Title page

Running title: LBP and lumbar kyphosis in knee OA

Coexistence of low back pain and lumbar kyphosis is associated with increased functional disability in knee osteoarthritis: the Nagahama Study

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On behalf of all authors, the corresponding author states that there is no conflict of interest.

Abstract

Objective: To examine the association of low back pain (LBP) and lumbar kyphosis with functional disabilities and knee symptoms in patients with knee osteoarthritis (OA).

Methods: We analyzed 586 participants (80.1% female; age, 68.8 ± 5.2 years) from the Nagahama Study who were aged ≥60 years and had radiographically confirmed knee OA. The Knee Scoring System (KSS) was used to assess functional disabilities and knee symptoms. LBP was defined as the presence of any persistent back pain for more than 3 months. Lumbar kyphosis was determined by skin-surface methods using a computer-aided electronic device called the Spinal Mouse. Multiple linear regression analysis was used for assessing the association of LBP and lumbar kyphosis with the KSS scores. Subgroup analyses based on sex were also performed.

Results: LBP and lumbar kyphosis were independently associated with a lower KSS function score after adjustment for covariates (mean difference [95%CI, confidence interval] = -4.96 [-7.56 to -2.36] points for LBP alone, -4.47 [-8.51 to -0.43] points for lumbar kyphosis alone, and -13.86 [-18.86 to -8.86] points for the coexistence of LBP and lumbar kyphosis, respectively). The coexistence of LBP and lumbar kyphosis in women was associated with a lower KSS symptom score (mean difference [95%CI] = -4.49 [-6.42 to -2.55] points).

Conclusion: These findings suggest that both LBP and lumbar kyphosis are useful clinical signals indicating functional disability and knee symptoms in patients with knee OA.

Keywords

Knee osteoarthritis, functional disability, knee symptoms, low back pain, lumbar kyphosis

Significance and Innovations

- Lumbar kyphosis in participants with knee OA was associated with functional disabilities in patients with knee OA.
- The coexistence of LBP and lumbar kyphosis was remarkably associated with functional disabilities in patients with knee OA.
- The coexistence of LBP and lumbar kyphosis had adverse associations on knee symptoms in women.
- These findings suggest that both LBP and lumbar kyphosis are useful clinical signs indicating functional disability and knee symptoms in patients with knee OA.

Knee osteoarthritis (OA) is a common musculoskeletal disorder and is the leading cause of knee pain and disability (1). A recent systematic review indicated that a greater burden of comorbidity was associated with functional disabilities and severe knee symptoms in patients with knee OA than in those without (2). In particular, low back pain (LBP) is a major comorbid condition in patients with knee OA (3). Both knee pain and LBP have potential deteriorative effects on functional disability (4).

Standing posture with decreased lumbar lordosis (i.e., lumbar kyphosis) and increased knee flexion are known as the knee-spine syndrome (5), and lumbar kyphosis is mostly linked to spinal stenosis (6). This malalignment may cause not only the spine but also knee joint overload via the kinetic chain. In community-dwelling older adults, age-related kyphosis, especially the lack of lumbar lordosis, reportedly causes impaired physical function, including reduced gait speed and quadriceps strength (7). Thus, increased mechanical stress of knee and spine joints and its related dysfunction may also be associated with functional disabilities in knee OA. Additionally, previous studies (8, 9) reported that degenerative changes with decreasing lumbar lordosis and the burden of restriction in activities were more common in women than in men. However, sex differences in the association of lumbar kyphosis and/or LBP with functional disability and knee symptoms have not been well investigated in knee OA patients.

Generally, decreased lumbar lordosis is related to the presence of LBP in middle-aged

and older adults (10). In contrast, Wang et al. (11) reported no differences in lumbar lordosis in patients with knee OA with or without LBP. Decreased lumbar lordosis in patients with knee OA could be caused by a compensatory strategy against knee flexion contracture and knee symptoms, regardless of the presence of LBP. Therefore, we assumed that LBP and lumbar kyphosis independently contributed to functional disabilities and severe knee symptoms in patients with knee OA. However, in recent literature, individual or coexistent associations of LBP and lumbar kyphosis with functional disabilities and knee symptoms in patients with knee OA remains unclear.

The primary objective of this study was to determine the association of LBP and lumbar kyphosis with functional disability and knee symptoms in patients with knee OA. The secondary objective was to determine the difference in these associations between the sexes. We hypothesized that the coexistence of LBP and lumbar kyphosis could be associated with functional disabilities and worse knee symptoms. We also hypothesized that those associations were stronger in women than in men. These findings will provide valuable information for the effective management of functional disability and knee symptoms in patients with knee OA who also have spinal problems.

Patients and Methods

Study participants and selection

We analyzed the data set of the Nagahama Prospective Cohort for Comprehensive Human Bioscience (the Nagahama Study), which was a population-based cohort. Our study was a cross-sectional analysis of the baseline measurements obtained between 2013 and 2016 from the general population of Nagahama City, which comprises 125,000 inhabitants located in a predominantly rural area of the Shiga Prefecture of central Japan (12). Community residents aged 30–74 years at recruitment, living independently without serious health problems, were recruited via mass communications in the local community such as public relation magazines and newspapers, and personal solicitations. From a total of 9,850 individuals in this cohort, we selected those older than 60 years who participated in the optional physical assessment, which included knee radiography and a sagittal spinal alignment evaluation. Among these, we selected participants who had unilateral or bilateral knee OA on radiographs and could walk for more than 10 m with or without a cane, after excluding those who meet the following exclusion criteria: acute LBP, rheumatoid arthritis, central nervous system impairments, and surgical history of the herniated intervertebral disk, spinal canal stenosis, and other lower limb joint diseases.

All study procedures were approved by the Ethics Committee of the Kyoto University Graduate School of Medicine and by the Nagahama Municipal Review Board. The study was conducted in accordance with the principles of the Declaration of Helsinki. Written informed

consent for the use of data was obtained from all participants in the Nagahama Study.

Definition of Knee Osteoarthritis

Participants who had unilateral or bilateral knee OA on radiographs were included in the present study. The tibiofemoral joints of both knees were evaluated using weight-bearing anteroposterior radiographs. Two experienced orthopedists, who were blinded regarding each patient's clinical status, evaluated each knee based on the Kellgren-Lawrence (KL) grading system, and radiographic knee OA was defined as KL grade ≥ 2 (13). If the grades were different between the two examiners, a third examiner evaluated and determined the final grade. This study classified the severity of radiographic knee OA as follows: either knee with KL grade = 2, both knees with KL grade = 2, either knee with KL grade 2 and the other ≥ 3, and both knees with KL grade ≥ 3.

Knee Society Score Functions and Symptoms

Self-reported functional disability and knee symptoms were evaluated using the new Knee Society Knee Scoring System (KSS, Japanese edition, 2011) (14). The 2011 KSS is a self-administered outcome measurement tool that consists of four subcategories, of which two, namely "functional activities" (0-100 points) and "symptoms" (0-25 points), were used in this study. The functional activities category further consists of four components, including walking

and standing (30 points), standard activities (30 points), advanced activities (25 points), and discretionary activities (15 points). The KSS symptom score relies on the degree of knee pain during walking and up-down stairs, and stiffness. For these two subcategories, lower scores indicate functional disabilities and poorer symptoms. The validity of the KSS 2011 in the Japanese population has previously been established (14).

Lumbar lordosis and Low Back Pain

Sagittal spinal alignment during quiet standing was measured using a Spinal Mouse (Index Ltd., Tokyo, Japan). The Spinal Mouse is a computer-aided electronic device that noninvasively measures intersegmental angles by tracing along the midline of the spine between the spinous process from C7 to S3. The measurement of spinal alignment by the Spinal Mouse has been validated with radiographic measurements, indicating a high correlation between these measurements for lumbar lordosis angle ($r = 0.794$) (15). The same examiner performed all measurements of lumbar lordosis angle. The lumbar lordosis angle was measured using the Spinal Mouse, which demonstrated high intra-rater reliability (intraclass correlation coefficients: 0.97). The lumbar lordosis was calculated as the sum of 6 segmental angles between Th12/L1 and L5/S1, and a negative value indicated lumbar kyphosis. Based on one standard deviation (SD) of mean lumbar lordosis angle (reference: 13.4 ± 12.4 degrees) reported using the Spinal Mouse in a previous study (12), lumbar kyphosis was defined in our

study as decreased lumbar lordosis (lumbar lordosis angle ≤1.0 degrees). Assessment test for lumbar lordosis angle was performed thrice, and the mean value was used for the analysis.

The presence of current LBP was identified using the self-reported questionnaire with the question, “Have you had any back pain continuously for more than three months until the present?”. We simultaneously obtained information on the surgical history for any spinal disorders, which was used as part of the exclusion criteria.

Gait speed

Maximum gait speed was measured using a wireless phototube (Brower Timing Systems, Co., Ltd., UT, USA) as the objective measure of physical function. The phototube was set at 4 and 10 m on a 12-m gait path, and the time taken to walk past the phototube was measured in 0.01-second unit. The participant was instructed to walk as fast as possible on the gait path. The maximum gait speed (m/s) was calculated from the taken-time of the 6-m distance.

Covariates

The body height and weight were measured to the nearest 0.1 cm and 0.1 kg and converted to body mass index (BMI: kg/m^2). History of diabetes and osteoporosis was retrieved from the cohort data. Moreover, depressive symptomatology in the previous week was

evaluated using the 20-item version of the Center for Epidemiological Studies Depression Scale (CES-D; range 0-60 point) (16, 17). A higher score indicated a more depressive status, and the presence of depressive symptoms was defined as a CES-D score of ≥16 points. We used the Japanese version of the CES-D with its validity previously established in the Japanese population (18).

Statistical Analysis

Continuous variables are expressed as mean ± SD and categorical variables as frequencies (%). Outcome measures and covariates were compared between women and men using unpaired t-test or chi-squared test. To investigate the associations of lumbar kyphosis with KSS function score, KSS symptom score, and gait speed in the total sample, univariate analysis of variance (ANOVA) was performed. The adjusted mean difference between the groups was also estimated, with adjustments for age, BMI, sex, OA severity, and the presence of LBP, diabetes, osteoporosis, and depression. Similarly, a univariate ANOVA was conducted in the subgroups for sex, and the adjusted mean difference was calculated, adjusting for the above covariates except for sex. For the KSS scores and gait speed, 3-way ANOVAs were conducted to assess the interaction among sex, lumbar kyphosis, and LBP, with adjustments for age, BMI, OA severity, and the presence of diabetes, osteoporosis, and depression. Then, we classified the participants into 4 subgroups based on the combinations of LBP and lumbar

kyphosis as follows: the absence of both LBP and lumbar kyphosis (reference category), LBP alone, lumbar kyphosis alone, and coexisting LBP and lumbar kyphosis. A multiple linear regression analysis was conducted using the KSS function score, KSS symptom score, and gait speed as the dependent variables and the 4 subgroup categories as the independent variables, with adjustments for the covariates including age, BMI, sex, OA severity, and the presence of LBP, diabetes, osteoporosis, and depression. As a secondary analysis, multiple linear regression analyses for each sex were conducted while adjusting for covariates except for sex. All statistical analyses were performed with SPSS software version 25.0 (SPSS Japan Inc., Tokyo, Japan). The level of significance was set at $p < 0.05$.

Results

Of a total of 9,850 individuals in this cohort, those over 60 years were 5,018. Among these, 1,682 participated in the optional physical assessment. After excluding participants who did not meet the inclusion criteria (participants without an X-ray confirmed knee OA, n = 983; could not walk for more than 10 m, n = 113), 586 participants with radiographic knee OA were included in the analysis (Fig. 1). The clinical characteristics of those included are summarized in Table 1. The mean age was 68.8 ± 5.2 (range; 60 – 81) years, and women accounted for 80.1% of the included participants with knee OA. There were no significant differences

between both sexes with respect to the KSS function and symptom score. However, the lumbar lordosis angle and comorbidities (diabetes and osteoporosis) were higher in women than in men, but women had a lower age and BMI. The clinical characteristics of the 4 subgroups classified by the absence or presence of LBP and/or lumbar kyphosis are shown in Table 2.

Associations between Lumbar Kyphosis and KSS Scores or Gait Speed

In total, 86 (14.7%) participants had lumbar kyphosis [women, 70 (14.9%); men, 16 (13.8%)]. Although the KSS symptom score was not significantly different between the two groups, the KSS function scores in those with lumbar kyphosis were significantly lower than those without lumbar kyphosis, and the gait speed was significantly slower (Table 3). The adjusted mean difference in women with lumbar kyphosis was -6.32 points (95% confidence interval, CI: -10.01 to -2.63) against those without lumbar kyphosis, and in men was -6.92 points (95% CI: -13.70 to -0.15).

Association of Individual or Coexisting LBP and Lumbar Kyphosis with KSS Scores and Gait Speed

Results of the 3-way ANOVA showed a significant interaction for the KSS symptom score ($F = 5.315$, $p = 0.021$), but not for the KSS function score and gait speed ($F = 0.070$, $p = 0.792$; $F = 0.114$, $p = 0.735$, respectively). Associations by multiple linear regression analysis

of the subcategories, stratified by the absence or presence of LBP and lumbar kyphosis, with KSS scores and gait speed are shown in Table 4. Multiple linear regression analysis showed that the presence of LBP and lumbar kyphosis in participants with knee OA were independently associated with the KSS function score after adjusting for the covariates (beta = -4.96; 95% CI: -7.56 to -2.36; p = <0.001, beta = -4.47; 95% CI: -8.51 to -0.43; p = 0.030, respectively). LBP coexisting with lumbar kyphosis was significantly associated with decreased KSS function scores (beta = -13.86; 95% CI: -18.86 to -8.86; p = <0.001) in participants with knee OA.

In addition, LBP alone or LBP coexisting with lumbar kyphosis was significantly associated with the KSS symptom score (beta = -1.72; 95% CI: -2.67 to -0.77; p = <0.001, beta = -3.43; 95% CI: -5.25 to -1.60; p = <0.001, respectively). The presence of LBP in women was associated with a lower KSS symptoms, after adjustment for covariates (beta = -1.87; 95% CI: -2.90 to -0.84; p = <0.001). The coexistence of LBP and lumbar kyphosis also reinforced the decrease in the KSS symptom score (beta = -4.49; 95% CI: -6.42 to -2.55; p = <0.001) in women. In contrast, these relationships were not confirmed in men.

Moreover, we found that lumbar kyphosis alone, or its coexistence with LBP was significantly associated with a slow gait speed (beta = -0.07; 95% CI: -0.13 to 0.00; p = 0.046, beta = -0.08; 95% CI: -0.16 to 0.00; p = 0.039, respectively).

Discussion

The primary objective of this study was to determine the association of lumbar kyphosis and LBP with KSS function and symptoms in patients with knee OA. Results of the univariate ANOVA showed that lumbar kyphosis in participants with knee OA was associated with a reduction of KSS function scores and slow gait speed, but not with KSS symptom score. Additionally, the association of the coexistence of LBP and lumbar kyphosis with functional disabilities was more remarkable than the individual association of these factors, which supported our hypothesis. A secondary objective was to determine the difference in these associations between the sexes. The coexistence of LBP and lumbar kyphosis was associated with a lower KSS symptom score in only women, and hence, this finding partially supports our secondary hypothesis. To the best of our knowledge, our study could be the first to determine the associations of both LBP and lumbar kyphosis with functional disabilities and knee symptoms in individuals with knee OA.

Concurring with the results of previous reports, which included community-dwelling older adults (7), our findings indicated that lumbar kyphosis was associated with a reduction of KSS function score and slow gait speed in patients with knee OA. In the knee-spine syndrome, a backward-tilting pelvis and knee-flexed posture produce dysfunction in the antigravity muscles (19). Miyazaki et al. (7) have reported that decreased lumbar lordosis significantly correlated with poor knee extensor strength and slow gait speed. It is also well

known that muscle weakness in patients with knee OA is one of the important factors causing functional disabilities (20). Therefore, lumbar kyphosis could induce muscle weakness and functional disabilities in patients with knee OA.

In contrast, lumbar kyphosis was not associated with a lower KSS symptom score in this study. We hypothesized that there is a significant relationship between lumbar kyphosis and knee symptoms because the postural changes caused by knee-spine syndrome could lead to increased knee shearing forces (21). One of the potential factors regarding this disparity could be the individual differences in compensatory patterns found in sagittal spinal malalignment. Since the compensatory strategy of the pelvis tilt in patients with knee OA varies according to the degree of femoral inclination, i.e., the knee flexion angle (11), this difference may have canceled the possible relationship between lumbar kyphosis and knee-related symptoms.

Our results showed no sex differences between lumbar kyphosis and functional disabilities, and the adjusted mean difference between participants with lumbar kyphosis and without lumbar kyphosis with respect to the KSS function score was nearly equal in women and men (women, -6.32 points; men, -6.92 points). Similar to the results of a previous report (8), we found a significant difference in the lumbar lordosis angles between women and men, but it was quite small. Therefore, although there was a small difference between sex in the lumbar lordosis angle, this difference had minimal effects on functional disabilities.

The results of our study showed the individual association as well as the coexisting association of LBP and lumbar kyphosis in participants with knee OA. A recent systematic review (2) concluded that the presence of LBP in patients with knee OA was associated with functional disabilities and severe knee symptoms; however, its effect size was small. Our study also showed that the individual association of LBP was small, but coexisting LBP and lumbar kyphosis was associated with a remarkable reduction in KSS function scores of 13.86 points. Given that the minimum clinically important difference for the KSS on functional activities after total knee arthroplasty was 4.1 points (22), the association of the coexistence of LBP and lumbar kyphosis with functional activities had a sufficient clinical impact. Decreased lumbar lordosis was one of the major risk factors predictive of severe LBP (10); hence, participants with LBP coexisting with lumbar kyphosis in this study could have more severe LBP than participants with LBP alone. Additionally, since patients with spinal stenosis often exhibit a reduced lumbar lordosis (6), an accompanying muscle weakness in the lower limb may also be associated with functional disabilities (23). These results suggest the necessity for a therapeutic approach focusing on LBP and lumbar kyphosis in patients with knee OA. Based on our findings, both symptom relief for LBP and back extensor strengthening (24) for preventing deterioration of lumbar kyphosis is needed for efficient management of functional disabilities in patients with knee OA with respect to the clinical scenario.

Our results confirmed the association of lower KSS symptom scores with LBP alone,

as well as with LBP coexisting with lumbar kyphosis in only women. Several previous studies (3, 25, 26) have reported the association between severe knee symptoms and LBP in patients with knee OA. One study (27) suggested that women with LBP have a higher risk of developing knee pain than men with LBP, implying a sex-related difference in the association of LBP and knee pain aggravation. In addition, women with knee-spine syndrome demonstrated a larger knee flexion angle than did men with the same degree of lumbar kyphosis (5). Therefore, increased mechanical stress caused by an increased knee flexion angle, together with LBP, possibly affected the knee symptoms in women in our study. Although the pathological mechanism of the observed sex difference is unclear, the association between severe knee symptoms and the coexistence of LBP and lumbar kyphosis needs attention from a clinical point of view.

This study had several limitations. First, although the sample size for data analysis in the total sample who had knee OA was large, the number of men was relatively small when classified into subgroups. Thus, we could not reach a definite conclusion about the association of the coexistence of LBP and lumbar kyphosis with functional disability and knee symptoms in men. Second, we did not perform radiographic examinations for spinal stenosis. In participants who had both knee OA and spinal stenosis, it should be noted that the effects of these diseases demonstrated mixed functional disabilities since spinal stenosis is also associated with physical dysfunction (23). Moreover, there was a lack of information regarding

the severity of LBP. Although the severity of LBP was higher in women than in age-matched men (28), the present study did not consider this factor. Finally, the cross-sectional design of this study does not allow us to determine any causal relationship between LBP and/or lumbar kyphosis and dysfunction in patients with knee OA. Future longitudinal studies are warranted to determine how LBP and/or lumbar kyphosis could influence functional disability and symptoms in patients with knee OA.

In conclusion, the presence of LBP and lumbar kyphosis are associated with functional disabilities in patients with knee OA, and the association is more remarkable in patients who had both LBP and lumbar kyphosis. In addition, the coexistence of LBP and lumbar kyphosis had adverse associations on knee symptoms in women. These findings suggest that both LBP and lumbar kyphosis are useful clinical signs indicating functional disability and knee symptoms in patients with knee OA.

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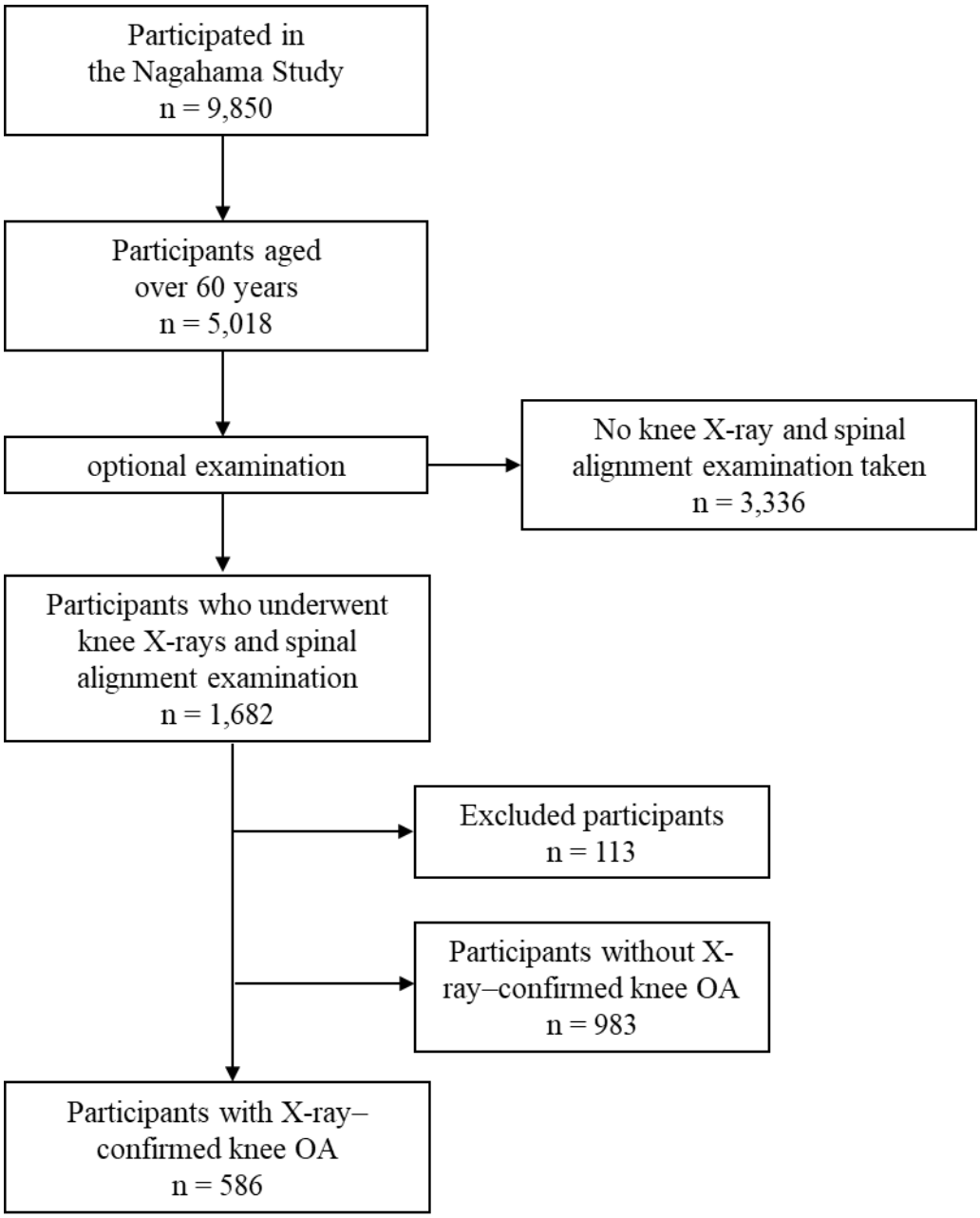

Figure 1. Flow chart for the selection of study participants.

Table 1. Clinical characteristics of the total participants stratified by sex

	Total (n = 586)	Women (n = 470)	Men (n = 116)	*p* Value	95%CI
KSS function, /100	84.8 (16.2)	84.5 (16.5)	86.1 (15.1)	0.361	[-4.84, 1.76]
KSS symptom, /25	19.8 (5.6)	19.9 (5.5)	19.2 (6.1)	0.235	[0.45, 1.84]
Gait speed, m/s	1.6 (0.2)	1.6 (0.2)	1.7 (0.3)	0.123	[-0.09, 0.01]
Lumbar lordosis, deg.	13.1 (13.1)	13.6 (13.6)	11.0 (10.9)	**0.049**	**[-5.34, -0.01]**
LBP, n (%)	195 (34.3)	156 (33.2)	39 (33.6)	0.93	[0.66, 1.57]
Age, years	68.8 (5.2)	68.5 (5.1)	70.2 (5.3)	**0.002**	**[-2.74, -0.63]**
BMI, kg/m^2	23.0 (3.3)	22.8 (3.3)	23.9 (3.3)	**0.001**	**[-1.78, -0.46]**
OA severity, n (%)					
either knee with KL grade = 2	171 (29.2)	127 (27.0)	44 (37.9)		
both knees with KL grade = 2	290 (49.5)	243 (51.7)	47 (40.5)	0.197	[0.69, 1.08]
either knee with KL grade 2 and the other ≥ 3	44 (7.5)	33 (7.0)	11 (9.5)		
both knees with KL grade ≥ 3	81 (13.8)	67 (14.3)	14 (12.1)		
Diabetes, n (%)	62 (10.6)	43 (9.1)	19 (16.4)	**0.023**	**[1.09, 3.49]**
Osteoporosis, n (%)	99 (17.4)	98 (20.9)	1 (0.8)	**<0.001**	**[0.01, 0.24]**
Depression, n (%)	159 (28.0)	128 (27.2)	31 (26.7)	0.912	[0.62, 1.54]

CI, Confidence interval; KSS, Knee society score; LBP, Low back pain; BMI, Body mass index; OA, Osteoarthritis; KL, Kellgren-Lawrence.

The continuous variables are shown as mean (SD), and categorical variables as frequencies (%). Sex differences in outcome measures and covariates were tested using unpaired t-test or chi-squared test. Bold type represents a statistically significant result.

Table 2. Clinical characteristics of subgroups classified by the absence or presence of low back pain and lumbar kyphosis

	Women				Men			
	Absence of LBP and lumbar kyphosis	LBP alone	Lumbar kyphosis alone	Coexisting of LBP and lumbar kyphosis	Absence of LBP and lumbar kyphosis	LBP alone	Lumbar kyphosis alone	Coexisting of LBP and lumbar kyphosis
	n = 273	n = 127	n = 41	n = 29	n = 66	n = 34	n = 11	n = 5
KSS function, /100	87.6 (15.1)	81.8 (16.1)	82.7 (17.2)	69.7 (19.5)	89.8 (10.6)	82.6 (18.3)	83.7 (14.6)	65.4 (24.3)
KSS symptom, /25	20.8 (5.1)	18.7 (5.5)	20.8 (5.0)	15.2 (6.3)	19.8 (5.5)	18.6 (6.6)	17.8 (6.5)	19.6 (9.1)
Gait speed, m/s	1.7 (0.2)	1.6 (0.2)	1.6 (0.2)	1.5 (0.2)	1.7 (0.3)	1.6 (0.3)	1.7 (0.2)	1.6 (0.4)
Age, years	67.6 (4.9)	68.5 (4.9)	70.7 (5.2)	73.7 (4.9)	70.0 (5.5)	70.2 (5.0)	70.7 (5.8)	71.2 (6.5)
BMI, kg/m^2	22.9 (3.4)	22.8 (3.1)	22.5 (3.2)	22.5 (2.8)	23.6 (2.8)	24.3 (3.7)	24.1 (3.9)	26.2 (4.4)
OA severity, n (%)								
either knee with KL grade = 2	75 (27.5)	31 (24.4)	15 (36.6)	6 (20.7)	25 (37.9)	13 (38.2)	5 (45.5)	1 (20.0)
both KL grades = 2	141 (51.6)	71 (55.9)	17 (41.5)	14 (48.3)	27 (40.9)	13 (38.2)	5 (45.5)	2 (40.0)
KL grade 2 and the other grades ≥ 3	20 (7.3)	11 (8.7)	2 (4.9)	0 (0)	7 (10.6)	4 (11.8)	0 (0)	0 (0)
both KL grades ≥ 3	37 (13.6)	14 (11.0)	7 (17.1)	9 (31.0)	7 (10.6)	4 (11.8)	1 (9.1)	2 (40.0)
Diabetes, n (%)	25 (9.2)	13 (10.2)	3 (7.3)	2 (6.9)	14 (21.2)	4 (11.8)	1 (9.1)	0 (0)
Osteoporosis, n (%)	37 (13.6)	39 (30.7)	11 (26.8)	11 (37.9)	1 (1.5)	0 (0)	0 (0)	0 (0)
Depression, n (%)	68 (24.9)	40 (31.5)	9 (22.0)	11 (37.9)	17 (25.8)	8 (23.5)	4 (36.4)	2 (40.0)

KSS, Knee society score; LBP, Low back pain; BMI, Body mass index; OA, Osteoarthritis, KL, Kellgren-Lawrence.

The continuous variables are shown as mean (SD), and categorical variables as frequencies (%). Outcome measures and physical characteristics in each subgroup based on the combinations of LBP and lumbar kyphosis are represented.

Table 3. Differences in functional disabilities and symptoms between participants with and without lumbar kyphosis

	Unadjusted mean (SD)		F Value	*p* Value	Adjusted mean difference [95%CI]
	Without lumbar kyphosis	With lumbar kyphosis			With lumbar kyphosis against without lumbar kyphosis
Total sample	n = 500	n = 86			
KSS function, /100	86.1 (15.3)	77.4 (19.1)	13.95	**<0.001**	**-6.14 [-9.36, -2.91]**
KSS symptom, /25	20.0 (5.5)	18.5 (6.4)	2.24	0.135	-0.90 [-2.08, 0.28]
Gait speed, m/s	1.7 (0.2)	1.6 (0.2)	5.32	**0.021**	**-0.06 [-0.11, -0.01]**
Women	n = 400	n = 70			
KSS function, /100	85.8 (15.7)	77.3 (19.2)	11.34	**0.001**	**-6.32 [-10.01, -2.63]**
KSS symptom, /25	20.2 (5.3)	18.5 (6.2)	2.69	0.102	-1.07 [-2.35, 0.21]
Gait speed, m/s	1.7 (0.2)	1.5 (0.2)	8.74	**0.003**	**-0.09 [-0.14, -0.03]**
Men	n = 100	n = 16			
KSS function, /100	87.4 (14.0)	78.0 (19.4)	4.10	**0.045**	**-6.92 [-13.70, -0.15]**
KSS symptom, /25	19.4 (5.9)	18.4 (7.2)	0.11	0.746	-0.51 [-3.59, 2.58]
Gait speed, m/s	1.7 (0.3)	1.7 (0.3)	0.00	0.992	0.00 [-0.12, 0.12]

KSS, Knee society score; SD, standard deviation; CI, confidence interval.

The adjusted mean differences between participants with and without lumbar kyphosis were estimated, with adjustments for age, BMI, sex, OA

grade, and the presence of LBP, diabetes, osteoporosis, and depression. Bold type represents a statistically significant result.

Table 4. Associations by multiple linear regression analysis of the subcategories, stratified by the absence or presence of LBP and lumbar kyphosis, with KSS scores and gait speed

	Total				Women				Men			
	Absence of LBP and lumbar kyphosis	LBP alone	Lumbar kyphosis alone	Coexisting of LBP and lumbar kyphosis	Absence of LBP and lumbar kyphosis	LBP alone	Lumbar kyphosis alone	Coexisting of LBP and lumbar kyphosis	Absence of LBP and lumbar kyphosis	LBP alone	Lumbar kyphosis alone	Coexisting of LBP and lumbar kyphosis
	n = 339	n = 161	n = 52	n = 34	n = 273	n = 127	n = 41	n = 29	n = 66	n = 34	n = 11	n = 5
KSS function												
Beta [95% CI]	reference	**-4.96 [-7.56, -2.36]**	**-4.47 [-8.51, -0.43]**	**-13.86 [-18.86, -8.86]**	reference	**-4.47 [-7.46, -1.48]**	-4.63 [-9.28, 0.02]	**-13.45 [-19.04, -7.86]**	reference	**-6.09 [-11.38, -0.80]**	-4.93 [-13.05, 3.19]	**-17.47 [-29.36, -5.59]**
Standard beta		**-0.137**	**-0.078**	**-0.200**		**-0.121**	-0.079	**-0.196**		**-0.184**	-0.096	**-0.236**
p Value		**<0.001**	**0.03**	**<0.001**		**0.003**	0.051	**<0.001**		**0.024**	0.232	**0.004**
KSS symptom												

Beta [95% CI]	reference	**-1.72 [-2.67, -0.77]**	-0.41 [-1.89, 1.07]	**-3.43 [-5.25, -1.60]**	reference	**-1.87 [-2.90, -0.84]**	-0.08 [-1.69, 1.52]	**-4.49 [-6.42, -2.55]**	reference	-1.02 [-3.41, 1.37]	-2.08 [-5.75, 1.59]	1.99 [-3.38, 7.37]
Standard beta		**-0.136**	-0.021	**-0.142**		**-0.151**	-0.004	**-0.196**		-0.077	-0.101	0.067
p Value		**<0.001**	0.584	**<0.001**		**<0.001**	0.919	**<0.001**		0.399	0.264	0.464
Gait speed												
Beta [95% CI]	reference	-0.03 [-0.07, 0.10]	**-0.07 [-0.13, 0.00]**	**-0.08 [-0.16, 0.00]**	reference	-0.02 [-0.06, 0.03]	**-0.09 [-0.16, -0.02]**	**-0.10 [-0.19, -0.01]**	reference	-0.08 [-0.18, 0.01]	-0.02 [-0.17, 0.12]	-0.04 [-0.26, 0.17]
Standard beta		-0.060	**-0.080**	**-0.084**		-0.031	**-0.108**	**-0.105**		-0.146	-0.021	-0.034
p Value		0.137	**0.046**	**0.039**		0.494	**0.017**	**0.024**		0.088	0.802	0.688

KSS, Knee society score; SD, standard deviation; CI, confidence interval.

A multiple linear regression analysis was conducted using the KSS scores and gait speed as a dependent variable and the 4 subgroup categories as independent variables, with adjustments for the covariates including age, BMI, sex, OA severity, and the presence of diabetes, osteoporosis, and depression. In the sub-analysis by sex, multiple linear regression analyses were conducted with adjusting covariates except for sex. Bold type represents a statistically significant result.