


The combination of osteoporosis and low lean mass correlates with physical function in end-stage knee osteoarthritis

A retrospective observational study

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Abstract

We aimed to investigate the prevalence of osteoporosis and low lean mass, either together or in isolation, and their association with physical function, pain, and quality of life (QOL) in patients with end-stage knee osteoarthritis (OA).

This retrospective cross-sectional observational study included 578 patients (77 males and 501 females) diagnosed with end-stage knee OA. Patients were divided into 4 groups based on body composition parameters: control, osteoporosis, low lean mass, and osteoporosis + low lean mass. All participants underwent performance-based physical function tests, including a stair climbing test (SCT), a 6-minute walk test, a timed up and go test, and instrumental gait analysis, to examine spatiotemporal parameters. Self-reported physical function and pain levels were measured using the Western Ontario McMaster Universities Osteoarthritis Index and visual analog scale, respectively. Self-reported QOL was measured using the EuroQOL 5 dimensions (EQ-5D) questionnaire.

Of 578 patients, 268 (46.4%) were included in the control group, 148 (25.6%) in the osteoporosis group, 106 (18.3%) in the low lean mass group, and 56 (9.7%) in the osteoporosis + low lean mass group. Analysis of variance revealed that the scores for the osteoporosis + low lean mass group in the SCT-ascent, SCT-descent, and timed up and go test were significantly higher, whereas those for the 6-minute walk test, gait speed, and cadence were significantly lower than those for the other groups ($P < .05$). After adjusting for age, sex, and body mass index, multiple linear regression analysis identified SCT-ascent ($\beta = 0.140$, $P = .001$, $R^2 = 0.126$), SCT-descent ($\beta = 0.182$, $P < .001$, $R^2 = 0.124$), gait speed ($\beta = -0.116$, $P = .005$, $R^2 = 0.079$), and cadence ($\beta = -0.093$, $P = .026$, $R^2 = 0.031$) as being significantly associated with osteoporosis + low lean mass.

Thus, osteoporosis + low lean mass correlates with poor physical function, but not pain and QOL, in patients with end-stage knee OA.

Abbreviations: 6MWT = 6-minute walk test, ANOVA = analysis of variance, ASM = appendicular skeletal muscle mass, ASM_{BMI} = ASM to BMI ratio, BMD = bone mineral density, BMI = body mass index, DXA = dual-energy X-ray absorptiometry, EQ-5D = EuroQOL 5 dimensions, FNHI = Foundation for National Institutes of Health, K-L = Kellgren–Lawrence, OA = osteoarthritis, QOL = quality of life, SD = standard deviations, SCT = stair climbing test, TKA = total knee arthroplasty, TUG = timed up and go, VAS = visual analog scale, WOMAC = Western Ontario McMaster Universities Osteoarthritis Index.

Keywords: knee, osteoarthritis, osteoporosis, physical function, prevalence, sarcopenia

1. Introduction

Osteoporosis and sarcopenia are chronic conditions that are common in frail older individuals.^[1–3] Osteoporosis is defined as

loss of bone mineral density (BMD),^[4,5] and sarcopenia refers to a reduction of muscle mass and strength accompanied by impaired muscle function.^[6] The combination of these 2 diseases, which exacerbates negative health outcomes, is known as the “hazardous

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and was approved by the institutional review board of Jeju National University Hospital.

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duet,” a phenomenon that increases the risk of falls and damage to bones.^[7] In addition, these diseases are significantly associated with physical disability and dependency.^[8,9] Changes in bone and muscle activate a vicious cycle, leading to accelerated weakness and, eventually, to physical disability.^[10] Yu et al^[11] showed that the fracture risk in men with osteosarcopenia increases by 3.5-fold; indeed, the risk is significantly higher than that for those with osteoporosis or sarcopenia alone. Yoo et al^[12] reported that 1-year mortality rates for hip fracture patients with osteosarcopenia were higher than for those without. The global population is aging rapidly and living longer; therefore, the burden of both osteoporosis and sarcopenia is expected to increase.

Knee osteoarthritis (OA) causes joint pain and swelling, reduced quality of life (QOL), and functional disability.^[13] In an aging population, the impact of OA is likely to increase, particularly as it often coexists with other comorbidities. Because many older adults, especially patients with end-stage knee OA, are prone to osteoporosis and sarcopenia, complications associated with these 2 diseases are expected to increase. Kadam and Croft^[14] showed that the presence of comorbidities in patients with OA increases the likelihood of physical disability; indeed, the combined effect of comorbidities is higher than that of OA or any individual condition alone. A meta-analysis of data from 17 studies revealed that as the number of comorbidities a patient with knee and/or hip OA has increases, pain levels increase and physical function decreases.^[15] OA and sarcopenia are closely related in that both are associated with aging, obesity, inflammation, and the risk of metabolic syndrome.^[16] In patients with OA, cytokines such as interleukin-1 β and tumor necrosis factor- α induce protein catabolism, leading to the development of sarcopenia.^[17] Conversely, in patients with sarcopenia, proinflammatory cytokines produced by adipose tissue, such as interleukin-6, tumor necrosis factor- α , vascular endothelial growth factor, and adipokines, may initiate low-grade systemic inflammation that can trigger local inflammation within vulnerable joints.^[18] Furthermore, although the relationship between OA and osteoporosis is highly complex and contextual, once OA is established, the patients experiences pain, reduced mobility, and decreased bone mass, particularly in the affected limb.^[19]

Therefore, we hypothesized that osteoporosis and low lean mass act synergistically in patients with end-stage knee OA, resulting in worse physical function, pain, and QOL. Although several studies have evaluated sarcopenia/low lean mass and osteopenia/osteoporosis, few have examined these parameters in patients with end-stage knee OA.

Therefore, the purpose of this study was to investigate the prevalence of end-stage knee OA in patients osteoporosis and low lean mass, either together or in isolation. We also examined the association between particular characteristics (osteoporosis + low lean mass, osteoporosis alone, low lean mass alone, or none of these conditions) and physical function, pain, and QOL.

2. Methods

2.1. Study participants

This was a retrospective cross-sectional observational study. Data from 578 patients (77 males and 501 females) diagnosed with end-stage knee OA and scheduled to undergo primary total knee arthroplasty (TKA) at the Department of Orthopaedic Surgery in OO National University Hospital between October 2013 and June 2019 were assessed. All participants met the radiographic criteria for end-stage knee OA: Kellgren–Lawrence (K-L) grade 3 and grade 4, on at least 1 side. The K-L grading system, accepted by World Health Organization in 1961, is the most commonly used knee OA severity grading system.^[20] The system classifies knee OA severity into 5 grades: grade 0 to grade 4. The criteria for each grade are shown in Figure 1.^[21] In addition, patients with uncontrolled hypertension, diabetes, or neurologically impaired motor function in the lower extremities (e.g., hemiplegia due to stroke), rheumatological diseases, or those who underwent a revision of TKA were excluded. The study protocol was approved by the institutional review board of Jeju National University Hospital. The requirement for informed consent was waived due to the retrospective nature of the study.

2.2. Body composition assessments

BMD was measured at the femur and lumbar spine (L1–L4) by dual-energy X-ray absorptiometry (Hologic Corp., Bedford, MA). According to the World Health Organization criteria, osteoporosis is defined as a BMD >2.5 standard deviations below that of a healthy young population (T-score \leq -2.5).^[22] Appendicular skeletal lean mass was obtained by summing the lean mass values for the upper and lower extremities, as measured by bioelectrical impedance analysis. A diagnosis of low lean mass was based on the values established by the Foundation for National Institutes of Health.^[23] Lean mass was calculated by dividing appendicular skeletal lean mass (in kilogram) by the

Kellgren and Lawrence (KL) Grading System

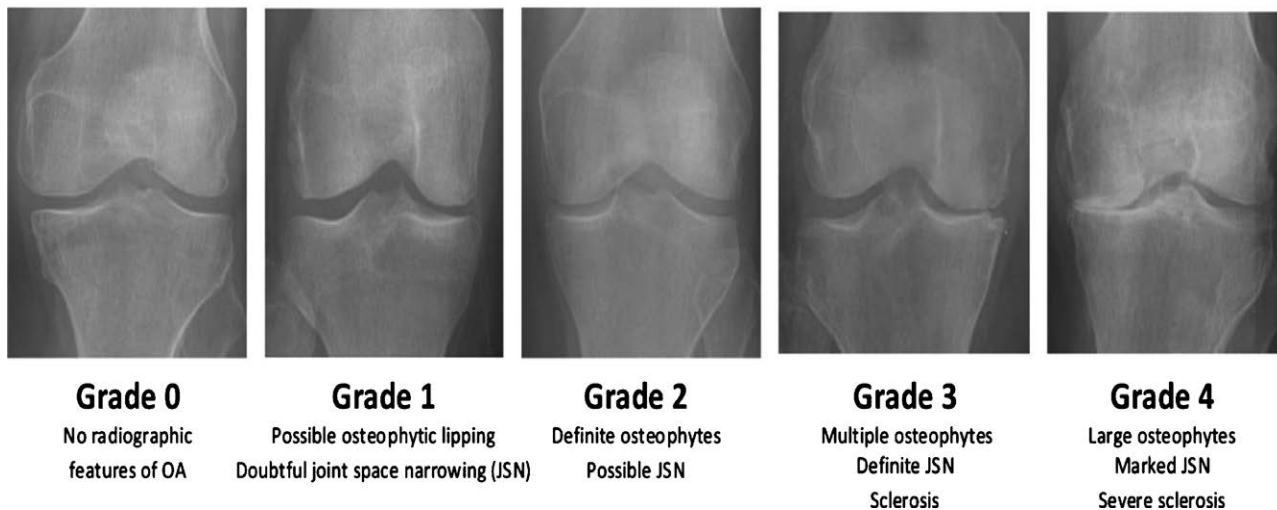


Figure 1. The K-L grading system to assess the severity of knee OA. K-L = Kellgren–Lawrence, OA = osteoarthritis.

body mass index (BMI; the cutoff reference values were <0.512 for women and <0.789 for men).

Based on the presence of osteoporosis and the low lean mass cutoffs, participants were classified into 4 groups: control (normal BMD and normal lean mass), osteoporosis (osteoporosis and normal lean mass), low lean mass (normal BMD and low lean mass), and osteoporosis + low lean mass.

2.3. Outcome measurements

All patients completed the following assessments before surgery: performance-based physical function tests, including a stair climbing test (SCT), a 6-minute walk test (6MWT), a timed up and go test (TUG), and instrumental gait analysis of spatiotemporal parameters. During the evaluation, patients were allowed to use an assistive device (e.g., a cane) if necessary. Self-reported physical function and pain were measured using the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC) and a visual analog scale, respectively, and self-reported QOL was measured using the EuroQOL 5 dimensions (EQ-5D) questionnaire.

2.4. Assessment of performance-based physical function

2.4.1. SCT. The SCT measures the time (in seconds) required to ascend and descend a flight of stairs (12 steps, each 17-cm high and 25-cm wide). Patients had to ascend and descend the stairs as quickly as possible, starting with the word “go.” There was a 5-minute interval between each trial and the shortest time was recorded.^[24] A higher score equated to worse performance (i.e., it takes longer to climb or descend the stairs).

2.4.2. 6MWT. The 6MWT assesses functional walking capacity and gait endurance in adults. Patients walked as far as possible for 6 minutes along a 50 m hallway. The distance traveled (in meters) was recorded.^[25] The higher the score, the better the performance.

2.4.3. Timed up and go. The TUG test evaluates dynamic balance. Each patient sat with their back against a chair (seat height, 44 cm; depth, 45 cm; width, 49 cm; arm rest height, 64 cm) placed at the end of a 3-m track. While being timed (in seconds), patients stood up on the word “go,” walked at a comfortable speed to the 3-m mark, turned around, walked back, and sat down again in the chair without physical assistance.^[26] A higher score in the TUG means equates to worse performance (i.e., the patient takes longer to get up and go).

2.4.4. Gait analysis. The spatiotemporal variables of gait were measured using a validated wireless inertial sensing device (G-Walk, BTS Bioengineering S.p.A., Milan, Italy). Each patient wore a semielastic back belt device around the waist, which measures acceleration along 3 anatomical axes (anteroposterior, mediolateral, and vertical). Patients were instructed to stand and remain standing for a few seconds and then to walk barefoot for 8 m as naturally as possible and at a comfortable speed. Gait data were collected and transmitted to a personal computer via Bluetooth. Data were processed using the BTS G-Walk system, a specialized software that measures gait variables (speed [meter per second], cadence [steps per minute], stride length [centimeter], gait cycle duration [second], stance phase duration [% of gait cycle], swing phase duration [% of gait cycle], and double and single support phase duration [% of gait cycle]).^[27]

2.5. Assessment of self-reported physical function, QOL, and pain

2.5.1. WOMAC. The multidimensional WOMAC questionnaire includes questions about pain, stiffness, and physical function.

The questionnaire has 5 pain, 2 stiffness, and 17 physical function variables. Each variable is scored on the Likert scale (0: none, 1: slight, 2: moderate, 3: very, and 4: extremely), which is used widely in rheumatology clinical trials. Higher scores indicate a greater degree of pain, stiffness, and difficulty in performing each of the 17 activities over the preceding 48 hours. The sum of the scores for pain, stiffness, and physical function determine the WOMAC pain (range, 0–20), WOMAC stiffness (range, 0–8), and WOMAC function (range, 0–68) subscores.^[28]

2.5.2. Visual analog scale. Patients were asked to evaluate their level of knee pain on a visual analog scale. Scores are based on self-reported measures of symptoms that are recorded with a single handwritten mark placed at 1 point along the length of a 10-cm line that stretches between 2 extremes (from no pain to worst pain).^[29]

2.5.3. EQ-5D questionnaires. The EQ-5D index is used widely to measure general health status. It is an evaluated self-reported QOL with 5 dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each question assesses each dimension on 3 severity levels (no problem, some or moderate problems, or extreme problems). The scores are transformed using utility weights derived from the general Korean population (ranging from -1 to 1). Higher scores indicate better overall health status.^[30]

2.6. Statistical analysis

All statistical analyses were performed using SPSS 20.0 (SPSS V 20.0K, SPSS Inc., Chicago, IL). Analysis of variance (ANOVA) with post hoc comparison using the Bonferroni test was used to test the significance of differences in performance-based physical function, self-reported physical function, pain, and QOL among the 4 groups. Stepwise multiple linear regression analysis adjusted for age, sex, BMI, and osteoporosis + low lean mass was used to evaluate the association between osteoporosis + low lean mass and performance-based physical function, self-reported physical function, pain, and QOL. To analyze the effect of osteoporosis + low lean mass, the osteoporosis + low lean mass group was compared with all of the 3 groups combined (i.e., the 3 other groups were treated as a single group). *P* values of $<.05$ were considered statistically significant.

3. Results

Table 1 shows the baseline demographic and disease-related characteristics of the patients. Of the 578 participants enrolled in the study, 86.7% were women, and the mean age was 71.47 ± 5.72 years. The prevalence of hypertension, diabetes, degenerative spine disease, osteoporosis, and sarcopenia according to the Foundation for National Institutes of Health criteria was 382 (65.1%), 105 (18.2%), 89 (15.4%), 204 (35.3%), and 162 (28.0%), respectively.

3.1. Comparison of performance-based physical function, self-reported physical function, QOL, and pain according to the presence or absence of osteoporosis and low lean mass

Table 2 compares the demographics, performance-based physical function, self-reported physical function, pain, and QOL according to the presence or absence of osteoporosis and low lean mass. Of the 578 participants, 46.4% ($n = 268$) were included in the control group, 25.6% ($n = 148$) in the osteoporosis group, 18.3% ($n = 106$) in the low lean mass group, and 9.7% ($n = 56$) in the osteoporosis + low lean mass group.

ANOVA with the Bonferroni post hoc test revealed that the time taken in the SCT-ascent and SCT-descent tests was

Table 1
Demographic characteristics of the subjects (N = 578).

	Total	Male	Female	P value
Number	578	77 (13.3)	501 (86.7)	
Age (yr)	71.47 (5.72)	72.32 (5.83)	71.34 (5.70)	.160
BMI (kg/m ²)	26.63 (3.47)	26.28 (3.21)	26.68 (3.51)	.340
ASM _{BMI} (m ²)	0.60 (0.13)	0.80 (0.14)	0.57 (0.10)	<.001
K-L grade				.420
Grade 3	122 (21.1%)	15 (19.5%)	107 (21.4%)	
Grade 4	456 (78.9%)	62 (80.5%)	394 (78.6%)	
Comorbidities				
Hypertension	382 (65.1%)	58 (75.3%)	324 (64.7%)	.040
Diabetes mellitus	105 (18.2%)	12 (15.6%)	93 (18.6%)	.330
Degenerative spine disease	89 (15.4%)	8 (10.4%)	81 (16.2%)	.130
Osteoporosis	204 (35.3%)	13 (16.9%)	191 (38.1%)	<.001
Sarcopenia*	162 (28.0%)	39 (50.6%)	123 (24.6%)	<.001

Values represent the mean (standard deviation) or number (%) of cases.

ASM = appendicular skeletal lean mass, ASM_{BMI} = ASM to BMI ratio, BMI = body mass index, K-L = Kellgren–Lawrence.

*Sarcopenia was defined according to the FNHI (Foundation for the National Institutes of Health) Criteria.

Table 2
Comparison of physical function, pain, and quality of life.

Variable	Control	Osteoporosis	Low lean mass	Osteoporosis + low lean mass	P value
Number (%)	268 (46.4)	148 (25.6)	106 (18.3)	56 (9.7)	
Age (yr)	70.83 (5.56)	71.64 (5.31)	71.80 (6.05)	73.45 (6.46)*	.014
BMI (kg/m ²)	26.33 (3.32)	25.39 (3.00)†	28.59 (3.58)‡,§	27.61 (3.40)*	<.001
Gender(M/F)	30 (11.2%)/238 (88.8%)	85.4 (5.4%)/140 (94.6%)	34 (32.1%)/72 (67.9%)	5 (8.9%)/51 (91.1%)	<.001
Comorbidities					
Hypertension	178 (66.4%)	93 (62.8%)	70 (66.0%)	41 (73.2%)	.58
Diabetes mellitus	56 (20.9%)	15(14.2%)	15 (14.2%)	9 (16.1%)	.42
Spine disease	44 (16.4%)	18 (12.2%)	16 (16.1%)	11 (19.5%)	.54
Osteoporosis	0	148	106	56	<.001
Sarcopenia	0	0	0	56	<.001
SCT-ascent (s)	13.04 (5.32)	13.67 (5.04)	13.80 (5.31)	16.81 (6.71) *, ,¶	<.001
SCT-descent (s)	15.41 (6.03)	16.40 (5.54)	16.50 (5.88)	20.69 (8.57) *, ,¶	<.001
6MWT (m)	326.63 (107.54)	308.77 (107.98)	299.24 (108.30)	276.79 (94.58) *	.005
TUG (s)	11.52 (3.26)	12.40 (5.51)	11.96 (3.24)	13.67 (5.96)*	.004
Gait analysis					
Gait speed (m/s)	0.93 (0.18)	0.89 (0.18)	0.87 (0.15) ‡	0.82 (0.15)*	<.001
Cadence (steps/min)	105.56 (14.65)	103.12 (15.95)	104.74 (12.99)	99.03 (17.60) *	.030
WOMAC pain	9.22 (3.12)	9.84 (3.13)	9.10 (2.76)	9.57 (3.20)	.170
WOMAC stiffness	2.87 (1.44)	2.89 (1.17)	2.68 (1.20)	2.70 (1.41)	.490
WOMAC function	28.54 (8.94)	28.70 (8.69)	30.09 (8.66)	31.80 (9.92)	.050
VAS	6.93 (1.72)	7.06 (1.56)	6.77 (1.81)	6.98 (1.50)	.600
EQ-5D	0.59 (0.16)	0.58 (0.16)	0.58 (0.16)	0.53 (0.19)	.080

Values represent the mean (standard deviation) or number (%) of cases.

6MWT = 6-minute walk test, BMI = body mass index, EQ-5D = EuroQOL 5 dimensions, SCT = stair climbing test, TUG = timed up and go, VAS = visual analog scale, WOMAC = Western Ontario McMaster Universities Osteoarthritis Index.

*Significant difference between the control group and the low lean mass + osteoporosis group ($P < .05$).

†Significant difference between control group and the osteoporosis group ($P < .05$).

‡Significant difference between control group and the low lean mass group ($P < .05$).

§Significant difference between osteoporosis group and the low lean mass group ($P < .05$).

||Significant difference between osteoporosis group and the low lean mass + osteoporosis group ($P < .05$).

¶Significant difference between low lean mass group and the low lean mass + osteoporosis group ($P < .05$).

significantly longer for the osteoporosis + low lean mass group than for the other 3 groups. In addition, the 6MWT, gait speed, and cadence scores were lower than those in the control group. Also, TUG time for the osteoporosis + low lean mass group was significantly longer than that for the control group.

3.2. Association between osteoporosis + low lean mass and physical function

Table 3 presents factors associated with physical function, including the combination of osteoporosis + low lean mass. After adjusting for age, sex, BMI, and osteoporosis + low

lean mass, multiple linear regression analysis identified osteoporosis + low lean mass as being significantly associated with SCT-ascent ($\beta = 0.140$, $P = .001$, $R^2 = 0.126$), SCT-descent ($\beta = 0.182$, $P < .001$, $R^2 = 0.124$), gait speed ($\beta = -0.116$, $P = .005$, $R^2 = 0.079$), and cadence ($\beta = -0.093$, $P = .026$, $R^2 = 0.031$). The 6MWT and TUG showed no statistically significant association with osteoporosis + low lean mass.

4. Discussions

Here, we present strong evidence that the combination of osteoporosis + low lean mass is associated significantly with physical

Table 3
Association between osteoporosis + low lean mass and physical function.

Outcome/independent predictor	Standardized β	P value	Adjusted R^2
SCT-ascent (s)			0.126
Age	0.292	<.001	
BMI	0.087	.037	
Sex	0.148	<.001	
Osteoporosis + low lean mass	0.140	.001	
SCT-descent (s)			0.124
Age	0.248	<.001	
BMI	0.085	.04	
Sex	0.164	<.001	
Osteoporosis + low lean mass	0.182	<.001	
Gait speed (m/s)			0.079
Age	-0.213	<.001	
Sex	-0.151	<.001	
Osteoporosis + low lean mass	-0.116	.005	
Cadence (steps/min)			0.031
Age	-0.149	<.001	
Osteoporosis + low lean mass	-0.093	.026	

BMI = body mass index, SCT = stair climbing test.

function in patients with end-stage knee OA. To the best of our knowledge, this is the first epidemiological study to assess the prevalence and effects of combined osteoporosis + low lean mass in patients with end-stage knee OA. The prevalence of osteoporosis + low lean mass in this study was 9.7% (56/578), 25.6% (148/578) had osteoporosis alone, and 18.3% (106/578) had low lean mass alone. Osteosarcopenia is a recently recognized disease entity, so its prevalence is unclear; to date, no study has examined the prevalence of osteosarcopenia in patients with OA. Studies of Japanese^[31] and Chinese^[10] community-indwelling elderly individuals show that the prevalence of osteosarcopenia is 8.4% and 12.7%, respectively, which is similar to that in our study. However, Huo et al^[32] reported the prevalence of osteosarcopenia in the elderly to be 38%, and Drey et al^[33] reported 27.9%, much higher than in our study. These discrepancies may be due to differences in patient demographics (age, sex, and diseases) and the definition of osteoporosis/sarcopenia used in these studies, making direct comparison difficult. In some studies, the definition of low bone density included both osteopenia and osteoporosis, whereas other studies defined sarcopenia using other validated diagnostic criteria, such as the Asian Working Group for Sarcopenia, the European Working Group on Sarcopenia in Older People, or the International Working Group on Sarcopenia.^[10,32,33] Although there is no consensus, it is still meaningful to assess the prevalence of osteoporosis and low lean mass in patients with end-stage knee OA.

The coexistence of osteoporosis and low lean body mass presents serious problems for patients. Previous reports focused on fractures and mortality^[12,32] in patients with osteosarcopenia, but few have examined physical function and QOL. Here, we show that the SCT-descent, SCT-ascent, gait speed, and cadence results are associated significantly with the combination of osteoporosis and low lean mass in those with end-stage knee OA. These tests measure functional status, the decline in which is a common problem for these patients; these parameters are not captured by self-reported measures.^[34] Previous studies show the validity of the SCT-descent, SCT-ascent, TUG, gait speed, and 6MWT for demonstrating impairment of physical performance in those with end-stage knee OA.^[24,35,36] The results presented herein suggest that, when compared with age-matched people, patients with end-stage knee OA have reduced physical function in important areas of daily activity such as maintaining gait speed and balance. In particular, the majority of falls in a domestic setting occur on stairs,^[37] and these falls may result in major injuries or even death. Valtonen et al^[38] reported that knee flexor and extensor muscle strength

in patients with knee OA are related to stair ascension time. Therefore, stair climbing is 1 of the important functional activities of daily living for maintaining mobility and independence in patients with OA. Also, Dunlop et al^[39] revealed that high levels of physical activity are closely related to greater functional performance (gait speed) in a cohort with knee OA. Marcum et al^[40] found that gait speed correlates with deterioration of function in elderly individuals with advanced knee OA. In view of these findings, our study highlights the impact of low bone mass and lean body mass on mobility and balance, both of which are important parameters of functional status in patients with end-stage knee OA. Thus, a preventive approach to managing osteosarcopenia might be warranted in those with end-stage knee OA who are scheduled to undergo primary TKA.

It can be assumed that the physical function of the control group will be better than that of the low lean mass only or osteoporosis only groups; however, we found that only the difference between the combined osteoporosis + low lean mass group was statistically significant. Thus, the synergic effect of osteoporosis and low lean mass is related to poor physical function. Furthermore, ANOVA plus a Bonferroni post hoc test revealed that the 6MWT and TUG results for the osteoporosis/low lean mass group were significantly worse than those of the control group; however, this was not the case for linear regression. This might be because the difference between the control group and the osteoporosis + low lean mass group was statistically significant, but that between the 3 groups excluding the control group was not.

An association between osteoporosis + low lean mass and impaired physical function was observed in previous studies.^[10,31,41] Kobayashi et al^[31] showed that osteosarcopenia is associated with muscle weakness in community-dwelling elderly people in Japan. Frisoli et al^[41] demonstrated an association between osteoporosis + low lean mass and impaired mobility, muscle weakness, and frailty in Brazilian older community-dwelling adult outpatients. The results of the present study are in line with these previous studies.

Kerr et al^[42] suggest that osteoporosis, especially when coupled with a fracture, can have a major impact on physical activity and function. The effects of osteoporosis accumulate over time through a cycle of disability: fracture results in long-term decline in physical function (immobilization, loss of muscle mass, and physical capacity), which in turn increases the risk of further fracture and the likelihood of further physical limitations. Osteoporosis and low lean mass have common biological

pathways and risk factors, which correlate with metabolic, cellular, vascular, and inflammatory factors.^[18,43]

Taken together, our results provide insight into factors related to progression of osteosarcopenia and will facilitate development of various preoperative rehabilitation strategies and guidelines for OA management and treatment. A regular exercise program that includes progressive resistance and balance training, along with proper nutrition, will preserve muscle mass and bone density; such programs should be considered for patients with knee OA.

4.1. Study limitations

First, the cross-sectional retrospective study design did not allow us to establish a cause and effect relationship; longitudinal research is needed to further explore the relationships between osteoporosis + low lean mass and physical function. Second, the results may not be generalizable to all patients with knee OA because we only analyzed data from patients scheduled to undergo TKA. In addition, this study enrolled more females than males, probably due to the predominance of knee OA in the former.^[44] Therefore, extrapolation of these results to males may be limited. Finally, we did not use the diagnostic criteria for sarcopenia when grouping; we used only lean mass. Further studies that measure gait speed and grip strength, which accurately reflect muscle strength or physical ability, are needed.

5. Conclusion

In patients with end-stage knee OA, the combination of osteoporosis and low lean mass increases the risk of impaired physical function when compared with osteoporosis alone, low lean mass alone, or neither condition. Therefore, we suggest that measurement of osteoporosis and appendicular skeletal lean mass will be helpful for assessing the physical function of frail patients with end-stage knee OA.

Author contributions

S.Y. Lee and B.R. Kim were involved in study conception and design. All authors contributed to acquisition, analysis and interpretation of the data. All authors were involved in critical revision of the article for important intellectual contents, and approved the final manuscript.

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