Dyslipidemia as a novel risk for the development of symptomatic ossification of the posterior longitudinal ligament

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Abbreviations: BMI, body mass index; CT, computed tomography; LDL, low-density lipoprotein; OLF, ossification of the ligamentum flavum; OPLL, ossification of the posterior longitudinal ligament; MAFLD, metabolic dysfunction-related fatty liver disease

Abstract

BACKGROUND CONTEXT

Obesity and visceral fat have been implicated as potential factors in the pathogenesis of the ossification of the posterior longitudinal ligament (OPLL); the details of the factors involved in OPLL remain unclear.

PURPOSE

We aimed to determine the association between dyslipidemia and symptomatic OPLL.

STUDY DESIGN

Single institution cross-sectional study.

PATIENT SAMPLE

Data were collected from Japanese patients with OPLL (n=92) who underwent whole-spine computed tomography scanning. Control data (n=246) without any spinal ligament ossification were collected from 627 Japanese participants who underwent physical examination.

OUTCOME MEASURES

Baseline information and lipid parameters, including triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) from fasting blood samples were collected to assess the comorbidity of dyslipidemia.

METHODS

Patient data were collected from 2020 to 2022. Patients with dyslipidemia were defined as those who were taking medication for dyslipidemia and who met one of the following criteria: TG ≥150 mg/dL, LDL-C ≥140 mg/dL, and/or HDL-C <40 mg/dL. The factors

associated with OPLL development were evaluated using multivariate logistic regression analysis.

RESULTS

The comorbidity of dyslipidemia in the OPLL group was more than twice that in the control group (71.7% and 35.4%, respectively). The mean body mass index (BMI) of the OPLL group was significantly higher than that of the control group (27.2 kg/m^2 and 23.0 kg/m^2). Multivariate logistic regression analysis revealed that dyslipidemia was associated with the development of OPLL (regression coefficient, 0.80; 95% confidence interval, 0.11–1.50). Additional risk factors included age, BMI, and diabetes mellitus.

CONCLUSIONS

We demonstrated a novel association between dyslipidemia and symptomatic OPLL development using serum data. This suggests that visceral fat obesity or abnormal lipid metabolism are associated with the mechanisms of onset and exacerbation of OPLL as well as focal mechanical irritation due to being overweight.

Keywords: ossification of the posterior longitudinal ligament (OPLL), symptomatic OPLL, dyslipidemia, whole-spine CT, obesity, visceral fat, abnormal lipid metabolism

Introduction

Ossification of the posterior longitudinal ligament (OPLL) is a progressive disease characterized by ectopic bone formation in the spinal ligament, causing spinal canal stenosis and severe myelopathy. [1-3] Currently, there are no preventive or therapeutic measures for OPLL. OPLL is the major cause of myelopathy in middle-aged to older populations in East Asia and predominantly affects the cervical spine. [1-5] Previous studies on patients with OPLL, mostly cervical OPLL, have shown that it is a multifactorial disease with complex environmental (e.g., sex, diabetes mellitus, mechanical stress, trauma, and eating habits) and genetic factors [5-9]; however, no obvious causative factors have been identified. Recent epidemiological studies have reported that, compared to patients with cervical OPLL, those with thoracic OPLL represent a distinctive subgroup with the following characteristics: 1) morbid obesity, 2) a strong tendency for ossification involving the entire spinal ligaments, and 3) a higher rate of younger age at onset. [7,10] In addition, obesity and metabolic dysfunction-related fatty liver disease (MAFLD) have been identified as exacerbating factors for OPLL, [11,12] suggesting that visceral fat obesity is involved in OPLL development. [10-13]

Dyslipidemia is closely related to atherosclerosis, MAFLD, genetic predisposition, nutritional disorders, and obesity. [14-17] Lipid metabolism regulates osteoblasts via the Wnt/β-catenin pathway, which is tightly linked to the mechanisms of calcification and bone formation. [18-20] Dyslipidemia also triggers oxidative stress and chronic inflammation, which leads to smooth muscle cell death, deficiency of calcification inhibitory factors, the transformation of smooth muscle cells to osteoblasts, and cellular senescence, resulting in

vascular calcification. [18,21] Although dyslipidemia and OPLL partially share cellular and molecular mechanisms, their relationship has not been studied in detail.

The present study aimed to identify the underlying etiologies responsible for the development and exacerbation of OPLL. We need to investigate whether dyslipidemia is associated with OPLL mechanisms based on the classification into subgroups that are strongly predicted to be associated with metabolic disorders and by the age of predilection for OPLL. Herein, we studied the association of dyslipidemia with OPLL and OPLL subgroups by comparing a large dataset, which included whole-spine computed tomography (CT) and fasting blood samples, of patients with symptomatic OPLL to a dataset of patients without spinal ligament ossification who underwent physical examinations.

Material and Methods

Study design

This was a cross-sectional study. The study included participants who visited our institution from 2020 to 2022. This study was approved by the ethics committee of our hospital and complies with the Declaration of Helsinki (1964). The need for obtaining patients' informed consent was waived owing to the retrospective nature of the study and the unidentified nature of the data used.

Inclusion/exclusion criteria for patients

Patients with symptomatic OPLL who regularly visited the orthopedic/spine surgery department of a single general hospital located in a city of 240,000 people in northern Japan

were included. These patients were diagnosed with OPLL by spine surgeons, orthopedic surgeons, and radiologists based on clinical symptoms and X-ray and CT images. Of 129 patients, 37 who did not have records of both fasting blood tests, including lipid parameters, and previous whole-spine CT scanning were excluded. Finally, 92 patients (43 men and 49 women) were included in the study (Figure 1).

As a control, a database of 13,700 Japanese patients from the same facility was used. Regardless of whether they were symptomatic, all patients underwent routine physical examinations once a year or every few years. The participants were community residents and facility employees, including physicians, nurses, nursing assistants, therapists, and clerical staff, and the majority underwent blood tests. They also underwent CT of the trunk at their discretion for screening purposes, mainly for cancer; they also selected the scan region (neck to chest, abdomen to pelvis, or neck to pelvis). In total, 627 patients were included, for whom CT images from the neck to the pelvis were available and lipid parameters could be assessed with blood test data. Of the 627 patients, 381 with any spinal ligament ossification, including ossification of the anterior longitudinal ligament (OALL), OPLL, and ossification of the ligamentum flavum (OLF) on axial CT planar images were excluded. Finally, 246 participants (102 men, 144 women) aged 34–78 years and without any spinal ligament ossification were included (Figure 1).

Demographics, comorbidities, and serological assessment

Demographic data of all participants were obtained. Data regarding age, sex, body mass index (BMI), previous OPLL-related operations, presence of comorbidities (hypertension, hyperuricemia, diabetes mellitus, and dyslipidemia), and current use of dyslipidemia

medication were assessed. All serological evaluations were performed on fasting blood samples. Serological evaluation parameters included total cholesterol (T-Cho), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). The LDL-C/HDL-C ratio (L/H ratio) was used as a parameter for the degree of dyslipidemia. [22,23] It is reported that the L/H ratio influences the lipid component of coronary plaques: L/H ratio ≤1.5 is unlikely to lead to plaque formation, L/H ratio ≥2.0 indicates gradual plaque formation, L/H ratio ≥2.5 indicates a high likelihood of thrombi formation, and L/H ratio ≥3.0 further increases the risk of thrombosis. [24,25]

Diagnostic criteria for dyslipidemia by the Japan Atherosclerosis Society

The 2022 guidelines of the Japan Atherosclerosis Society define dyslipidemia in adults as the following: TG ≥150 mg/dL, LDL-C ≥140 mg/dL, and/or HDL-C <40 mg/dL. [26] This study defined patients with dyslipidemia as those who met any of the above criteria and those who were taking medication for dyslipidemia.

Assessment of OPLL and grouping of patients by OPLL type

The distribution of OPLL (cervical, thoracic, and/or lumbar) in patients with symptomatic OPLL was assessed using whole-spine CT. Patients with OPLL were divided into two groups according to the OPLL type: a “localized OPLL” group that had OPLL only in the cervical spine (Figure 2A), and a “diffuse OPLL” group with OPLL in the thoracic spine, with or without OPLL in the cervical and lumbar spine (Figure 2B). This grouping rationale was based on our previous studies as follows: compared with patients with OPLL only in the cervical spine, those with OPLL involving the thoracic spine tended

to have 1) more pronounced obesity and 2) more advanced ossification of ligaments throughout the spine. [10,27,28] All CT images were obtained using the Aquilion One™/Genesis Edition system (Canon Medical Systems, Inc., Tochigi, Japan).

Assessment of the absence of spinal ligament ossification in participants undergoing physical examinations (i.e., exclusion criteria regarding the controls)

Axial CT planar images from the neck to the pelvis were used to evaluate the absence of spinal ligament ossification in the participants undergoing physical examinations. OALL, OPLL, and OLF were evaluated as per our previously reported methods, and participants who did not have any of the aforementioned spinal ligament ossifications were enrolled as controls (Figure 3). Briefly, OALL was defined as a thickness of ≥4 mm with bridging of adjacent vertebrae; OPLL was defined as a thickness of ≥2 mm; OLF was defined as a thickness of ≥3 mm, clearly visible even if the thickness was <3 mm, or mushroom-shaped ossifications localized in the central lamina. [13] All CT scans were evaluated by two board-certified spine surgeons (TE and RF). Discrepancies were resolved by consensus to minimize intra- and inter-observer biases and errors.

Grouping of presence or absence of concomitant dyslipidemia

All participants were additionally categorized into two groups according to the presence or absence of dyslipidemia: DL(+) and DL(-).

Grouping by the presence or absence of previous OPLL-related operations

Patients in the localized and diffuse OPLL groups were further categorized into the operative OPLL and non-operative OPLL groups, respectively, according to the presence or absence of previous OPLL-related operations.

Statistical analyses

Data were analyzed using the Bell Curve for Excel (version 4.02; Social Survey Research Information Co., Ltd., Tokyo, Japan). The normality of the data distribution was evaluated using the Shapiro–Wilk test. The results are presented as mean ± standard deviation or median (minimum–maximum). Differences in continuous variables among the groups were evaluated using the Student's or Welch's t-test (for normally distributed data) or Mann–Whitney U test (for non-normally distributed data). Differences in proportions of categorical variables among the groups were evaluated using Fisher's exact test. Statistical significance was set at $P<0.05$ in two-group comparisons; it was set at $P<0.016$ (0.05/3) in three-group comparisons with a Bonferroni correction considering multiple testing. Univariate analysis was performed for age, BMI, sex, comorbidities (hypertension, hyperuricemia, diabetes mellitus, and dyslipidemia), and the L/H ratio as potential risk factors for developing OPLL. In the multivariate logistic regression analysis, explanatory variables were determined based on previous reports and expert opinions, and dyslipidemia was added, all of which met $P<0.10$ in univariate analysis. A positive regression coefficient (β) implied a positive association and a negative β implied a negative association; a 95% confidence interval (CI) that included the value zero was not considered significant.

Results

Clinical characteristics

Among all patients with OPLL, the proportion of patients with localized OPLL was 42.4% (39/92) and that with diffuse OPLL was 57.6% (53/92). We first examined whether patients with the two OPLL types, localized and diffuse, differed in body size and comorbidities, compared with controls. The characteristics of each group are shown in Table 1. The mean ages of both the localized and diffuse OPLL groups were significantly higher than that of the control group. The mean BMI of the diffuse OPLL group was the highest among the groups. The diffuse OPLL group also had the highest proportion of patients with BMI ≥25.0 kg/m^2, ≥27.5 kg/m^2, ≥30.0 kg/m^2, and ≥35.0 kg/m^2 among the groups. Both the localized and diffuse OPLL groups had significantly higher proportions of patients with BMI ≥25.0 kg/m^2 and ≥30.0 kg/m^2 than the control group. The co-existence rates of hypertension and diabetes mellitus in the localized and diffuse OPLL groups were also significantly higher than those in the control group; however, the co-existence rate of hyperuricemia was not different among the groups. The proportions of previous OPLL-related operations were 66.7% in the localized OPLL group and 50.9% in the diffuse OPLL group.

Dyslipidemia

We next assessed the co-existence rate and severity of dyslipidemia in participants with each OPLL type. The co-existence rates of dyslipidemia in the localized and diffuse OPLL groups (82.1% and 64.1%, respectively) were significantly higher than that in the control group (35.4%) (Figure 4A). The rates of medication use in the localized and diffuse OPLL groups (53.8% and 41.5%, respectively) were significantly higher than that in the control

group (10.2%) (Figure 4B). The co-existence rates of dyslipidemia in both OPLL groups were also higher than that in the control group for each age group, and the rate in the localized OPLL group was significantly higher than that in the control group in the middle-aged group (aged 60–69 years) (Figure 4C). The co-existence rate of dyslipidemia in the diffuse OPLL group in the age group of 40–49 years and in the localized OPLL group in the age group of 50–59 years was 100% but not significantly different from that in the control group (control vs. diffuse OPLL group in the age group of 40–49 years, P=0.035; control vs. localized OPLL group in the age group of 50–59 years, P=0.019). These rates in both OPLL groups were also higher than the rates of suspected dyslipidemia in the different age groups of the general Japanese population (30–39 years: 7.4%; 40–49 years: 7.1%; 50–59 years: 17.1%; 60–69 years: 26.5%; ≥70 years: 37.2%). [29] The rates of medication use for dyslipidemia in both OPLL groups were higher than that in the control group in the relatively young age group of 40–49 years, and it was 100% in the diffuse OPLL group (Figure 4D).

Additionally, we assessed the L/H ratio, an indicator of dyslipidemia severity. The proportion of participants with an L/H ratio ≤1.5 in the localized OPLL group was significantly lower than in the control group (12.8% vs. 31.3%) (Table 1).

Proportion of co-existing OPLL between participants with and without dyslipidemia

We also assessed the effect of dyslipidemia on the differences in the proportion of OPLL types (Supplemental Table 1). The proportion of participants without ligament ossification was significantly lower in the DL(+) group than in the DL(−) group (56.9% vs. 85.9%,

respectively; P<0.001). The proportion of participants with both localized and diffuse OPLL was significantly higher in the DL(+) group than in the DL(−) group (P<0.001).

Proportion of dyslipidemia in patients with and without OPLL-related operations

To assess the association of dyslipidemia with the severity of OPLL symptoms, we compared items, including lipid parameters, between operative and non-operative patients in the localized and diffuse OPLL groups (Supplemental Table 2). There were no significant differences in all parameters, including the co-existence rate of dyslipidemia, between operative and non-operative patients in both the localized and diffuse OPLL groups.

Risk factors for the development of OPLL

We conducted a multivariate logistic regression analysis to identify the risk factors for OPLL development (Table 2). β and standardized β-values were examined. OPLL development was associated with dyslipidemia (β=0.80; 95% confidence interval [CI], 0.11–1.50). Furthermore, age, BMI, and diabetes mellitus were associated with OPLL development. To determine the relative contribution of the risk factors, we compared the standardized β-values for each risk factor. The standardized β-value of dyslipidemia was higher than that of diabetes mellitus but lower than that of age and BMI; age was the strongest risk factor for OPLL development. We further identified the risk factors for localized and diffuse OPLL development, respectively. Dyslipidemia was a stronger risk factor for localized OPLL development (β, 1.33; 95% CI, 0.32–2.34) than for diffuse OPLL development (β, 0.33; 95% CI, -0.57–1.23). BMI was a stronger risk factor for diffuse

OPLL development (β, 0.34; 95% CI, 0.21–0.46) than for localized OPLL development (β, 0.13; 95% CI, 0.005–0.26). In comparison with standardized β-values, age (1.26) was more strongly associated with localized OPLL development, and BMI (1.47) was more strongly associated with diffuse OPLL development.

Discussion

The current study revealed that the proportion of comorbid dyslipidemia among patients with symptomatic OPLL was 82.1% for localized OPLL and 64.1% for diffuse OPLL, which was more than twice as high as that for controls without spinal ligament ossification (35.4%). The proportion in patients with OPLL was higher than that of suspected dyslipidemia (22.8%) in the general Japanese population (40‐74 years) as surveyed by the Ministry of Health, Labor, and Welfare. [29] This study also clarified that OPLL development was associated with dyslipidemia. The clinical significance of these findings is that one-third of patients with OPLL with comorbid dyslipidemia have not been previously diagnosed or medically treated for dyslipidemia, which may be due to the uniqueness of most patients with dyslipidemia remaining asymptomatic. All patients were evaluated for the presence of dyslipidemia based on fasting blood sampling data. This was the first case-control study to report the comorbidity of dyslipidemia in symptomatic Japanese patients with OPLL and the association between dyslipidemia and OPLL compared with controls.

The association between dyslipidemia and OPLL was supported by the high proportion of comorbid dyslipidemia in both localized and patients with diffuse OPLL. Interestingly,

in the assessment of the relative risk using standardized β-values, dyslipidemia was equivalent to or higher than diabetes mellitus, which has been previously reported as a risk factor for OPLL development. [4,8,30,31] We also found that patients with diffuse OPLL had a high prevalence of comorbid dyslipidemia at a relatively young age. It was unexpected that the proportion of comorbid dyslipidemia was not significantly different between the OPLL groups, and dyslipidemia was associated with localized OPLL, even though BMI was significantly higher in patients with diffuse OPLL than in those with localized OPLL. This was because a recent study reported that approximately 80% of patients with symptomatic OPLL had MAFLD and that the severity of spinal ligament ossification was associated with the severity of their fatty liver. [11] All of these findings, however, suggest that visceral fat obesity or abnormal lipid metabolism rather than focal mechanical irritation may be associated with the mechanisms of onset or exacerbation of OPLL.

At present, it is unclear whether abnormal lipid metabolism can induce heterotopic ossification of the spinal ligaments; however, various studies suggest this possibility. First, subendothelial retention of lipoproteins by proteoglycans is an initiating event in atherosclerosis; the elongation of chondroitin sulfate chains, which is critical for calcifying effects, is associated with increased LDL binding and progression of atherosclerosis. [15,16] Second, the mechanism of OLF has been postulated to be the production of cartilage matrix by chondrocytes within the ligamentum flavum and calcification around the chondrocytes, which eventually fuse and become ossified. Biochemical studies on glycosaminoglycans in the ossified ligamentum flavum suggest that OLF development is associated with the promotion of proteoglycan synthesis, which is mainly composed of

chondroitin-6 sulfate and chondroitin-4 sulfate. [32,33] Third, the oxidative stress environment caused by high LDL-C also activates Wnt signaling, and LDL receptor-related protein (LRP5) promotes bone formation through osteoblast proliferation. [20,21,34]

Multivariate logistic regression analysis identified age, BMI, and diabetes mellitus as additional factors associated with OPLL development. These results support previous findings that the general onset age of OPLL is middle age or older, [1,2,6,30] that patients with OPLL tend to be obese, [8,10,12,34], and that glucose metabolism may be associated with the mechanism of OPLL development. [4,8,30,31] We should note that the risk factors for localized and diffuse OPLL did not necessarily coincide because the study showed that factors associated with localized OPLL were male sex, age, and BMI, whereas factors associated with diffuse OPLL were female sex, age, BMI, and diabetes mellitus. β and standardized β values also showed that diffuse OPLL was less associated with dyslipidemia and more strongly associated with BMI compared to localized OPLL. These results supported the findings that localized OPLL is twice as common in men than in women and diffuse OPLL is three times as common in women than in men, [3,35,36] and that diffuse OPLL has a higher prevalence of severe obesity (BMI >35 kg/m^2) and is more strongly associated with BMI than localized OPLL. [7,10,11,13,28] Based on these facts and the results of multivariate logistic regression analysis adjusting for each factor, we speculated that, compared to localized OPLL, diffuse OPLL is strongly influenced by factors including BMI, resulting in a relatively lower association with dyslipidemia. The presence of multiple risk factors for OPLL and the variation in risk in the OPLL subgroups indicates that the pathogenesis of OPLL is multifactorial.

The present study has several limitations. First, because the study design was cross-sectional, a causal relationship between dyslipidemia and OPLL could not be determined. Second, the risk of selection bias could not be eliminated because many patients with OPLL might have relatively severe myelopathy, and patients with slightly symptomatic or asymptomatic OPLL were likely not included in this study. Third, because all data were collected from Japanese individuals, the results may not be applicable to other populations.

In conclusion, the present study revealed that Japanese patients with symptomatic OPLL had a high incidence of comorbid dyslipidemia. Furthermore, in addition to age, BMI, and diabetes mellitus (as previously reported), dyslipidemia was newly found to be associated with symptomatic OPLL development. These findings may help elucidate the pathogenesis of OPLL, the details of which are still unknown, and suggest that OPLL may be preventable through the control of lipid metabolism. For futures studies, animal models should be used to verify whether abnormal lipid metabolism causes heterotopic ossification of the spinal ligaments.

Competing Interests

The authors declare no competing interests.

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Figure Legends

Figure 1. Inclusion and exclusion criteria for patients with OPLL and control participants.

OALL, ossification of the anterior longitudinal ligament; OPLL, ossification of the posterior longitudinal ligament; OLF, ossification of the ligamentum flavum

Figure 2. Representative cases of OPLL

A. Localized OPLL: OPLL present only in the cervical spine (arrow)

B. Diffuse OPLL: OPLL present throughout the spine, including the thoracic spine (arrow)

OPLL, ossification of the posterior longitudinal ligament

Figure 3. The assessment of spinal ligament ossification in controls (i.e., exclusion criteria)

A. OALL: located in the paramedian region of the anterior vertebral body with a thickness ≥4 mm (arrow)

B. OPLL: with a thickness ≥2 mm (arrow)

C. OLF: with a thickness ≥3 mm (arrow)

D. OLF: with a mushroom-shape that is localized at the center of laminae (arrow)

OALL, ossification of the anterior longitudinal ligament; OPLL, ossification of the posterior longitudinal ligament; OLF, ossification of the ligamentum flavum

Figure 4. Comparison of the proportion of dyslipidemia among the ossification types

A, C. The proportion of co-existing dyslipidemia in the participants

B, D. The proportion of participants using medication for dyslipidemia

1 * indicates P<0.016

2 OPLL, ossification of the posterior longitudinal ligament

Table 1. Comparison of clinical characteristics between the control, localized OPLL, and diffuse OPLL groups

Variable	Control (n=246)	Localized OPLL (n=39)	Diffuse OPLL (n=53)
Age (years)	50 (34－78)	68 (42－81)*	68 (33－81)*
Age range (%)			
30–39 years	11.4	0	3.8
40–49 years	33.7	7.7*	5.7*
50–59 years	30.5	12.8	15.1
60–69 years	13.8	35.9*	32.1*
≥70 years	10.6	43.5*	43.3*
BMI (kg/m^2)	23.0 ± 3.3	26.0 ± 4.5*	28.1 ± 5.8*
BMI ≥25.0 kg/m^2 (%)	26.8	59.0*	69.8*
BMI ≥27.5 kg/m^2 (%)	10.2	23.1	50.9*†
BMI ≥30.0 kg/m^2 (%)	1.6	15.3*	34.0*
BMI ≥35.0 kg/m^2 (%)	0	5.1	9.4*
Male sex (%)	41.4	79.5*	22.6*†
Comorbidity (%):			
Hypertension	16.7	59.0*	60.3*
Diabetes mellitus	3.6	25.6*	37.7*
Hyperuricemia	11.8	12.8	11.3
OPLL-related operations (%):	0	66.7*	50.9*
T-Cho (mg/dL)	209.5 ± 37.1	187.2 ± 33.7*	194.7 ± 37.2*
TG (mg/dL)	94.6 ± 54.6	161.5 ± 76.9*	149.6 ± 86.6*
HDL-C (mg/dL)	65.7 ± 16.6	51.4 ± 12.4*	59.9 ± 15.0†
LDL-C (mg/dL)	122.1 ± 34.5	109.6 ± 29.5	109.1 ± 29.9
L/H ratio	1.98 ± 0.81	2.23 ± 0.73	1.89 ± 0.56†
L/H ≤1.5 (%)	31.3	12.8	18.9
L/H ≥2.0 (%)	43.5	57.9	35.8
L/H ≥2.5 (%)	23.6	36.8	15.1
L/H ≥3.0 (%)	12.2	18.4	3.8

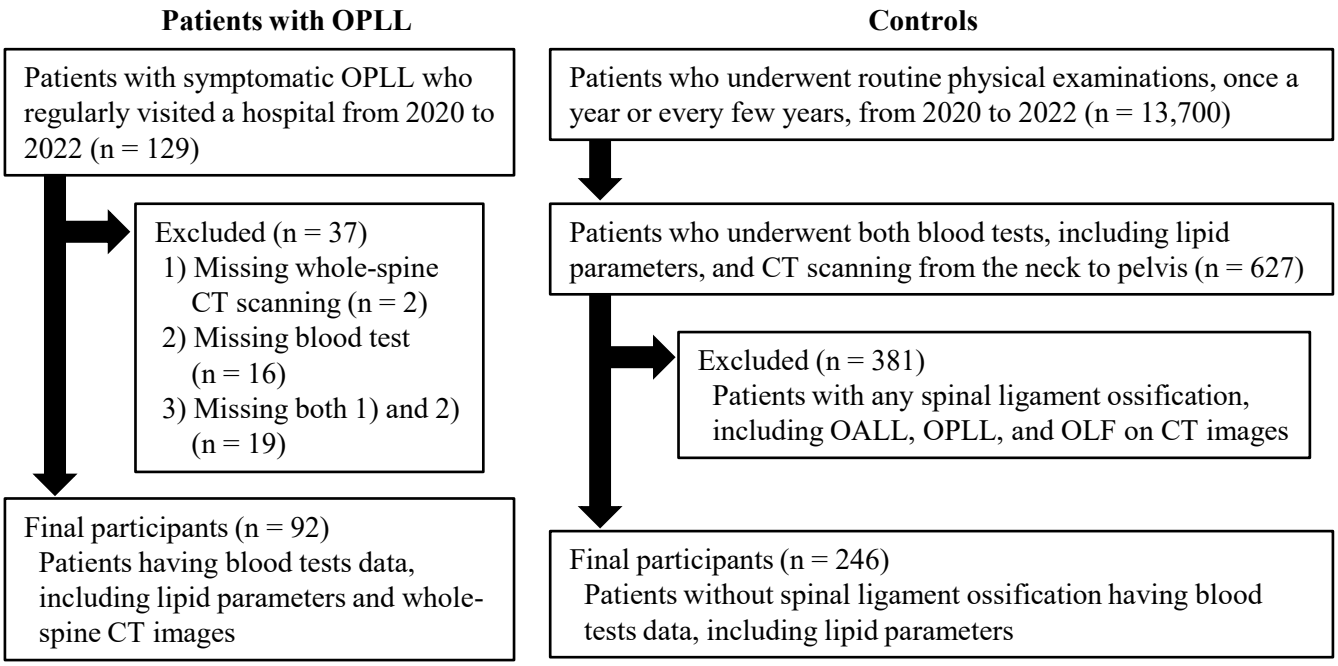
Data are shown as mean ± standard deviation for normally distributed variables, as median (minimum–maximum) for non-normally distributed variables, and as percentages for categorical variables. L/H ratio represents LDL-C/HDL-C.
(* indicates $P<0.016$ vs. the control group)
(† indicates $P<0.016$ vs. the localized OPLL group)

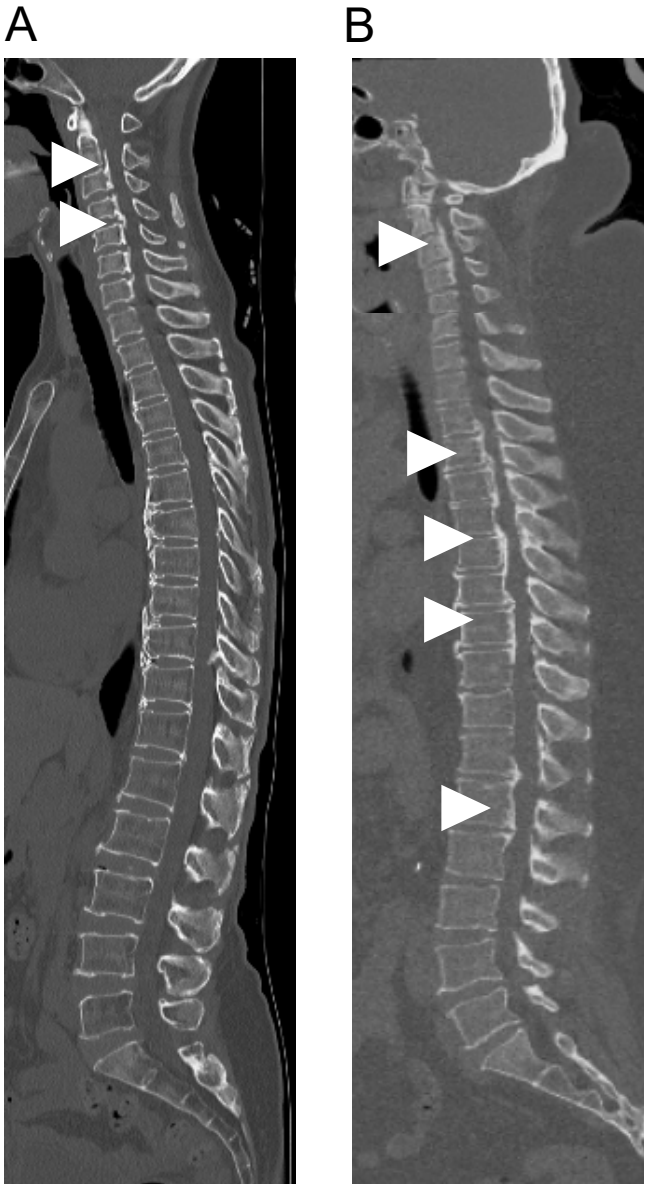
OPLL, ossification of the posterior longitudinal ligament; BMI, body mass index; T-Cho, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol

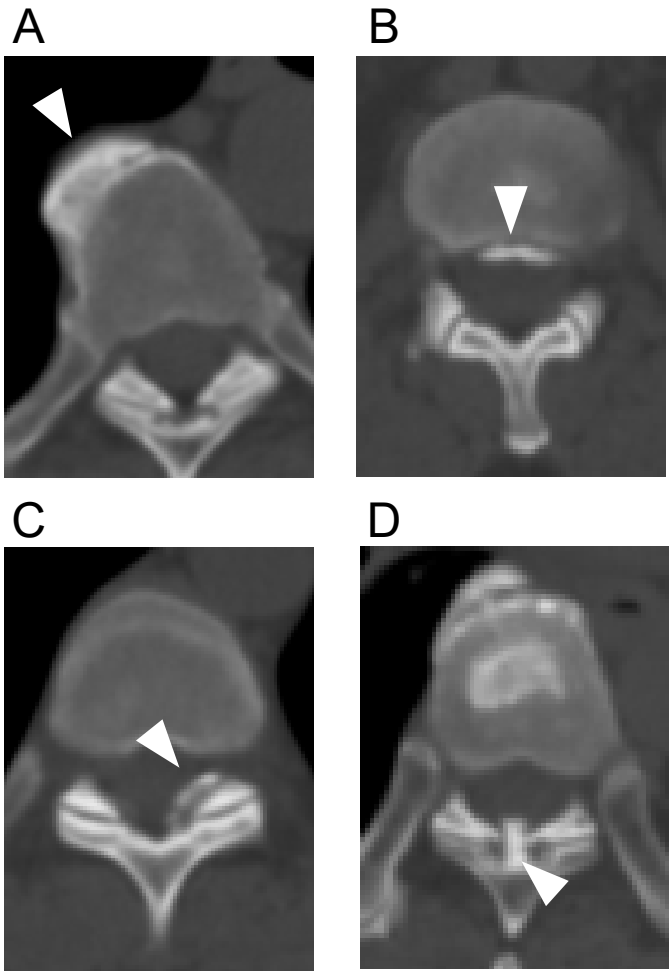
Table 2. Multivariate logistic regression analysis of risk factors for developing OPLL, localized OPLL, and diffuse OPLL

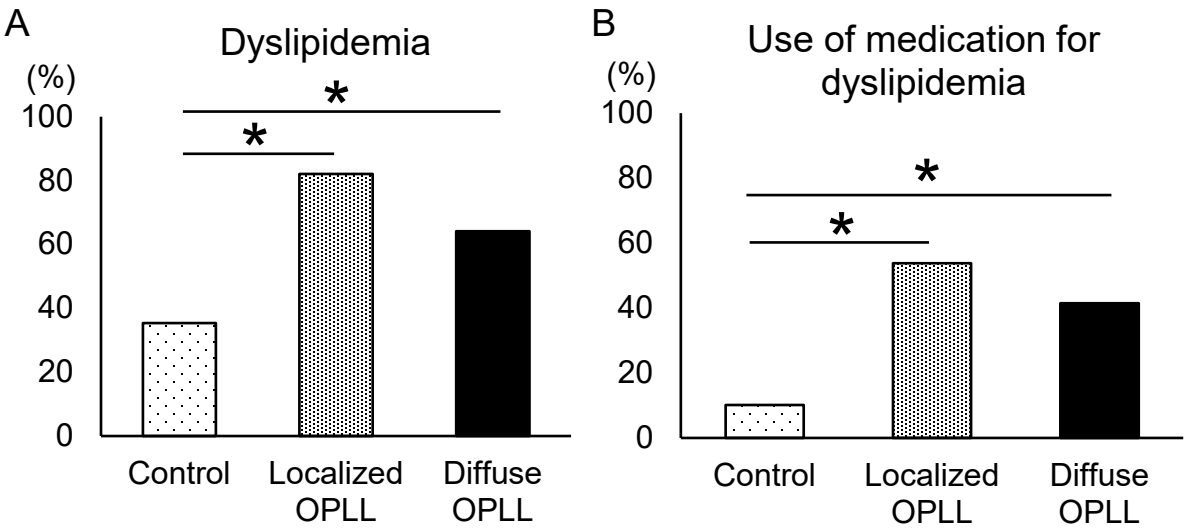
Independent variables	β	Standardized β	95% CI	P-value
(OPLL)				
Dyslipidemia	0.80	0.40	0.11－1.50	0.02
Male sex	-0.34	-0.17	-1.03－0.34	0.32
Age (years)	0.11	1.39	0.07－0.14	<0.001
BMI (kg/m^2)	0.24	1.08	0.15－0.33	<0.001
Hypertension	0.36	0.16	-0.36－1.09	0.33
Diabetes mellitus	1.07	0.34	0.13－2.00	0.02
(Localized OPLL)				
Dyslipidemia	1.33	0.65	0.32－2.34	0.009
Male sex	1.13	0.56	0.13－2.12	0.02
Age (years)	0.10	1.26	0.06－0.15	<0.001
BMI (kg/m^2)	0.13	0.50	0.005－0.26	0.04
Hypertension	0.60	0.25	-0.32－1.52	0.20
Diabetes mellitus	-0.19	-0.04	-1.40－1.02	0.75
(Diffuse OPLL)				
Dyslipidemia	0.33	0.16	-0.57－1.23	0.47
Male sex	-2.10	-1.02	-3.26－-0.94	<0.001
Age (years)	0.11	1.43	0.06－0.17	<0.001
BMI (kg/m^2)	0.34	1.47	0.21－0.46	<0.001
Hypertension	0.32	0.14	-0.61－1.27	0.49
Diabetes mellitus	1.86	0.55	0.73－2.99	0.001

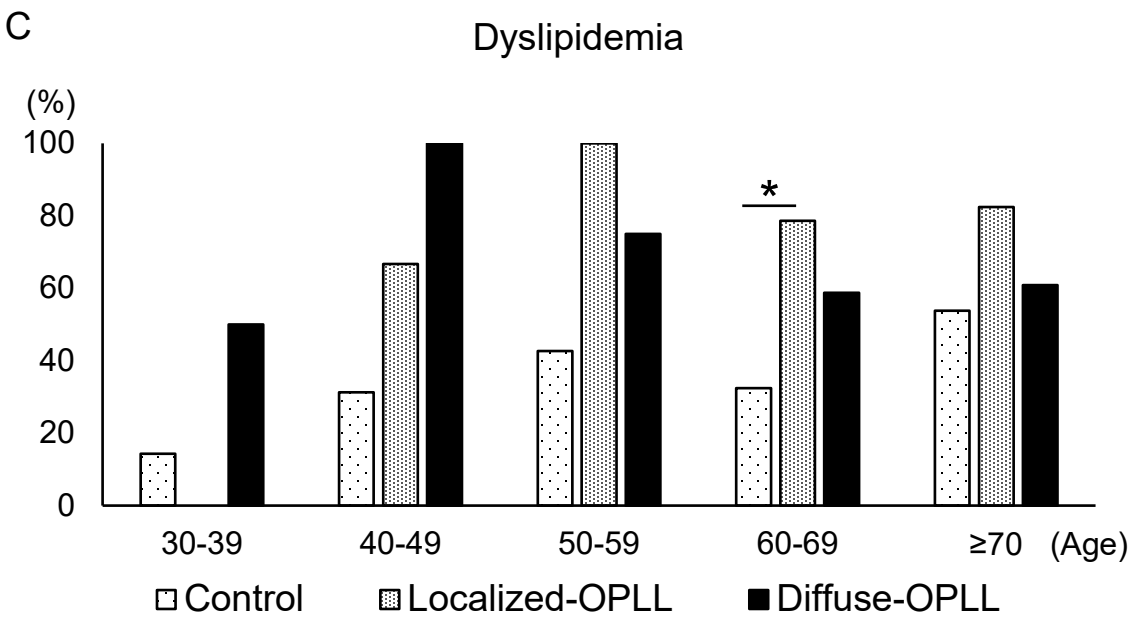
OPLL, ossification of the posterior longitudinal ligament; β, regression coefficient; CI, confidence interval; BMI, body mass index.

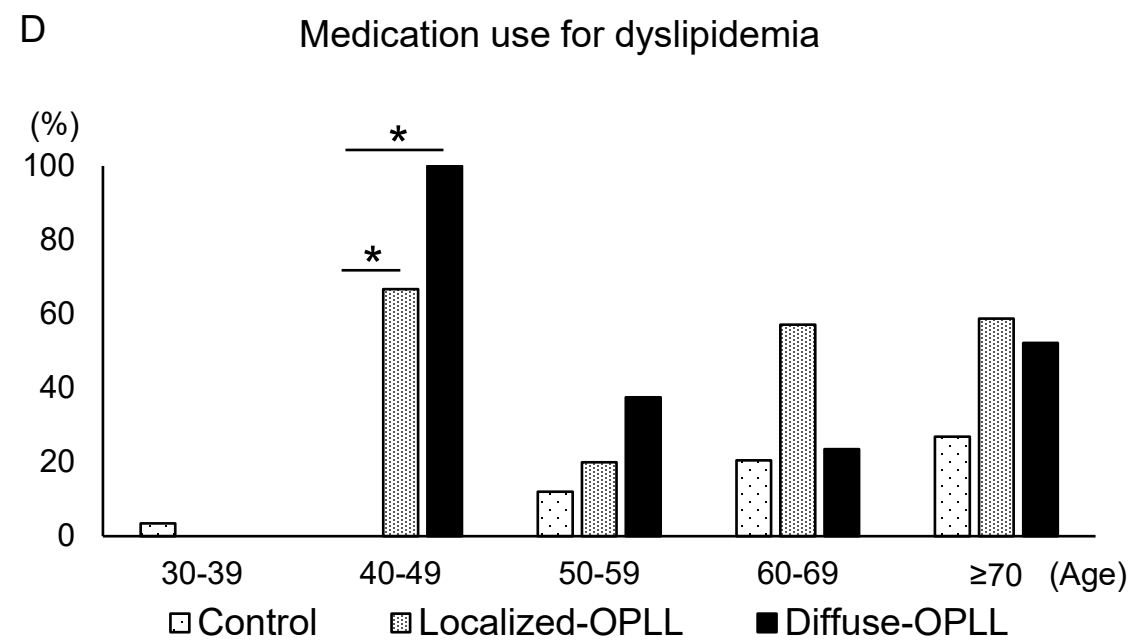

Patients with OPLL
Controls
Patients with symptomatic OPLL who regularly visited a hospital from 2020 to 2022 (n = 129)
Excluded (n = 37)
1) Missing whole-spine CT scanning (n = 2)
2) Missing blood test (n = 16)
3) Missing both 1) and 2) (n = 19)
Final participants (n = 92)
Patients having blood tests data, including lipid parameters and whole-spine CT images
Patients who underwent routine physical examinations, once a year or every few years, from 2020 to 2022 (n = 13,700)
Patients who underwent both blood tests, including lipid parameters, and CT scanning from the neck to pelvis (n = 627)
Excluded (n = 381)
Patients with any spinal ligament ossification, including OALL, OPLL, and OLF on CT images
Final participants (n = 246)
Patients without spinal ligament ossification having blood tests data, including lipid parameters


A
B


A
B
C
D


A
Dyslipidemia
(%)
100
80
60
40
20
0
*
*
Control
Localized OPLL
Diffuse OPLL
B
Use of medication for dyslipidemia
(%)
100
80
60
40
20
0
*
*
Control
Localized OPLL
Diffuse OPLL


C
Dyslipidemia
(%)
100
80
60
40
20
0
*
30-39
40-49
50-59
60-69
≥70
(Age)
Control
Localized-OPLL
Diffuse-OPLL


D
Medication use for dyslipidemia
(%)
100
80
60
40
20
0
*
*
30-39
40-49
50-59
60-69
≥70
(Age)
Control
Localized-OPLL
Diffuse-OPLL