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Does Diabetes Affect the Surgical Outcomes in Cases With Cervical Ossification of the Posterior Longitudinal Ligament? A Multicenter Study From Asia Pacific Spine Study Group

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Abstract

Study Design: Retrospective multicenter study.

Objectives: To evaluate the surgical outcomes of cervical ossification of the posterior longitudinal ligament (OPLL) in diabetes mellitus (DM) patients.

Methods: Approximately 253 cervical OPLL patients who underwent surgical decompression with or without fixation were registered at 4 institutions in 3 Asian countries. They were followed up for at least 2 years. Demographics, imaging, and surgical information were collected, and cervical Japanese Orthopaedic Association (JOA) scores and the visual analog scale (VAS) for the neck were used for evaluation.

Results: Forty-seven patients had DM, showing higher hypertension and cardiovascular disease prevalence. Although they presented worse preoperative JOA scores than non-DM patients (10.5 $\pm$ 3.1 vs. 11.8 $\pm$ 3.2; $P = 0.01$), the former showed comparable neurologic recovery at the final follow-up (13.9 $\pm$ 2.9 vs. 14.2 $\pm$ 2.6; $P = 0.41$). No correlation was noted between the hemoglobin A1c level in the DM group and the pre- and postoperative JOA scores. No significant difference was noted in VAS scores between the groups at pre- and postsurgery. Regarding perioperative complications, DM patients presented a higher C5 palsy frequency (14.9% vs. 5.8%; $P = 0.04$). A similar trend was observed when surgical procedure was limited to laminoplasty.

Conclusions: This is the first multicenter Asian study to evaluate the impact of DM on cervical OPLL patients. Surgical results were favorable even in DM cases, regardless of preoperative hemoglobin A1c levels or operative procedures. However, caution is warranted for the occurrence of C5 palsy after surgery.

Keywords

cervical ossification of the posterior longitudinal ligament, Asian multicenter study, diabetes mellitus, surgical outcomes, perioperative adverse events

Introduction

Degenerative cervical myelopathy (DCM) is the most common cause of spinal cord dysfunction and encompasses various forms of cord compressive disorders that includes cervical spondylotic myelopathy (CSM), ossification of the posterior longitudinal ligament (OPLL), disk herniation, and subluxation.[1] Among these pathologies, OPLL is the major disease involving ossified spinal ligaments, with most of its cases

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found in Asian countries.[2,3] Around half of the cervical OPLL patients present with a progression of ossification, which induces myelopathy in the middle- to older-aged population. To halt the symptom progression and to improve the neurological status, surgical treatment has been frequently performed due to its effectiveness reported in previous studies.[4]

Several studies have indicated the association of OPLL pathology with diabetes mellitus (DM). Kobashi et al. reported that the frequency of having a history of DM was >20.0% in patients with OPLL, whereas the ratio was <5.0% in healthy volunteer.[5] Furthermore, Akune et al. revealed that abnormal glycometabolism was positively associated with the extent of ossification.[6] Because DM has an adverse effect on the microvascular and nervous systems,[7,8] a concern remains regarding the relation of this metabolic pathology with surgical outcomes for the cervical OPLL.

Under the umbrella of DCM, several studies evaluated the impact of DM on the surgical outcomes,[9-14] and a recent systematic review clarified worse baseline neurologic status and postoperative functional recovery.[15] However, those studies assessed the outcomes for mixed pathologies, such as spondylosis and disk herniation in addition to OPLL, and, consequently, the numbers of patients with only OPLL were inevitably small. Moreover, most studies had patients only from a single country, which introduced a potential bias when assessing its comprehensive clinical picture.

Recently, we have established the cervical OPLL database in collaboration with 4 facilities from 3 Asian countries, which we believe will have the evidence to clarify the detailed pathology and clinical outcomes of the OPLL. The purpose of this study is to examine the impact of DM on surgical outcomes for cervical OPLL using this Asian population-based dataset.

Materials and Methods

Subjects

This study included 253 clinically and radiographically confirmed cervical OPLL patients who were treated at 4 institutions in 3 countries (China, Korea, and Japan) between 2010 and 2016. All investigators were experienced orthopedic spine surgeons or neurosurgeons. This study received ethical approval from the institutional review boards of the participating institutions: Keio University School of Medicine (20 110 142), Yonsei University (2014-1270-001), the 4th Teaching Hospital of Peking University (202 007-24), Hong Kong University (UW 17-134).

For patients to be included in the study, they had to meet the following criteria: (1) evidence of cervical spinal cord compression by the OPLL on magnetic resonance imaging (MRI) or computed tomography (CT) and (2) no previous cervical spine surgery. Patients were excluded if they were diagnosed with active infection, neoplastic spinal disease, rheumatoid arthritis, or ankylosing spondylitis.

DM was diagnosed if any or all of the following criteria were met: (1) fasting blood sugar level over 126 mg/dL, (2) causal blood sugar level over 200 mg/dL, (3) blood sugar level over 200 mg/dL under 2 hours of 75 g oral glucose-tolerance test, and (4) hemoglobin A1c level over 6.5%.[16] The patients were also included in the DM group if they were previously diagnosed with DM and continued to undergo its treatment.

For surgical techniques, cervical laminoplasty, laminectomy, and anterior and/or posterior fixation were chosen at the discretion of the surgeons at each institute. For the DM patients, specialists of diabetes at each hospital controlled the blood sugar levels well in the immediate term during the perioperative period.

Data Collection

We retrospectively collected demographic information, medical history, imaging, surgical summary, and other data for all subjects, which were followed up at least 2 years after the surgery. Clinical outcomes were assessed before surgery and at the final follow-up using the cervical Japanese Orthopaedic Association (JOA) scores and the visual analog scale (VAS) for the neck. All surgery-related events that occurred within 30 days of the operation were defined as perioperative complications. C5 palsy was defined as the deterioration of muscle strength with one or more grades of manual muscle testing on the deltoid and the biceps after surgery without any deterioration of other neurologic symptoms.[17] Surgical site infections (SSIs) included both superficial and deep incisional infection.

Imaging

OPLL classification[18] and K-line[19] were assessed using plain radiographs in the neutral position. The occupying ratio was calculated using the diameters of the spinal canal and OPLL at a maximal compressive level on the preoperative axial CT scan.[20]

We evaluated an increase in the intramedullary signal intensity (SI) at the narrowest level of the spinal cord as "grade 0" if no intramedullary high SI appeared on the T2-weighted MR images; "grade 1" if there is a predominantly faint and indistinct border; and "grade 2" if there is a predominantly intense and well-defined border.[21]

Statistical Analysis

Continuous variables and frequencies were presented as means ± standard deviation and categorical variables as percentages. Baseline demographics, preoperative scores, and surgical characteristics in the DM and non-DM groups were compared using unpaired t-test for continuous variables and chi-square test for categorical variables. Multivariate logistic regression analysis was performed to identify the predictor for C5 palsy, and factors that yielded a P-value of <0.20 in univariate analyses were explored in the multivariable models. Pearson's product moment correlation coefficient was performed to analyze the association of hemoglobin A1c levels with the cervical JOA

Table 1. Demographics of DM or Non-DM Patients.

	DM group (n = 47)	Non-DM group (n = 206)	*P*-value
Age (y)	61.9 ± 9.1	59.0 ± 9.4	0.06
Gender (% male)	72.3	71.4	0.89
BMI (kg/m^2)	25.6 ± 4.2	25.6 ± 3.6	0.94
Smoker (%)	19.1	17.6	0.79
Duration of symptoms (months)	28.4 ± 43.3	32.7 ± 52.6	0.61
Comorbidities			
Hypertension (%)	51.1	30.1	0.01
Cardiac disease (%)	23.4	5.8	<0.01
Renal disease (%)	4.3	5.8	0.50
Cerebrovascular disease (%)	2.1	5.8	0.27
Respiratory disease (%)	4.3	3.9	0.58
Rheumatologic disease (%)	4.3	3.4	0.52
Psychiatric disease (%)	2.1	1.0	0.46

DM, diabetes mellitus; BMI, body mass index.

scores. All statistical analyses were performed using SPSS version 26.0 (SPSS Inc., Chicago, IL). P < 0.05 was considered statistically significant.

Results

Demographics and Imaging Characteristics

Table 1 showed the demographic data of DM (n = 47) and non-DM (n = 206) patients (prevalent rate of DM: 18.6%). The age of DM patients was older than those without DM, although no significant difference was noted (61.9 ± 9.1 vs. 59.0 ± 9.4, $P = 0.06$). Comparable results were observed in gender ($P = 0.89$), body mass index (BMI) ($P = 0.94$), frequency of smoking ($P = 0.79$), and duration of symptoms ($P = 0.61$). Among the DM patients, the average level of hemoglobin A1c was 6.4 ± 1.1%. Regarding comorbidities, the DM group presented with a significantly higher frequency of hypertension (51.1% vs. 30.1%, $P = 0.01$) and cardiac disease (23.4% vs. 5.8%, $P < 0.01$) than the non-DM group. No statistical significance was noted among other frequencies of comorbidities.

Table 2 outlined the imaging characteristics and revealed no statistically significant differences in the types of ossification ($P = 0.32$), preoperative K-line ($P = 0.14$), occupying ratio ($P = 0.47$), and intramedullary SI on MRI ($P = 0.88$) between the groups.

Surgical Procedures and Perioperative Complications

Of the surgical techniques, laminoplasty was performed most frequently in both the DM (78.7%) and the non-DM groups (80.1%) (Table 3). Posterior fixation and anterior fixation were performed in 14.9% and 6.4% of the DM patients, respectively. In the non-DM group, these procedures were conducted in 8.3% and 9.2%, respectively. Both anterior and posterior fixations as a primary surgery were conducted in only one non-DM patient (0.5%). All procedures showed no statistically significant difference ($P = 0.51$).

Table 2. Imaging Characteristics.

	DM group (n = 47)	Non-DM group (n = 206)	*P*-value
Types of ossification[18] (%)			0.32
Continuous	40.0	29.9	
Segmental	22.2	26.0	
Mixed	33.3	31.9	
Others	4.4	12.3	
K-line[19] (% plus)	72.3	72.3	0.14
Occupying ratio[20] (average %)	47.6 ± 13.6	46.0 ± 13.2	0.47
MRI SI[21] (%)			0.88
0 (no intensity)	27.7	31.2	
1 (faint and indistinct border)	36.2	35.6	
2 (intense and well-defined border)	36.2	33.2	

DM, diabetes mellitus; MRI, magnetic resonance imaging; SI. Signal intensity.

Table 3. Surgical Factors and Perioperative Complications.

	DM group (n = 47)	Non-DM group (n = 206)	*P*-value
Surgical methodology			
Laminoplasty (%)	78.7	80.1	0.51
Laminectomy (%)	0	1.9	
Posterior fixation (%)	14.9	8.3	
Anterior fixation (%)	6.4	9.2	
Anterior and posterior fixation (%)	0	0.5	
Perioperative complications			
C5 palsy (%)	14.9	5.8	0.04
Surgical site infection (%)	0	0.5	0.81
Epidural hematoma (%)	0	0	-
Dural tear (%)	2.1	0.5	0.34
Neurological deterioration (%)	0	2.3	0.54
Dysphagia (%)	0	2.3	0.54
Dysphonia (%)	0	0.5	0.81
Hardware failure	2.1	1.5	0.56

DM, diabetes mellitus.

Regarding perioperative complications, the DM group showed a significantly higher frequency of C5 palsy (14.9% vs. 5.8%; $P = 0.04$). Other complication rates showed no significant differences: SSI ($P = 0.81$), dural tear ($P = 0.34$), neurological deterioration ($P = 0.54$), dysphagia ($P = 0.54$), dysphonia ($P = 0.81$), and hardware failure ($P = 0.56$). Infection occurred in only one patient with superficial SSI in the non-DM group, which was cured by means of following longer administration of antibiotics without any additional surgical intervention.

When examining the status of C5 palsy during the follow-up period, 83.3% (10/12) in the non-DM group showed complete recovery as opposed to only 42.9% (3/7) in the DM group, although no significant difference was observed between the groups ($P = 0.10$). Among the subjects who gained complete

Table 4. Clinical Outcomes.

	DM group (n = 47)	Non-DM group (n = 206)	*P*-value
Cervical JOA score			
Preoperation	10.5 ± 3.1	11.8 ± 3.2	0.01
Final follow-up	13.9 ± 2.9	14.2 ± 2.6	0.41
ΔJOA score	3.3 ± 3.0	2.4 ± 2.9	0.04
VAS for neck			
Preoperation	34.6 ± 31.5	35.3 ± 28.9	0.70
Final follow-up	19.9 ± 26.7	21.4 ± 25.2	0.73
ΔVAS	−15.0 ± 34.7	−14.0 ± 29.6	0.85

DM, diabetes mellitus; JOA, Japanese Orthopaedic Association; VAS, visual analog scale; Δ, change from preop to final follow-up values.

recovery from the C5 palsy, the duration of recovery was 5.7 ± 5.5 months and 7.6 ± 6.8 months in the DM and non-DM groups, respectively ($P = 0.43$).

Subanalysis was performed to identify the predictor for C5 palsy. Univariate analysis revealed no significant differences between the patients with and without postoperative palsy in age ($P = 0.29$), hypertension ($P = 0.08$), and cardiac disease ($P = 0.24$). In addition to these parameters, we analyzed clinically-relevant factors that were reported as predictors for the C5 palsy[22-24]; however, significant differences were not observed with respect to the duration of symptoms ($P = 0.46$), presence of T2-weighted MRI SI ($P = 0.25$), occupying ratio ($P = 0.15$), surgical techniques ($P = 0.76$), and preoperative cervical JOA score ($P = 0.36$). Based on these results, multivariate logistic regression analysis was performed, and results demonstrated that DM was the sole predictor for this adverse event (OR 2.8, 95% CI 1.0-7.6, $P = 0.04$).

Surgical Outcomes

As shown in Table 4, the baseline JOA score before surgery was significantly lower in the DM group than in the non-DM group (10.5 ± 3.1 vs. 11.8 ± 3.2, $P = 0.01$). In contrast, the changes in scores from the preoperative status were significantly higher in the DM group (3.3 ± 3.0 vs. 2.4 ± 2.9, $P = 0.04$), resulting in statistical insignificance between the groups at final follow-up (13.9 ± 2.9 vs. 14.2 ± 2.6, $P = 0.41$). Hemoglobin A1c levels had no correlation with the JOA scores either at preoperation ($r = 0.24$, $P = 0.13$) or at final follow-up ($r = 0.17$, $P = 0.29$).

No significant difference was noted in the VAS for neck pain between the groups before surgery (34.6 ± 31.5 mm vs. 35.3 ± 28.9 mm; $P = 0.70$) or at the final follow-up (19.9 ± 26.7 mm vs. 21.4 ± 25.2 mm; $P = 0.73$).

Demographics and Outcomes in Patients Treated Using Laminoplasty

Table 5 showed the results of patients who underwent laminoplasty only to evaluate the clinical outcomes for the majority with a single surgical technique. Similar to the overall results

Table 5. Demographics, Perioperative Complications, and Surgical Outcomes in Patients Who Underwent Laminoplasty.

	DM group (n = 37)	Non-DM group (n = 165)	*P*-value
Age (y)	62.5 ± 9.3	59.3 ± 8.9	0.06
Gender (% male)	73.0	71.5	0.86
BMI (kg/m^2)	25.6 ± 4.4	25.4 ± 3.6	0.84
Perioperative complications			
C5 palsy (%)	16.2	5.5	0.04
Surgical site infection (%)	0	0.6	0.81
Epidural hematoma (%)	0	0	-
Dural tear (%)	2.7	0	0.18
Neurological deterioration (%)	0	1.2	0.67
JOA scores			
Preoperation	9.9 ± 3.0	11.8 ± 3.3	< 0.01
Final follow-up	13.9 ± 2.7	14.2 ± 2.6	0.58
ΔJOA scores	4.0 ± 2.9	2.4 ± 3.0	< 0.01
VAS for the neck			
Preoperation	38.6 ± 31.1	37.4 ± 28.9	0.83
Final follow-up	23.3 ± 28.6	21.5 ± 25.8	0.77
ΔVAS	−15.4 ± 35.2	−14.9 ± 29.0	0.94

DM, diabetes mellitus; BMI, body mass index; JOA, Japanese Orthopaedic Association; VAS, visual analog scale; Δ, change from preop to final follow-up values.

described earlier, the demographics were comparable between the DM group (n = 37) and the non-DM group (n = 165), whereas perioperative complications showed a higher frequency of C5 palsy in the DM group than in the non-DM group (16.2% vs. 5.5%, $P = 0.04$). Other perioperative complications had no significant differences. Regarding the surgical outcomes, preoperative JOA scores were significantly lower in the DM group (9.9 ± 3.0 vs. 11.8 ± 3.3, $P < 0.01$) but were comparable at the final follow-up (13.9 ± 2.7 vs. 14.2 ± 2.6, $P = 0.58$) with larger changes in the DM group (4.0 ± 2.9 vs. 2.4 ± 3.0, $P < 0.01$). For the analysis using the VAS for the neck, the results were almost comparable between the groups.

Discussion

This is the first international study with the largest sample size to evaluate the impact of DM on the surgical outcomes for cervical OPLL patients. Overall incidence of DM was 18.6% in the enrolled subjects, and this was a larger ratio compared to those in the general population which was estimated as 8.8%.[25] Although preoperative neurologic function was significantly worse in the DM group, they reached a comparable functional status postoperatively. Among the perioperative complications; however, the frequency of C5 palsy in the DM group was approximately 3 times greater than that in the non-DM group, which was also identified when laminoplasty was utilized as the single surgical procedure. Therefore, even if cervical OPLL patients have DM, surgeons should not hesitate to perform operation, but the possibility of postoperative C5 palsy should be kept in mind and carefully explained to the patients before surgery.

In the current study, the baseline severity of neurologic status was significantly worse in DM patients. One of the potential explanations for this pathology was severe spinal cord compression due to a larger size of ossification in these patients, but in our results, no difference was noted in the size of ossified ligaments between the groups. Therefore, this severe myelopathy could be due to the pathological condition of the spinal cord itself affected by abnormal glycometabolism. Although a few studies examined the spinal cord degeneration in the pathology of DM, previous reports demonstrated a dysfunction of synaptic connection at both ventral and dorsal horns, which led to motor deterioration and sensory disturbance, respectively.[7,26] The blood vessels damaged by hyperglycemia had a reduced number of endothelial cells, which resulted in disruption of blood-spinal cord barrier and increased vascular permeability.[8,27] Some studies clarified that DM patients suffer from degradation of conduction velocity in motor and somatosensory evoked potentials, indicating a decrease of myelinated fibers in the spinal cord.[28,29] These pathological disadvantages in DM could be sufficiently attributed to the preoperative impairments of the OPLL cases.

Despite the adverse baseline severity, the present study revealed that surgical intervention had a beneficial effect for neurologic recovery even among DM patients. Similar results were observed in previous studies, which examined the JOA or modified JOA scores in cases with cervical myelopathy and showed comparable postoperative neurologic function between the DM and non-DM groups.[9,10,13,14,30] Since the average hemoglobin A1c level before surgery was relatively controlled at 6.4% in our cases, this glycometabolic status might be the contributing factor for the favorable surgical outcomes to be achieved. Therefore, surgical treatment is expected to acquire fair functional recovery under strictly controlled blood sugar levels.

In contrast, the current results clarified that DM patients have a high frequency of C5 palsy. With regard to the risk factors for postoperative segmental paralysis in cervical OPLL, previous reports proposed a longer duration of symptoms, the presence of intramedullary SI at T2-weighted MRI, a larger occupying ratio, and the performance of posterior instrumented fusion surgery.[22-24] However, all predictors were not associated with the occurrence of palsy in the present study as shown in our results. Due to the fact that the baseline cervical JOA score was significantly lower in the DM group, this inferior neurologic status might affect the occurrence of postoperative C5 palsy. However, several studies have demonstrated that there is no relation between this adverse event and preoperative severe myelopathy, thus indicating that baseline severity is not a predictor for paralysis.[23,31,32] Therefore, we suspected that the incidence of C5 palsy could be due to polyneuropathy, which is a well-known pathology of DM. For peripheral motor neurons, degeneration mainly occurs at the distal axonal terminals and disrupts its integrity of motor units at neuromuscular junctions.[33] Decompression surgery for cervical OPLL causes a posterior shift of the spinal cord and subsequent nerve root traction, which could damage the fragile distal terminals and trigger the C5 palsy. Although it is necessary to increase the number of cases and verify this hypothesis in the future, care should be taken regarding the occurrence of C5 palsy when treating OPLL in diabetic patients.

Previous studies have demonstrated a frequent incidence of SSI in patients with DM due to lower immunity and microvascular angiopathy.[14,34] However, recent large-scale studies targeting DCM revealed no significant difference in its occurrence between the DM and non-DM groups.[9,12,35] Consistent with these results, our study also demonstrates that there is no significant increase in SSI frequency in the DM group. This favorable consequence could be attributed to a strict control of blood glucose conducted by diabetes specialists during the perioperative period.

Our results demonstrated a higher prevalence of hypertension and cardiac diseases among DM patients. Hypertension is a risk factor for developing DM, both of which promote atherogenesis.[36] These combined comorbidities markedly increase the prevalence of cardiovascular disease. Thus, when treating cervical OPLL in DM patients, it is necessary to pay close attention to the systemic management during the perioperative period.

Several limitations were noted in this study. First, this is a retrospective study, which inevitably carries a low evidence level. Second, decisions about surgical methods and the number of decompression levels were made at the discretion and preference of the surgeons. Third, intervertebral foramen was not measured due to the property of multicenter registry in our database. Wu et al. reported that narrowing of the intervertebral foramen was involved in the development of C5 palsy, although the authors included patients with OPLL and with other forms of DCM.[22] Whether intervertebral foraminal stenosis is a risk factor for the paralysis that occurs in patients with OPLL remains an issue to be evaluated in the future. And finally, only cervical JOA scores and VAS for the neck were used for the assessment of surgical outcomes. Further study will be necessary to evaluate additional outcomes including cervical function and quality of life to comprehend the impact of DM on the overall clinical pictures of cervical OPLL. Despite these limitations, the strength of the current study was the utilization of international database from 3 Asian countries where the OPLL prevalence was frequent compared to the other areas or regions to investigate the surgical outcomes of cervical OPLL. Since the analysis for the evaluation of DM was conducted with the largest sample size that consisted of cervical OPLL patients only, the present research will make a new avenue to elucidate the pathophysiology and therapeutic outcomes in the field of ossification of the spinal ligaments.

In conclusion, this is the first multicenter Asian study to evaluate the impact of DM on cervical OPLL patients. Even in the DM cases, surgical results were favorable regardless of preoperative hemoglobin A1c levels or operative procedures. However, caution is warranted for the occurrence of C5 palsy after the surgery in the DM patients, which also require careful perioperative management due to systematic comorbidities such as hypertension and cardiovascular diseases.

Declaration of Conflicting Interests

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References

1. Nouri A, Tetreault L, Singh A, Karadimas SK, Fehlings MG. Degenerative cervical myelopathy: epidemiology, genetics, and pathogenesis. *Spine*. 2015;40(12):E675-E693.
2. Matsunaga S, Sakou T. Ossification of the posterior longitudinal ligament of the cervical spine: etiology and natural history. *Spine*. 2012;37(5):E309-E314.
3. Nagoshi N, Tetreault LA, Nakashima H, et al. Do Caucasians and East Asians have different outcomes following surgery for the treatment of degenerative cervical myelopathy?: Results from the prospective multicenter AOSpine international study. *Spine*. 2016;41(18):1428-1435.
4. Nakashima H, Tetreault L, Nagoshi N, et al. Comparison of outcomes of surgical treatment for ossification of the posterior longitudinal ligament versus other forms of degenerative cervical myelopathy: results from the prospective, multicenter AOSpine CSM-International Study of 479 Patients. *J Bone Joint Surg Am*. 2016;98(5):370-378.
5. Kobashi G, Washio M, Okamoto K, et al. High body mass index after age 20 and diabetes mellitus are independent risk factors for ossification of the posterior longitudinal ligament of the spine in Japanese subjects: a case-control study in multiple hospitals. *Spine*. 2004;29(9):1006-1010.
6. Akune T, Ogata N, Seichi A, Ohnishi I, Nakamura K, Kawaguchi H. Insulin secretory response is positively associated with the extent of ossification of the posterior longitudinal ligament of the spine. *J Bone Joint Surg Am*. 2001;83(10):1537-1544.
7. Benitez SU, Carneiro EM, de Oliveira AL. Synaptic input changes to spinal cord motoneurons correlate with motor control impairments in a type 1 diabetes mellitus model. *Brain Behav*. 2015;5(10):e00372.
8. Ved N, Da Vitoria Lobo ME, Bestall SM, et al. Diabetes-induced microvascular complications at the level of the spinal cord: a contributing factor in diabetic neuropathic pain. *J Physiol*. 2018;596(16):3675-3693.
9. Arnold PM, Fehlings MG, Kopjar B, et al. Mild diabetes is not a contraindication for surgical decompression in cervical spondylotic myelopathy: results of the AOSpine North America multicenter prospective study (CSM). *The Spine J*. 2014;14(1):65-72.
10. Dokai T, Nagashima H, Nanjo Y, Tanida A, Teshima R. Surgical outcomes and prognostic factors of cervical spondylotic myelopathy in diabetic patients. *Arch Orthop Trauma Surg*. 2012;132(5):577-582.
11. Kusin DJ, Ahn UM, Ahn NU. The influence of diabetes on surgical outcomes in cervical myelopathy. *Spine*. 2016;41(18):1436-1440.
12. Machino M, Yukawa Y, Ito K, et al. Impact of diabetes on the outcomes of cervical laminoplasty: a prospective cohort study of more than 500 patients with cervical spondylotic myelopathy. *Spine*. 2014;39(3):220-227.
13. Tanishima S, Mihara T, Tanida A, et al. Influence of diabetes mellitus on surgical outcomes in patients with cervical myelopathy: a prospective, multicenter study. *Asian Spine J*. 2019;13(3):468-477.
14. Kawaguchi Y, Matsui H, Ishihara H, Gejo R, Yasuda T. Surgical outcome of cervical expansive laminoplasty in patients with diabetes mellitus. *Spine*. 2000;25(5):551-555.
15. Liu Y, Ban DX, Kan SL, Cao TW, Feng SQ. The impact of diabetes mellitus on patients undergoing cervical spondylotic myelopathy: a meta-analysis. *Eur Neurol*. 2017;77(1-2):105-112.
16. Committee of the Japan Diabetes Society on the diagnostic criteria of diabetes mellitus; Seino Y, Nanjo K, et al. Report of the committee on the classification and diagnostic criteria of diabetes mellitus. *J Diabetes Investig*. 2010;1(5):212-228.
17. Kaneyama S, Sumi M, Kanatani T, et al. Prospective study and multivariate analysis of the incidence of C5 palsy after cervical laminoplasty. *Spine*. 2010;35(26):E1553-E1558.
18. Tsuyama N. Ossification of the posterior longitudinal ligament of the spine. *Clin Orthop Relat Res*. 1984:(184):71-84.
19. Fujiyoshi T, Yamazaki M, Kawabe J, et al. A new concept for making decisions regarding the surgical approach for cervical ossification of the posterior longitudinal ligament: the K-line. *Spine*. 2008;33(26):E990-E993.
20. Choi S, Lee SH, Lee JY, et al. Factors affecting prognosis of patients who underwent corpectomy and fusion for treatment of cervical ossification of the posterior longitudinal ligament: analysis of 47 patients. *J Spinal Dis Tech*. 2005;18(4):309-314.
21. Shin JJ, Jin BH, Kim KS, Cho YE, Cho WH. Intramedullary high signal intensity and neurological status as prognostic factors in cervical spondylotic myelopathy. *Acta Neurochir*. 2010;152(10):1687-1694.
22. Wu FL, Sun Y, Pan SF, Zhang L, Liu ZJ. Risk factors associated with upper extremity palsy after expansive open-door laminoplasty for cervical myelopathy. *Spine J*. 2014;14(6):909-915.
23. Liu G, Reyes MR, Riew KD. Why does C5 palsy occur after prophylactic bilateral C4-5 foraminotomy in open-door cervical laminoplasty? A risk factor analysis. *Global Spine J*. 2017;7(7):696-702.
24. Kimura A, Seichi A, Hoshino Y, et al. Perioperative complications of anterior cervical decompression with fusion in patients with ossification of the posterior longitudinal ligament: a retrospective, multi-institutional study. *J Orthop Sci*. 2012;17(6):667-672.

25. Ogurtsova K, da Rocha Fernandes JD, Huang Y, et al. IDF Diabetes Atlas: global estimates for the prevalence of diabetes for 2015 and 2040. *Diabetes Res Clin Pract*. 2017; 128:40-50.
26. Morgado C, Pinto-Ribeiro F, Tavares I. Diabetes affects the expression of GABA and potassium chloride cotransporter in the spinal cord: a study in streptozotocin diabetic rats. *Neurosci Lett*. 2008;438(1):102-106.
27. Zhao Y, Liu X, Yu A, Zhou Y, Liu B. Diabetes-related alteration of occludin expression in rat blood-spinal cord barrier. *Cell Biochem Biophys*. 2010;58(3):141-145.
28. Kucera P, Goldenberg Z, Varsik P, Buranova D, Traubner P. Spinal cord lesions in diabetes mellitus. Somatosensory and motor evoked potentials and spinal conduction time in diabetes mellitus. *Neuro Endocrinol Lett*. 2005;26(2):143-147.
29. Varsik P, Kucera P, Buranova D, Balaz M. Is the spinal cord lesion rare in diabetes mellitus? Somatosensory evoked potentials and central conduction time in diabetes mellitus. *Med Sci Monit*. 2001;7(4):712-715.
30. Okada M, Minamide A, Yoshida M, Kawakami M, Enyo Y, Endo T. Observations in the diagnosis of cervical myelopathy in patients suffering from diabetes mellitus. *Spinal Cord*. 2012; 50(12):878-881.
31. Fehlings MG, Wilson JR, Kopjar B, et al. Efficacy and safety of surgical decompression in patients with cervical spondylotic myelopathy: results of the AOSpine North America prospective multicenter study. *J Bone Joint Surg Am*. 2013;95(18):1651-1658.
32. Chiba K, Toyama Y, Matsumoto M, Maruiwa H, Watanabe M, Hirabayashi K. Segmental motor paralysis after expansive open-door laminoplasty. *Spine*. 2002;27(19):2108-2115.
33. Zochodne DW, Ramji N, Toth C. Neuronal targeting in diabetes mellitus: a story of sensory neurons and motor neurons. *Neuroscientist*. 2008;14(4):311-318.
34. Olsen MA, Nepple JJ, Riew KD, et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. 2008;90(1):62-69.
35. Nori S, Nagoshi N, Yoshioka K, et al. Diabetes does not adversely affect neurological recovery and reduction of neck pain after posterior decompression surgery for cervical spondylotic myelopathy: results from a retrospective multicenter study of 675 patients. *Spine*. 2020.
36. Grossman E, Messerli FH. Hypertension and diabetes. *Adv Cardiol*. 2008;45:82-106.