Consensus statement on diagnosis and treatment of cervical ossification of posterior longitudinal ligament from Asia Pacific Spine Society (APSS) 2020

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Abstract
Purpose: The study aimed to develop an evidence-based expert consensus statement on diagnosis and treatment of cervical ossification posterior longitudinal ligament (OPLL). Method: Delphi method was used to perform such survey, and the panel members from Asia Pacific Spine Society (APSS) 2020 were invited to answer the open-ended questions in rounds 1 and 2. Then the results were summarized and developed into a Likert-style questionnaire for voting in round 3, and the level of agreement was defined as 80%. In the whole process, we conducted a systematic literature search on evidence for each statement. Results: Cervical OPLL can cause various degrees of neurological symptoms, it’s thought to be more common in Asia population. CT reconstruction is an important imaging examination to assist diagnosis and guide surgical choice. Segmental, continuous, mixed, and focal type is the most widely used classification system. The non-surgical treatment is recommended for patients with no or mild clinical symptoms, or irreversible neurological damage, or failed surgical decompression, or condition cannot tolerate surgery, or refusing surgery. As OPLL may continue to develop gradually, surgical treatment would be considered in their course inevitably. The surgical choice should depend on various conditions, such as involved levels, thickness, and type of OPLL, skill-experiences of surgeons, which are listed and discussed in the article. Conclusion: In this statement, we describe the clinical features, classifications, and diagnostic criteria of cervical OPLL, and review various surgical methods (such as their indications, complications), and provide a guideline on their choice strategy.

Keywords: consensus statement, diagnosis, ossification posterior longitudinal ligament, treatment

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Introduction

Cervical ossification posterior longitudinal ligament (OPLL) refers to ectopic calcification of the posterior longitudinal ligament in the cervical spine, which may result in cervical myelopathy due to the compression of spinal cord or nerve roots. Patients usually develop into various degrees of neurological symptoms, such as paresthesia of limbs and trunk, motor paralysis, and bladder and rectal dysfunction. It was first reported by Japanese scholar Tsukimato in 1960. Epidemiological studies demonstrated that the incidence of OPLL varies regionally, such as Asian populations presented higher prevalence compared with non-Asian populations. Among them, the prevalence in Japanese population over 30 years of age is 1.9% to 4.3%, about 1.6% to 1.8% in mainland China, and about 2.8% in Taiwan. Gender and age also affect its morbidity, such as, men is more susceptible than women, and the middle aged aged around 50 to 55 years old accounts for about 90% of patients. However, previous epidemiological investigations were based on X-ray examinations. With the popularity of CT examinations, the diagnosis of OPLL is more sensitive. Recently, scholars based on CT examination found that the prevalence of OPLL was as high as 6.3% in the Japanese population, while the prevalence of OPLL was 2.2% in the non-Asian population.

However, there is currently no unified and accepted guidelines for the diagnosis and treatment of OPLL. In view of the fact that OPLL is relatively common in China and Japan, plenty of researches have been carried out on the disease. Special experts from China and Japan have comprehensively reviewed existing publications, and conducted in-depth discussions on the difficulties and priorities in the diagnosis and treatment of OPLL, and reached the following consensus statement.

Pathogen

Cervical OPLL is a ligament degenerative disease under the combined effects of genetic and environmental factors. The etiology of this disease is not completely understood so far, and several speculative theories may explain its pathology, such as intervertebral disc degeneration, systemic bone hypertrophy, metabolic disorders, and stress stimulation. OPLL has an obvious genetic predisposition, and its related genes and molecular factors are mainly collagen gene 11A2 (collagen11A2, COL11A2), COL6A1, bone morphogenetic protein 2 (BMP2), transforming growth factor β, TGF-β), Runt-related transcription factor 2 (RUNX2), etc. A recent whole-genome study found that OPLL is closely related to several genetic loci of HAO1A. Abnormalities also present close correlations with the processes of OPLL.

The diagnosis

(A) Clinical manifestations
The patients with cervical OPLL may present no clinical symptoms in the early stage, then it could develop slowly with the ossified mass thickened and widened. When the subsequent cervical spinal stenosis develops to a certain extent, the related neurological symptoms appear and progress after middle age generally. Additionally, the disease can also progress rapidly when accompanied by trauma, developmental spinal stenosis, and other intraspinal occupying lesions.

In the early stage, patients may suffer mild cervicodynia, and their range of motion (ROM) of cervical spine are normal or slightly restricted. The ROM generally is limited in the extension direction, and it may cause neck pain or soreness when the passive movement exceeds its normal range. The neurological symptoms mainly present as intermittent, chronic, progressive numbness and weakness of the extremities. Generally, upper extremity symptoms are secondary to the lower extremities, in a few cases, upper extremity symptoms may occur first, or they develop simultaneously. Others include urethral sphincter dysfunction (which is manifested as difficulty urinating or urinary incontinence), defecation dysfunction, and zonesthesia in the chest and abdomen.

(B) Imaging examination
Imaging examination is the main method for diagnosing OPLL. It is mainly based on high-density shadows on plain radiography or tomography of the vertebral body. CT or MRI can be used for patients who cannot be diagnosed clearly, such as those with mild ossification. CT reconstruction can not only be used to assist the diagnosis of OPLL, but also guide the choice of surgical strategy.

It is worth noting that the concomitant ossification in other region should not be missed, such as cervical ossification of the ligamentum flavum, thoracic and lumbar OPLL. In addition, dural sacral ossification should be diagnosed and identified accurately, which may present double-layer sign and meningeal tail sign on preoperative CT.

(C) Classification
The classification of OPLL is mainly based on imaging results. Currently, there are many types of classification systems. The most widely used are as follows:

1. Japan’s Ministry of Health, Labour and Welfare Investigation Committee for Ossification of Spine Ligaments established a widely used classification, which account for 92.81% of the published literature. This system classified OPLL into four types according to cervical X-rays: (1) Segmental type, with several separate ossification behind vertebral bodies, which indicates the type of early stage and may originate from the degenerative and protrusive intervertebral disc, but its clinical symptoms can show severe; (2) Continuous type, with continuous ossification extending over several vertebral bodies, which cross several intervertebral spaces, and its
clinical symptoms are usually not very serious for its flat characteristic. (3) Mixed type, a combination of segmented and continuous type, which can be identified most commonly, and its clinical symptoms are usually severe. (4) Focal type, with ossification limited to the posterior of the intervertebral space, and its clinical symptoms generally are severe.

2. Goto et al.\textsuperscript{11} classified the cervical OPLL into three types according to the location of the ossification: (1) high-position type, which refers to ossification at the level of C1–C3; (2) low-position type, which refers to at the level of C4–C7 (3) Extensive type, which refers to the type of ossification that is involved in both the upper and lower positions. Kawaguchi et al.\textsuperscript{12} further divided into C1 (+) and C1 (−) according to whether ossification was involved in C1 level.

3. K-line is another widely used typing method proposed by Fujiyoshi et al., which assists to choose the surgical approach.\textsuperscript{13} This method defines the straight line connecting the midpoints of the C2 and C7 spinal canals on the X-rays of patients with OPLL as the K-line. If the ossification has not exceeded the K-line, it is a K-line (+), and if it has exceeded the K-line, it is a K-line (−).

4. The nine points method is a typing method proposed by the Chinese scholar Yang et al. to evaluate whether osteosynthesis can be safely removed.\textsuperscript{14} This method is based on a CT cross-section of the most severe ossification segment. The posterior edge of the vertebral body is defined as the baseline. The space between the posterior edge of the vertebral body and the root of the spinous process is divided into three equal parts by two lines, which is safe line and danger line. At the same time, the left and right spinal canals are also divided into three equal parts to form a nine-grid pattern. If the ossification is between the baseline and the safety line, it is considered safe to remove. If the ossification is between the safety line and the danger line, the width of the ossification should be paid attention to; the risk increases with the width broadens. If the ossification is beyond the danger, anterior osteotomy will be at great risk. In general, complications, such as cerebrospinal fluid leakage and spinal cord injury, increased significantly when ossification occupied six or more of the nine regions.

5. MRI-based typing. Otake et al.\textsuperscript{15} divided the cervical OPLL into three types according to the shape of ossification on the MRI axial imaging, namely rectangular, mushroom-type and mountain-type. Their shapes were defined by a pair of tangential lines to the bilateral margins of the ossified mass. Others have typed according to the morphology of the spinal cord after compression on the MRI cross-section, namely the boomerang type, the teardrop type and the triangle.\textsuperscript{16}

6. Dural ossification is not uncommon in patients with OPLL, and its accuracy identification can reduce the risk of cerebrospinal fluid leakage after anterior decompression. Hida et al.\textsuperscript{17} classified the ossification on CT into single-layer sign and double-layer sign, and the double-layer sign highly suggested the presence of ossified dural sac. Mizuno et al.\textsuperscript{18,19} further divided dual ossification into three types based on its association with OPLL: (1) Isolated type, with dural ossification presenting no relationship with OPLL; (2) Double-layer sign, with an epidural space located between dural ossification and OPLL; (3) Meningeal tail sign in the sagittal position, with dual ossification fused with OPLL.

### Treatment

1. Non-surgical treatment

The indications for non-surgical treatment of cervical OPLL are: no clinical symptoms or mild symptoms; imaging and clinical examinations have confirmed irreversible neurological damage; surgical decompression has failed to restore neural function; patient’s condition cannot tolerate surgery; refusing surgery treatment (Table 1).\textsuperscript{20}

Non-surgical treatment methods include: drugs therapy (such as non-steroidal anti-inflammatories, neurotrophic drugs), physical therapy, cervical immobilization and activity modification to maintain the stability of the cervical spine and avoid the high-risk activities.

The current views on the non-surgical treatment of cervical OPLL are still inconsistent. One long-term study demonstrated that the JOA score was greater than 14 for asymptomatic patients that underwent non-surgical treatment. Patients can get satisfactory outcomes by non-surgical treatment methods, such as reducing neck movements. Excessive neck movements can cause repeated friction of the spinal cord on the ossified lesions, which may be a risk factor for the progressive spinal cord injury.\textsuperscript{21,22}

2. Surgical treatment

As reported, OPLL may continue to develop gradually. Long-term follow-up have shown that the ossification progressed laterally for 42\% patients and longitudinally for up to 86\% patients.\textsuperscript{20} Therefore, surgical intervention would be considered in their course inevitably. Surgical indications include: serious or progressive clinical symptoms; severe ossification that resulting obvious spinal stenosis; combined with cervical spondylotic myelopathy, spinal canal stenosis, disc herniation, or cervical instability; and those who have failed conservative treatments (Table 1).\textsuperscript{3,4,23–25} The surgical principle is to relieve the spinal cord compression,
reconstruct the physiological curvature of the cervical spine, and create good conditions for neural function recovery.

1. Posterior approach

For patients with multilevel OPLL and excellent cervical curvature accompanied, posterior surgery should be recommended. Although posterior approach cannot resect the ossified mass which compress spinal cord ventrally, it can enlarge the spinal canal volume and drift the spinal cord dorsally, which indirectly decompresses the compressed spinal cord. For K-line (− ) OPLL patients, posterior decompression can achieve satisfactory results. Laminctomy and laminoplasty are the most commonly used surgical methods (Table 2).

1. Laminctomy

Laminctomy or hemi-laminctomy is relatively simple to operator, which can decompress effectively by spinal cord drifting dorsally. However, cervical kyphotic changes may arise following the surgeries due to the remove of posterior structure. And the ossification has been reported to progress commonly.26 Although it is believed not directly related to the postoperative neurological status of patients, this procedure is currently less commonly used.27

2. Laminctomy with instrumented fusion

Laminctomy with instrumented fusion can provide immediate and long-term stability of the cervical spine, and reduce the incidence rate of secondary kyphosis. Lateral mass screws and pedicle screws are commonly used for internal fixation.28,29 The instrumented system can also correct the preoperative cervical curvature and drift spinal cord dorsally to a sufficient extent, but it increases the risk of vascular and nerve injury.30 Moreover, the postoperative C5 nerve root palsy is closely related to the excessive increase of cervical lordosis after laminctomy with instrumented fusion.31

3. Laminoplasty

Laminoplasty was first proposed by Japanese scholars, and it is also a common posterior decompression technique for the treatment of cervical OPLL. The advantages are that it enlarges the spinal canal and decompresses the spinal cord with the posterior structure preserved, which can maintain postoperative stability, reduce the formation of epidural scars, and preserve the movement of cervical spine.32,33 Some factors may affect the efficacy of laminoplasty, such as severe compression, hill-shaped ossification, spinal canal stenosis > 60%, cervical curvature loss, and the elderly.34 The main procedures of laminoplasty are: single-door laminoplasty, double-door laminoplasty, “Z” angioplasty, and spinous process suspension, etc. At present, single-door laminoplasty is used commonly.

The surgical segment of laminoplasty can be formulated by the compressed segment, but it should be noted that the drifting spinal cord can form a new compression at the upper and lower ends. In most cases, the decompression involves C3–C7. C2 can also be decompressed when the osteoid extends to C2. However, segmental OPLL tends to be mobile, and auxiliary fixed fusions are recommended for segments with abnormal movements.35

2. Anterior approach

The advantages of anterior approach are that it can not only remove the ossification directly to obtain a sufficient decompression effect, but also reconstruct the cervical curvature and provide a good biomechanical environment for neural function recovery (Table 2). The neurological improvement rate is approximately between 51% and 71.1% as reported.36,37

1. Anterior cervical discectomy and fusion (ACDF)

ACDF can be selected in such conditions: the ossification is mainly limited to the intervertebral space, or it can be expected resected through the intervertebral space, or the protruding disc is the main compressive origination. Patients with multilevel OPLL are often uncomfortable with this procedure.38

2. Anterior cervical corpectomy and fusion (ACCF)

ACCF is the most commonly used anterior approach for the treatment of cervical OPLL. It is mainly applied to patients with ossification that extends less than three segments and does not exceed the lower edge of C2 and the upper edge of T1.37,39,40 Although five-segmental ACCF has been reported successful, such long segmental resection significantly increased the complications and reoperation rates.41 The type of OPLL also should be taken into consideration for the surgical choice: a recent study compared ACCF with laminoplasty and concluded that ACCF could achieve better neurological recovery, especially in patients with segmental-type OPLL; as segmental-type OPLL are more likely to develop postoperative kyphosis and induce late neurologic deterioration than other types OPLL after LAMP. Therefore, ACCF is recommended for patients with OPLL involves less than three levels, especially for segmental-type.

The risk of complications in ACCF cannot be ignored, such as cerebrospinal fluid leakage and spinal cord injury, especially for those with severe adhesion between the ossification and dural sac. To deal with the ossified dural sac, the “floating method” is recommended: after the ossified dural sac is separated as far as possible, OPLL is thinned and transacted around it; then the preserved ossified dural sac will float anteriorly.42 If the ossified dural sac attached with OPLL tightly and cannot be separated, the OPLL can be thinned and released from the surrounding vertebral body and achieve anterior float integrally.44,45 However,
delayed deterioration is a concerned problem after floating method due to the insufficient decompression and progression of OPLL. Recently, Chen X et al. has introduced a new method, that the released ossification was further lift up and resected from caudal to cranial to avoid the problem mentioned above, which was named anterior cervical ossified posterior longitudinal ligament en bloc resection (ACOE). In some cases, dural defect may be unavoidable after remove of the ossified dura mater. Then attention should be paid to minimize the deficient area and keep the arachnoid membrane intact. After decompression, the defect can be repaired by autologous fascia, gelatin sponge or biological protein.

3. Anterior controllable antidisplacement and fusion (ACAF)

OPLL more than three levels cannot be managed well by traditional anterior decompression surgery. In recent years, the team of Shi Jiangang from Shanghai Changzheng Hospital, has reported a direct decompression technique for severe cervical OPLL, named ACAF.46,47 This method is guided by the theory of in-situ-decompression of spinal cord. In its procedures, anterior vertebral bodies were partly resected and the remained vertebrae-OPLL complex (VOC) was hoisted via plate-screw system. Then OPLL is moved ventrally to restore the space of the spinal canal and achieve direct decompression. Without resecting the ossification, the incidence rate of cerebrospinal fluid leakage and spinal cord injury was significantly decreased, and the preserved vertebral body increased stability of the cervical spine after surgery. Additionally, the cervical curvature can be restored appropriately, which effectively avoided excessive drifting of spinal cord and related complications, such as C5 nerve root paralysis.48,49 By this method, long-level OPLL will not be a contraindication for anterior approach any more, even the patients with OPLL extending to the upper cervical and thoracic spine have been reported to get satisfactory outcomes.50 The indication of ACAF covers almost all types of OPLL.

3. Anterior and posterior combined approach

Either anterior or posterior approach has its own indications and disadvantages. In some cases, a single approach cannot solve problems effectively, then a combined approach should be considered. For examples, anterior approach alone is risky and ineffective for severe and multilevel OPLL, the combined method is recommended for these cases. For those with a kyphotic cervical spine, spinal cord cannot be drift dorsally to a sufficient extent by posterior decompression alone. Then anterior surgery can be added priorly to correct the curvature.51 The combined approach can be performed in one-stage or two-stages. Though it combines the advantages of direct and indirect decompressions, its high risk should be paid attention.

Summary

There is no recognized guideline for the diagnosis and treatment of cervical OPLL, especially for the choice of surgical methods. Various decompression methods have their own advantages and disadvantages. Moreover, the incidence of complications is more common in OPLL surgery, compared with other cervical surgeries. As reported, the total complication rate of OPLL surgery can reach up to 21.8%. Their complications include dysphagia, hoarseness,

Table 1. The indications for conservative and surgical treatments.

| Treatment Method | Indications                                                                 |
|------------------|-----------------------------------------------------------------------------|
| Non-surgical Treatment | No or mild symptoms | Confirmed neurological damage | Failed surgical decompression | Patient’s factors (healthy condition, refuse surgery) |
| Surgical Treatment | Serious or progressive symptoms | Severe ossification | Concomitant disease (cervical spondylotic myelopathy, spinal canal stenosis, disc herniation, or cervical instability) | Failed conservative treatments |

Table 2. The surgical choice in different conditions.

| Surgical Approach | Recommended Cases                                                                                     |
|------------------|--------------------------------------------------------------------------------------------------------|
| Anterior Approach | ACDF: The ossification is limited to the intervertebral space, or it can be resected through the intervertebral space, or the protruding disc is the main compressive origination |
|                  | ACCF: The ossification extends less than 3 segments and does not exceed the lower edge of C2 and the upper edge of T1, especially for segmental-type OPLL |
|                  | ACAF: Almost all types, especially severe and multilevel OPLL |
| Posterior Approach | Laminectomy: Rarely used |
|                  | Laminectomy with instrumented fusion or Laminoplasty: Multilevel OPLL with negative K-line |
| Hybrid Approach  | A single approach cannot solve problems effectively |

ACDF, Anterior cervical discectomy and fusion; ACCF, Anterior cervical corpectomy and fusion; ACAF, Anterior controllable antedisplacement and fusion; OPLL, Ossification posterior longitudinal ligament.
cough, cerebrospinal fluid leakage, neural damage, axial pain, hematoma, and implant-related complications. According to the published data, cerebrospinal fluid leakage and neural damage usually arise following the anterior approach, while axial pain and C5 nerve root paralysis are common after posterior approach. The new ACAF surgery has reduced the risk of complications and is expected to change the traditional strategy of diagnosis and treatment. Various factors should be considered for the surgical choice, such as the involved levels, the severity of compression, the cervical curvature, and the learning curve of operators.

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XS and YW contributed equally to the work.

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