The Clinical Implications and Complications of Anterior Versus Posterior Surgery for Multilevel Cervical Ossification of the Posterior Longitudinal Ligament; An Updated Systematic Review and Meta-Analysis

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Objective: Theoretically, the optimal approach is determined by the status of ossification of the posterior longitudinal ligament (OPLL) and sagittal alignment. However, there have long been disputes about the optimum surgical approach of OPLL. This study is to compare risk-effectiveness between anterior decompression and fusion (ADF) and laminoplasty and laminectomy with fusion (LP/LF) for the patient with cervical myelopathy due to multilevel cervical OPLL.

Methods: We searched core databases, and compared complication and outcomes between ADF and LP/LF for patients with multiple OPLL for the cervical spine. The incidence of complications such as neurologic deterioration, C5 palsy, and dura tear was assessed. Changes in JOA score between baseline and final evaluations were assessed for 2 groups. The minimal clinically important difference (MCID) was utilized for evaluating clinical significance. We calculated Peto odds ratio (POR) and mean difference for the incidence and continuous variables, respectively.

Results: We included data from 21 articles involving 3,872 patients with cervical myelopathy with OPLL. Major neurologic deficits such as paraplegia, quadriplegia, and dura tear was assessed. Changes in JOA score between baseline and final evaluations were assessed for 2 groups. The minimal clinically important difference (MCID) was utilized for evaluating clinical significance. We calculated Peto odds ratio (POR) and mean difference for the incidence and continuous variables, respectively.

Conclusion: Anterior surgery often led to rare but critical complications, and the difference of neurological improvement between 2 groups was below a clinically meaningful level. Posterior surgeries may be appropriate in the treatment of multilevel cervical myelopathy with OPLL.

Keywords: Anterior decompression and fusion, Laminoplasty, Ossification of the posterior longitudinal ligament, Recovery rate, Complication
INTRODUCTION

Ossification of the posterior longitudinal ligament (OPLL) of the cervical spine is characterized by ectopic bone formation in spinal ligaments, and one cause of cervical myelopathy. Several surgical options for cervical OPLL have been established and involve anterior surgery or posterior surgery. The anterior decompression and fusion (ADF) for the treatment of cervical OPLL is theoretically reasonable, as the lesion exists anteriorly, and can provide direct decompression to the spinal cord and can stabilize the involved segments.\(^1\)\(^2\) However, the procedure is complex and technically demanding, and is associated with serious complications, such as intraoperative spinal cord injury, dura tear, symptomatic cerebrospinal fluid (CSF) leakage, dysphonia, dysphagia, graft slippage, and adjacent-segment disease.\(^3\)\(^-\)\(^5\)

Posterior decompressive surgery, such as laminoplasty and laminectomy with fusion (LP/LF), is relatively simple, and known to achieve good results with low complication rates in the treatment of patients with OPLL.\(^6\)\(^7\) However, the effect of indirect decompression of the spinal cord is limited for patients with massive OPLL.\(^1\) Patients may experience such as persistent deficit due to incomplete decompression, C5 palsy, postoperative pain, postoperative kyphosis and late deterioration because of disease progression.\(^7\)\(^-\)\(^15\) The optimal approach is known to be determined by the depth and length of OPLL, sagittal alignment in the cervical spine, severity of stenosis, and history of previous surgery.\(^16\)\(^-\)\(^18\) However, there have long been disputes about the optimum surgical approach of OPLL.\(^16\)\(^,\)\(^17\)

Several meta-analyses were comparing anterior versus posterior surgery for cervical myelopathy with OPLL.\(^19\)\(^-\)\(^24\) They focused only on the recovery of neurological status at the final follow-up, and underestimate clinical implication of the effect size of the recovery and critical complications of the surgeries. Information regarding the surgical risks of these treatment options is critically important for surgical decision making because severe morbidity such as tetraplegia, paraplegia, and death can occur.\(^25\) They did not investigate the risk-effectiveness of the decompressive surgery for cervical myelopathy with OPLL.

The primary goal of the study is to compare neurological outcomes and complications between ADF and LP/LF for the patients with cervical myelopathy due to multilevel cervical OPLL. The secondary goal is to introduce appropriate surgical methods of multilevel cervical myelopathy with OPLL in consideration of the risk-effectiveness.

MATERIALS AND METHODS

1. Search Strategy and Study Selection Criteria

In accordance with the PRISMA (preferred reporting items for systematic reviews and meta-analyses) guidelines, we performed a meta-analysis of clinical studies that directly compared ADF and posterior surgeries such as laminoplasty and laminectomy for cervical myelopathy due to cervical OPLL. A systematic search of PubMed, Embase, Web of Science, the Cochrane Database, and KoreaMed was conducted on the 7th of July 2019 independently by 2 separate reviewers CHL and DHK. The search terms used were “ossification of the posterior longitudinal ligament” AND (laminoplasty OR laminectomy) AND (decompression OR corpectomy). Search results were screened by scanning abstracts for the following exclusion criteria: case reports, letters, comments, reviews, or technical note; animal studies; duplicate studies; cervical myelopathy not related with OPLL; single group studies; lack of outcomes of interest (neurological change, surgical mortality, and complications); and not population of interest (adults > 18 years). After removing excluded abstracts, full articles were obtained, and studies were screened again more thoroughly using the same exclusion criteria. The papers that dealt with cervical spondylotic myelopathy without OPLL, single group studies, thoracic or lumbar spine, other techniques, and diagnostic accuracy were also excluded. If data was absent in the included studies, we contacted corresponding authors of the papers to request data. The search was not restricted by language. Any discrepancies between the 2 reviewers were resolved by discussion after the search and a consensus was achieved.

2. Inclusion Criteria, Data Extraction, Endpoints, and Definitions

The goal of the search was to find articles that met the following inclusion criteria: direct comparison between ADF and laminoplasty (or laminectomy) for the cervical myelopathy due to OPLL in adults; clinical outcomes at preoperative and postoperative state and/or recovery rate were assessed; surgical complications were assessed; and results were presented as mean ± standard deviation (SD). Studies were included in data extraction if they reported surgical procedure performed and at least 1 outcome of interest resulting from these surgeries. Characteristics of the starting study sample, such as the number of patients, age, sex, country, study period, level, and occupying ratio, were collected when available. The occupying ratio was defined as a thickness of the OPLL at the level of the greatest canal narrow-
ing divided by proper anteroposterior diameter of spinal canal. For clinical outcome scores, the Japanese Orthopedic Association (JOA) scoring system and a recovery rate were used to evaluate the neurologic status before and after the operation. The recovery rate of neurologic outcome was calculated using the Hirabayashi method as Recovery Rate = (postoperative JOA score−preoperative JOA score)/(17−preoperative JOA score) × 100%.

These scores measured the severity of neurological status as a numerical value preoperatively and postoperatively. Conversion of units to keep data consistent was performed when necessary. Other outcomes such as complications, operation duration and amount of blood loss during each surgery, were also retrieved from the studies either from the writing or tabular data.

### 3. Quality Appraisal of Studies

Quality assessment was conducted independently in pairs and a consensus reached by discussion. Study quality was determined for controlled observational cohort studies with the RoBANS (risk of bias assessment tool for nonrandomized studies) and for randomized controlled trials with the ROB (risk of bias) tool. Two authors performed a quality appraisal of the studies independently, any discrepancies among reviewers were resolved through discussion.

### 4. Statistical Analyses

The relative weight of each study was determined by utilizing the meta-analytical inverse-variance. This involved computing the intervention effect estimate and its standard error for each study. The pooled results of the JOA and recovery rate were analyzed by calculating the effect size based on the mean difference (MD). All mean and SDs were calculated on the assumption that the data was a normal distribution. The minimal clinically important difference (MCID) was utilized to measure if the changes to JOA scores were significant enough to make a clinical difference. The MCID used in this study to determine clinical significance were 2.5 points for JOA.

The number of each complication during the anterior or posterior surgery was identified, and the Peto odds ratio (POR) was calculated to avoid statistical problems caused by zero or rare events in each study. In the case of zero events in one treatment arm, the calculation of relative measures such as risk ratio and odds ratio necessitated the use of additional approaches for the case of zero events. The POR can be calculated without a continuity correction which is currently the relative effect estimation method of choice for binary data with rare events. For the pooled effects, MD and 95% confidence intervals (CIs) were calculated for continuous variables according to the consistency of measurement units.

To assess the heterogeneity of the results of individual studies, we used the Cochran Q test and the Higgins I² statistic (Q was < 0.1 or I² > 50% was used as a threshold to indicate significant heterogeneity). Random-effects or fixed-effects models were used depending on the clinical diversity of each study included in the analysis. Publication bias was determined by studying funnel plots, and a statistically significant one-tailed p-values (< 0.05) for the Egger intercept. Statistical analyses of the pooled data were conducted using the Comprehensive Meta-Analysis software ver. 3.3 (Biostat, Englewood, NJ, USA).

### RESULTS

#### 1. Search Results for Relevant Studies

An initial literature search using the chosen subject headings identified 149 studies in PubMed, 191 in Embase, 252 in Web of Science, 1 in the Cochrane Central Register of Controlled Trials, and 11 in KoreaMed. Among these 604 studies, 265 were duplicates and were thus excluded. Also, 61 of the 339 remaining papers were excluded from our analysis for being a case report, review article, letter, technical note, or patent. After screening titles and abstracts, 44 studies about cervical myelopathy without OPLL and 78 studies about single group studies were excluded. The remaining 156 studies were subjected to a full-text review, and another 135 were excluded. These articles were excluded because the studies used new surgical techniques (n = 39), diagnostic tool (n = 22), thoracic or lumbar spine (n = 17), not described clinical outcomes such as JOA or recovery rate (n = 54), and no description of the SD (n = 3). Therefore, a total of 21 studies were included in our meta-analysis. Detailed results of the selection process are shown in Fig. 1. Studies could contribute to more than 1 analysis.

#### 2. Participant Characteristics

The characteristics of the included studies and participants are described in Table 1. Eleven studies were conducted in Japan, 6 in China, 3 in Korea, and 1 in India. Two studies shared the same patients and reported different outcome variables. Therefore, it is labeled as one. A study was conducted using a national inpatient database in Japan from April 1, 2010 to March 31, 2016. Two studies were performed in Japan at that time, and patients of the studies may be overlapped. Both studies were included and analyzed because they are not redundant papers. Two studies compared anterior surgery with laminectomy with fusion, and the other 19 compared with laminoplasty.
A total of 3,872 patients were included in our analyses. Among studies reporting participants’ information, 1,957 patients underwent anterior surgery such as ADF, and 1,915 patients underwent LP/LF. Mean age was 55.9 (95% CI, 52.44–59.35) years for the ADF group and 56.6 (95% CI, 52.73–60.40) years for the LP/LF group, male was 64.6% and 67.2%, involved level was 2.72 (95% CI, 2.68–2.76) and 4.10 (95% CI, 4.04–4.16), occupying ratio was 52.4% (95% CI, 38.93–65.91) and 51.0% (95% CI, 33.30–68.66), and baseline JOA was 9.60 (95% CI, 9.16–10.03) and 9.43 (95% CI, 9.85–10.01), respectively in Table 2. Involved spine level has a significant difference between the 2 groups (p < 0.01), and other baseline characteristics have no significant differences (age, p = 0.67; occupying ratio, p = 0.21; baseline JOA, p = 0.99) in Table 2.

3. Operative Morbidity and Postoperative Complications
Postoperative complications were depicted in Fig. 2. Major neurologic deficits such as paraplegia, quadriplegia developed 2.17% in the ADF group and 1.11% in the LP/LF group, and POR was 2.16 (95% CI, 1.14–4.07, p = 0.017). The POR of postoperative neurologic deficit was significantly high in the ADF group. The POR of C5 palsy was 0.65 (95% CI, 0.29–1.44), which showed no statistically significant difference in incidence of C5 palsy based on surgical procedure, although there was a trend toward high rates with LP/LF. Iatrogenic dura tear and CSF leakage was 3.74% (62 of 1,658) in the ADF group and 0.96% (13 of 1,453) in the LP/LF group, which showed that the dura tear was significantly frequent in the ADF more than the LP/LF group (POR, 3.36; 95% CI, 2.09–5.40).

4. Postoperative Clinical Outcomes
Clinical outcomes, evaluated in terms of the JOA score, were found to have improved after the surgeries in both the ADF (MD, 4.72; 95% CI, 4.34–5.10) and the LP/LF (MD, 3.59; 95% CI, 2.83–4.35) groups. MD of improvement in JOA score between the 2 groups was 1.30 (95% CI, 0.57–2.03), and the MD showed a statistical significance in Fig. 3. However, 1.3 points of JOA improvement cannot reach 2.5 points of the MCID. The ADF group was also superior to the LP/LF group for the Recovery rates, calculated by the JOA score in preoperative and postoperative state. The MD of recovery rate between 2 groups was 11.09% (95% CI, 2.66–19.51).

Fig. 1. Study attrition diagram. OPLL, ossification of the posterior longitudinal ligament; JOA, Japanese Orthopedic Association Score; SD, standard deviation.

References identified in database search PubMed (n = 149), Embase (n = 191), Web of Science (n = 252), Cochrane Library (n = 1), and Korea Med (n = 11)

Identification

Screening of titles and abstracts (n = 339)

Excluded according to selection criteria
- Review, case report, letter, and experiments (n = 61)
- No OPLL (n = 44)
- Single group study (n = 78)

Full-text articles assessed for eligibility (n = 156)

Excluded because of
- Other techniques (n = 39)
- Diagnostic tool (n = 22)
- Thoracic or lumbar disease (n = 17)
- No description of JOA or recovery rate (n = 54)
- No description of SD (n = 3)

Studies included in quantitative synthesis (n = 21)
Table 1. Baseline characteristics of studies and patients

| Study         | Country | Study period | No. of patients (male) | Mean age | Mean level | Mean occupying ratio | Mean baseline JOA score | Mean follow-up (mo) |
|---------------|---------|--------------|------------------------|----------|------------|-----------------------|------------------------|---------------------|
| Tomita, 1988  | Japan   | ND           | 17/23                  | 60.13 ND | 4.4 ND     | ND ND                 | 8.5/13.25             | ND/31.6             |
| Cheng, 1994   | China   | 1986.1–1992.6| 8(6)/11(10)            | 51.5/50.6| 3.7/3.7    | ND ND                 | ND ND                 | 32.0/32.0           |
| Goto, 1995    | Japan   | 1968–1993    | 50/65                  | 54.6/58.7| ND ND      | >50/50                | 7.8 ND                | 104.4/84.0          |
| Tan, 2002     | Japan   | 1991–2000    | 14(11)/12(9)           | 62/66    | 3.5/4      | 63/67                 | 9.4/10.1              | 49.0/50.0           |
| Jain, 2005    | India   | 1996.1–2004.1| 14/13                  | 51.5/56.1| ND ND      | 59.1/53.7             | 7.5 ND                | ND ND               |
| Mizuno, 2006  | Japan   | 1993–2002    | 111/10                 | ND ND    | 1–2 ND     | ND ND                 | ND ND                 | ND ND               |
| Iwasaki, 2007 | Japan   | 1996–2003    | 27(15)/66(51)          | 58/57    | 3/4        | 56.6/44.4             | 9.5 ND                | 72.0/122.4          |
| Masaki, 2007  | Japan   | 1993.6–2002.7| 19(14)/40(30)         | 51.8/62.6| 2.9/4.1    | 56/55.9               | 8.3/13                | >12/12              |
| Lee, 2008     | Korea   | 2001–2005    | 20(15)/27(26)          | 56.8/54.7| 2.4 ND     | ND ND                 | ND ND                 | 21.8/29.1           |
| Chen, 2011    | China   | 1997.6–2004.6| 22(14)/25(16)        | 57.2/54.2| 3–4/4      | 55.4/54.3             | 9.3/10.9              | >48/ND              |
| Chen, 2012    | China   | 2004.1–2007.12| 91(63)/41(33)      | 48.7/46.3| 2.7/4.1    | 43.6/46.3             | 9.8/14.6              | >48/ND              |
| Lin, 2012     | China   | 2005.1–2008.12| 26(15)/30(17)     | 54.7/56.2| 3.3/3.2    | 54.2/44.2             | 9.3/13.7              | 36.3/37.6           |
| Sakai, 2012   | Japan   | 1996–2004    | 20/22                  | 59.5/58.4| 3.1/4.5    | 43.4/46.9             | 11.4/14               | >60/ND              |
| Tian, 2012    | China   | 2007.7–2010.11| 40/120               | ND ND    | 1–2/1–5    | ND ND                 | ND ND                 | ND ND               |
| Fujimori, 2014| Japan   | 1986–2010    | 12(7)/15(12)          | 55.6/58.7| 3.3/5.4    | 67.5/66               | 9.5/11.7              | 118.8/122.4         |
| Kim, Moon, 2015/2019| Korea | 2005–2012    | 70(50)/63(48)        | 57.2/55.3| ND ND      | 56.4/54.8             | 11.9/ND               | 47.9/40.4           |
| Koda, 2016    | Japan   | ND           | 15(10)/16(12)         | 57.7/60.3| >3/>3      | 64.4/62.3             | 9.8/10.3              | 58.6/46.0           |
| Yoshii, 2016  | Japan   | 2006–2013    | 39(31)/22(18)         | 61.1/60.6| 2.7/3.4    | 58.8/57.1             | 11.1/14.2             | 44.5/37.2           |
| Hou, 2017     | China   | 2010.7–2014.6| 150(86)/102(61)    | 47.8/45.9| ND ND      | 61.9/63.4             | 9.5/15.2              | 35.4/36.1           |
| Morishita, 2019| Japan   | 2010.4–2016.3| 1,192(847)/1,192(859)| 60.9/60.8| ND ND      | ND ND                 | ND ND                 | ND ND               |

JOA, Japanese Orthopedic Association; ADF, anterior decompression and fusion; LP/LF, laminoplasty and laminectomy with fusion; ND, no description.
Average surgical time was 266.0 minutes (95% CI, 205.2–326.7) in the ADF group and 162.6 minutes (95% CI, 138.3–187.0) in the LP/LF group. The LP/LF group demonstrated an average operative time that was 96.3 minutes shorter than that of the ADF group (95% CI, 53.4–139.3; Fig. 4). Average intraoperative blood loss was 405.1 mL (95% CI, 138.8–671.5) in the ADF group and 329.8 mL (95% CI, 194.1–465.6) in the LP/LF group, which did not demonstrate a significant difference between the 2 groups.
5. Sensitivity Analysis and Publication Bias

Single elimination of each study affected the overall results of the meta-analysis in terms of neurologic deficit. Tani et al. reported that postoperative neurologic deficit occurred 0% (0 of 14) in the ADF group and 33% (4 of 12) in the LP. We could not find a reasonable cause of this results and it was hard to review the raw data because the study was performed from 1991 to 2000. Therefore, we eliminated the data of Tani et al. Sensitivity analysis of the other variables did not affect the overall results of the meta-analysis. All funnel plots were symmetric, indicating an absence of significant publication bias within the studies. The Egger test results were 0.67 (p = 0.24), -1.04 (p = 0.30), -0.83 (p = 0.44), 0.70 (p = 0.69), 14.81 (p = 0.36), 4.84 (p = 0.07), and 2.38 (p = 0.26) for neurologic deterioration, C5 palsy, CSF leakage, JOA change, recovery rate, operation time, and blood loss, respectively. These results indicated that there was no substantial evidence of publication bias in the dataset.

**DISCUSSION**

We conducted an up-to-date and comprehensive systematic review and meta-analysis. Especially, we evaluated risks and benefits associated with the cervical OPLL surgery. There are 2 ways of surgery for patients with cervical myelopathy due to OPLL. Although anterior surgery accomplished better clinical outcomes than posterior surgeries at the final follow-up, the difference between anterior and posterior surgeries did not exceed MCID. However, postoperative neurologic deterioration such as paraplegia or quadriplegia that is one of the most critical complications following spine surgery was more frequent in anterior surgeries than posterior surgeries. Considering the risk-effectiveness, posterior surgery such as laminoplasty or laminectomy with fusion may be a safe and effective surgery.

Anterior decompression can remove OPLL directly and offer...
decompression of the spinal cord with maintaining cervical lordosis. However, anterior surgery is plagued by a high risk of neurologic decline, CSF leakage, and pseudarthrosis because spinal cord was severely compressed, and the dura was frequently attached to OPLL. Despite this potential risk, the incidence of complications in patients with OPLL has not been fully established because of the relatively small number of patients included in previous studies. A previous report addressed that paraplegia occurred from 0% to 14.3% after ADF. In this study, major neurologic deficits developed 2.17% in the ADF group and 1.11% in the LP/LF group. The incidence of the complications was low, but anyone of them may leave fatal sequelae for both patients and surgeons. A reported incidence of CSF fistulas was 5.1%–25% during cervical surgery for OPLL. This meta-analysis displayed that iatrogenic dura tear and CSF leakage was 3.74% in the ADF group. Dura tear was closely related with adhesion to OPLL, the incidence might be underestimated. CSF leakage can be stopped spontaneously or with lumbar drainage, but some cases may need revision surgery and progress meningitis or encephalitis.

The posterior approach provides a relatively simple and safe means to decompressing the entire cervical spinal cord. However, patients may experience late deterioration because of progressive kyphosis, and expansion of the ossification, especially in patients with preexisting kyphosis. Some studies reported that neurological recovery following ADF was superior to that following posterior decompression. In contrast, other studies reported no significant difference in surgical outcomes between anterior and posterior decompression. Our findings are consistent with previous literature that LP/LF has lower morbidity and complication rates than ADF, and the difference of recovery between the 2 groups was clinically insignificant.

There are several meta-analyses dealt with anterior versus posterior surgery for OPLL. Although all the reported meta-analyses included 8–13 papers, we found 21 relevant papers. We tried to find out why other studies did not include the studies we included, but we could not find it. Our paper may be more reliable given the definition of meta-analysis which should synthesize all existing evidence. A meta-analysis by Yoshii et al used wrong data that was different from the included primary studies. Almost all papers concluded that ADF achieves better neurological improvement compared with laminoplasty in the treatment of cervical myelopathy due to OPLL. In accordance with previous systematic reviews and meta-analyses, we found significant superiority of anterior surgery in terms of neurological improvement after the surgery. However, they emphasized...
that the difference in neurological improvement was statistically significant, and overlooked the fact that there was no clinical significance.

Surgery-related complications are a key factor in deciding surgical procedure, especially if the complications are fatal. Surgeries for OPLL may lead to paraplegia or quadriplegia, it is fatal to the patient even if it is rare. Some papers reported complication rate including neurologic deficit, hematoma, infection, and neck pain.18,20 We analyzed the incidence of major complications such as neurologic deterioration, C5 palsy, and dura tear. The results showed a significant increase in the risk of neurological deterioration during anterior surgery. Our findings are consistent with previous literature that the complication rates were significantly higher in the anterior group compared with the posterior group.45 Unfortunately, Liu et al.18 reported the only incidence of each study groups and did not show results of statistical tests.

Based on the results of this meta-analysis, we recommend the posterior surgery in the treatment of multilevel cervical myelopathy due to OPLL. Although ADF accomplished better postoperative neurological outcomes than LP/LF, the difference was less than MCID in the neural function recovery between the 2 surgical approaches. The critical complication rates were significantly higher in the anterior group compared with the posterior group. The surgical trauma associated with ADF was significantly higher than that associated with posterior laminoplasty.45 Previous researchers also reported that laminoplasty remained as a salvage procedure, especially if the complications are fatal. Surgeries for OPLL may lead to paraplegia or quadriplegia, it is fatal to the patient even if it is rare, and the difference of neurological improvement between 2 groups was below a meaningful level. Posterior surgeries may be appropriate in the treatment of multilevel cervical myelopathy due to OPLL.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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