Association of Weight Change and Physical Activity with Knee Pain and Health-Related Quality of Life in East Asian Women Aged 50 Years and Older with Knee Osteoarthritis: A Population-Based Study

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Objectives: This study aimed to investigate the association of self-reported weight change and physical activity with the level of knee pain and health-related quality of life in East Asian women with knee osteoarthritis using population-based data.
Methods: A total of 564 women (mean age, 68.2 years, standard deviation, 8.9 years) aged 50 years or older with knee osteoarthritis (Kellgren-Lawrence (K-L) grade ≥ 2) were included in the data analyses from the fifth Korea National Health and Nutrition Examination Survey. Data regarding the radiographic grade, self-reported weight change during the past year, physical activity, level of knee pain, and health-related quality of life (EuroQOL five- dimension (EQ-5D) index) were collected. Multiple regression analysis was performed to identify factors significantly associated with the level of knee pain and health-related quality of life in subgroups according to the body mass index (BMI) range (≤ 22.5, between 22.6 and 27.5, and > 27.5 kg/m^2).
Results: In the whole group, the level of knee pain was significantly associated with K-L grade ($P < 0.001$), and EQ-5D was negatively associated with age ($P < 0.001$), the level of knee pain ($P < 0.001$), and weekly hours of vigorous-intensity activity ($P = 0.026$). In the subgroup analysis, weight gain showed significant association with the level of knee pain only in women with 22.5 kg/m^2 $<$ BMI ≤ 27.5 kg/m^2 ($P = 0.006$). Weight gain showed significant association with EQ-5D in women with BMI ≤ 22.5 kg/m^2 ($P = 0.047$) whereas weekly hours of moderate-intensity activity was negatively associated with EQ-5D in women with BMI > 27.5 kg/m^2.
Conclusions: The association of weight change and physical activity with knee pain and health-related quality of life might be different according to BMI ranges. Well-designed interventions to improve both knee pain and health-related quality of life need to be investigated in future studies that would strictly control physical activity, diet, and weight changes.

Key Words: Health-related quality of life, Knee pain, Osteoarthritis, Physical activity Weight change

Knee osteoarthritis is one of the most prevalent orthopedic disorders that adversely affects the patients' health-related quality of life, especially in the elderly population.[1,2] Knee pain is an important clinical parameter when determining the necessity of surgical treatment and the treatment

outcomes.[3,4] Therefore, physicians need to understand the factors affecting the level of knee pain and quality of life in patients with knee osteoarthritis.

Previous studies showed that various factors could affect arthritic knee pain, including the radiographic grade of osteoarthritis, presence of spine or hip diseases, obesity, and psychiatric disorders.[5] Obesity is known to affect arthritic pain by increasing mechanical load on the joint as well as by increasing inflammatory cytokine through the arachidonic pathway, which eventually could lead to development and progression of knee osteoarthritis.[6-8] Therefore, obesity has been acknowledged as an important modifiable factor that affects the prognosis of knee osteoarthritis.[6,9-14]

A study reported that weight loss and moderate activity were effective in improving function and pain in obese patients with knee osteoarthritis.[15] However, there is little evidence that weight loss is an effective treatment in nonobese patients, especially in the Asian population. Theoretically, body weight and physical activity can exert complicated effects on the mechanical load on joints, and their relationship could be a confounding factor when analyzing this effect because although physical activity helps reduce body weight, it could also increase joint loading.

Therefore, the authors hypothesized that categorization of body mass index (BMI) and physical activity would provide more clinically relevant analysis. This study aimed to investigate the association of self-reported weight change and physical activity with knee pain and health-related quality of life in Asian women with knee osteoarthritis (Kellgren- Lawrence grade ≥ 2) using population-based data.

MATERIALS AND METHODS

Subjects

The Korean National Health and Nutrition Examination Survey (KNHNES) is a national population-based study conducted by the Korean Centers for Disease Control and Prevention annually from 1998. The subjects are noninstitutionalized civilians who were randomly selected through stratified, multistage probability samples, which were based on age, sex, and residence area. This study includes questionnaires regarding health behavior and nutrition intake and health examinations such as body weight, height, blood pressure measurements, and blood tests. Specific health examinations are included according to the demand of national healthcare policies. Knee osteoarthritis examination and survey were performed in 2011.

A total of 10,589 population-based subjects were invited to participate in the 2011 survey, and 8518 agreed to participate, with a response rate of 80.4%. Of these, 1956 women aged 50 years and older were selected from the parent study. Knee osteoarthritis was defined radiographically as Kellgren-Lawrence grade ≥ 2,[16,17] which was evaluated by two skeletal radiologists. A total of 830 women with knee osteoarthritis were selected, and exclusion criteria were use of osteoarthritis medication,[18,19] pres-

ence of malignancies, and incomplete dataset. Finally, 564 women with knee osteoarthritis were analyzed after implementing the inclusion and exclusion criteria (Fig. 1).

Written informed consent was obtained by the Korean Centers for Disease Control and Preven-

tion from all participants. Approval from the ethical committee was exempted by the institutional review board at our hospital because this study utilized a publicly available database and did not have any potential violation of patient rights.
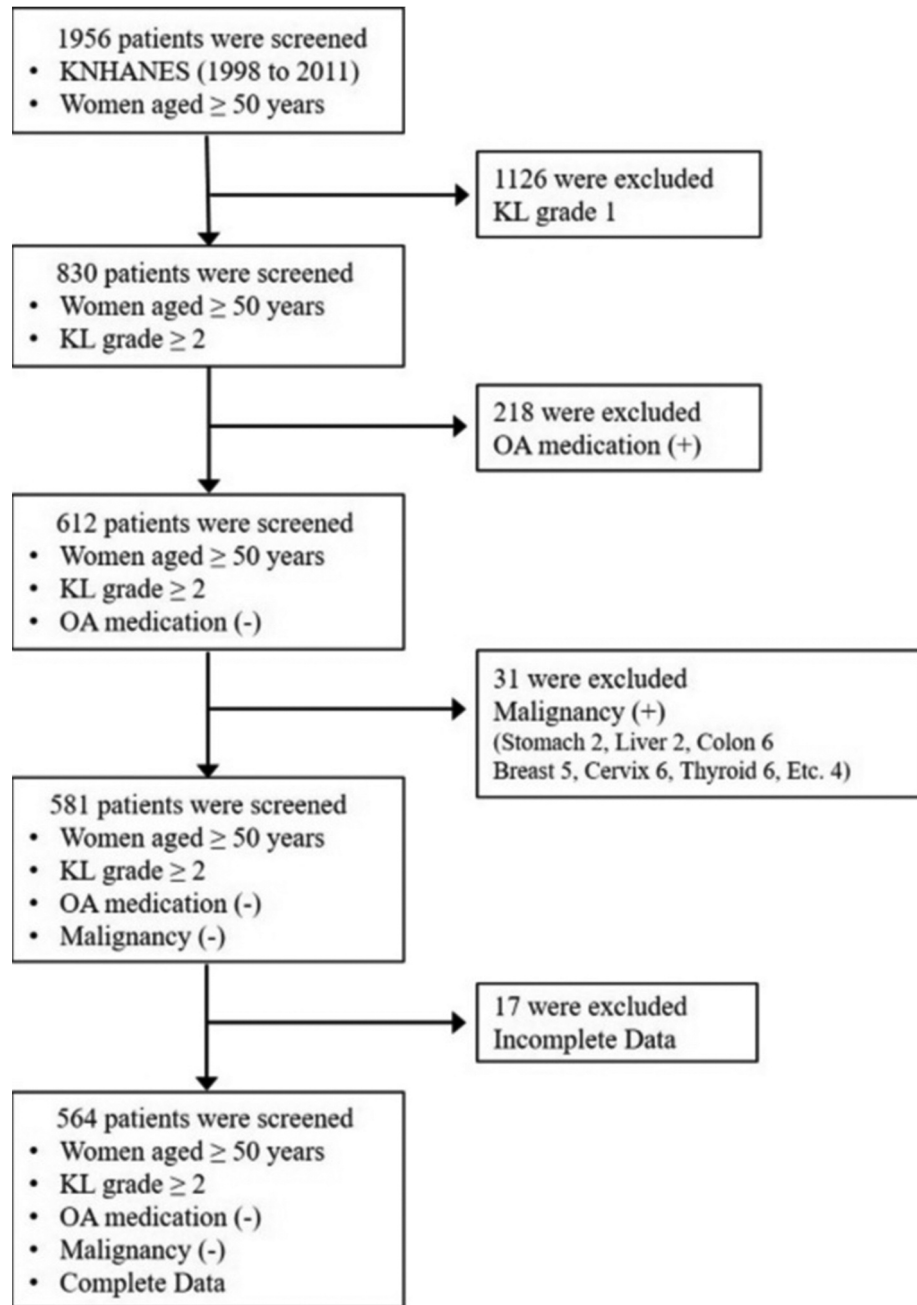

Fig. 1. Flow diagram of the inclusion and exclusion criteria for the Korea National Health and Nutrition Examination Survey (KNHNES). A total of 564 women aged 50 years or older were included.

Data collection from the fifth KNHNES database

Demographic data including age, sex, body mass index (BMI), self-reported weight change in the past year (gain > 10 kg, gain of 6–10 kg, gain of 3–6 kg, gain < 3 kg, no change, loss < 3 kg, loss of 3–6 kg, loss of 6–10 kg, and loss > 10 kg) was collected. The parameters of height and weight were measured using standardized instruments, and BMI was calculated using the height and weight measurements. The percentage of weight change was calculated by dividing the weight change with body weight. Presence of malignant diseases and use of osteoarthritis medication were recorded using a health information questionnaire. The short form of the International Physical Activity Questionnaire[20] was used to evaluate the subjects' activity level, and weekly hours of vigorous-intensity, moderate-intensity, and walking activities were recorded.

Health-related quality of life was measured using the EuroQOL five-dimension (EQ-5D) index. The system comprises five dimensions including mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.[21,22]

The knee osteoarthritis survey included severity of knee pain and radiographic examination. The severity of knee pain was evaluated using a 10-point numerical rating scale (NRS) (0 = no pain, 10 = severe pain). Knee X-rays were taken bilaterally with the subjects' weight-bearing using an SD 3000 Synchro Stand (Accele Ray, SYFM Co., Seoul, South Korea), and the radiographic images were digitally stored. Severity of radiographic knee osteoarthritis was evaluated using the Kellgren-Lawrence grading system[16,17] (grade 0, no features of osteoarthritis; grade 1, small osteophytes of uncertain significance; grade 2, definite osteophytes without impairment of joint space; grade 3, definite osteophytes with moderate joint space reduction; grade 4, definite osteophytes with substantial joint space narrowing and subchondral bone sclerosis). Presence of knee osteoarthritis was defined as Kellgren-Lawrence grades 2, 3, and 4.[16,17] Radiographic evaluation was performed by two radiologists, and the agreement between the two was 85.2% for 81 randomly selected radiographic images with an intraclass correlation coefficient of 0.767 (95% confidence interval, 0.659 to 0.844). If a disagreement in radiographic findings between the two radiologists occurred, the higher grade was adopted.

Data analysis and statistics

Women with knee osteoarthritis were categorized into three groups according to BMI measurements considering the number of women in each group: those with BMI < 23.0 kg/m² (underweight and normal weight for Asian population), those with 23.0 kg/m² < BMI ≤ 27.5 kg/m² (overweight), and those with BMI > 27.5 kg/m² (obesity).[25] Descriptive statistics included mean and standard deviation (SD) for continuous variables and proportion for categorical variables. Normal distribution of the data was tested using the Kolmogorov-Smirnov test. Means and frequency were compared using analysis of variance (ANOVA) test and chi-square test among the three groups, respectively. Correlation be-

tween the variables was analyzed using Pearson's correlation coefficient or Spearman's correlation coefficient according to data normality.

Multiple regression analysis was performed to identify the variables that significantly contributed to the level of knee pain (NRS) and health-related quality of life (EQ-5D), which were dependent variables. Candidate independent variables were selected and included in the regression model as enter mode when the variable showed $P < 0.1$ in the correlation tests. All statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA), with statistical significance set at $P < 0.05$.

RESULTS

The characteristics of the patients included in the analysis are given in Table 1.

In all subjects, the severity of radiographic os-

teoarthritis (Kellgren-Lawrence grade) ($P < 0.001$) was the significant factor associated with the level of knee pain, whereas age ($P < 0.001$), level of knee pain ($P < 0.001$), and weekly hours of vigorous-intensity activity ($P = 0.026$) were the significant factors negatively associated with EQ-5D (Table 2). In the subgroup of women with BMI < 23.0 kg/m^2, Kellgren-Lawrence grade ($P < 0.001$) was the significant factor associated with the level of knee pain, and age ($P < 0.001$), level of knee pain ($P < 0.001$), and percentage change of weight during the past year ($P = 0.032$) were significantly associated with EQ-5D (Table 3). In the subgroup of women with 23.0 kg/m$^2 \leq$ BMI $\leq$ 27.5 kg/m^2, the Kellgren-Lawrence grade ($P < 0.001$) and percentage change of weight during the past year ($P = 0.007$) were found to be significant factors associated with the level of knee pain. Age ($P = 0.006$), level of knee pain ($P < 0.001$) and weekly hours of walking ($P = 0.018$) were the factors significantly associated with EQ-5D

Table 1. Data summary

	All subjects with knee osteoarthritis (n=564)	BMI subgroups			
		BMI < 23.0 kg/m^2 (n = 168)	23.0 kg/m$^2 \leq$ BMI $\leq$ 27.5 kg/m^2 (n = 297)	BMI > 27.5 kg/m^2 (n = 99)	P-Value
Age (years)	68.2 (8.9)	71.4 (8.9)	67.3 (8.7)	65.6 (8.2)	<0.001
BMI (kg/m^2)	24.8 (3.6)	21.1 (1.5)	25.2 (1.3)	30.2 (3.3)	<0.001
Percentage change of body weight (%)	−1.0 (4.7)	−2.3 (5.6)	−0.5 (4.2)	−0.3 (4.1)	<0.001
Kellgren-Lawrence grade (2/3/4)	257/227/80	85/63/20	154/127/45	33/48/18	0.101
Activity (weekly hours)					
Vigorous intensity	0.88 (3.8)	0.88 (4.4)	0.95 (4.0)	0.67 (2.1)	0.829
Moderate intensity	1.2 (3.9)	0.86 (2.9)	1.51 (4.4)	1.1 (3.3)	0.205
Walking	3.4 (5.1)	3.5 (4.9)	3.55 (5.5)	2.5 (4.0)	0.208
Level of knee pain	2.02 (3.33)	1.85 (3.28)	1.94 (3.27)	2.57 (3.56)	0.193
EQ-5D	0.867 (0.174)	0.851 (0.208)	0.878 (0.159)	0.858 (0.148)	0.234

Values are presented as mean (standard deviation) or n.

Table 2. Multiple regression analysis in all subjects with knee osteoarthritis aged 50 years and older

	Level of knee pain (dependent variable)						EQ-5D (dependent variable)				
	Nonstandardized		Standard-ized beta	t	P-Value		Nonstandardized		Standard-ized beta	t	V-value
	B	Standard error					B	Standard error			
Age	0.026	0.016	0.069	1.639	0.102	Age	−0.004	0.001	−0.207	−5.279	<0.001
Kellgren-Lawrence grade	1.220	0.197	0.259	6.187	<0.001	Level of knee pain	−0.018	0.002	−0.341	−8.704	<0.001
Percentage change of weight	−0.026	0.029	−0.037	−0.901	0.368	Kellgren-Lawrence grade	−0.017	0.010	−0.067	−1.677	0.094
Weekly hours of walking	−0.043	0.026	−0.066	−1.613	0.107	Percentage change of weight	0.001	0.001	0.030	0.787	0.431
Coefficient	−2.896	1.097	-	−2.641	0.008	Weekly hours of vigorous activity	-0.004	0.002	-0.084	-2.231	0.026
						Weekly hours of walking	0.002	0.001	0.051	1.361	0.174
						Coefficient	1.221	0.054	-	22.816	<0.001

Table 3. Multiple regression analysis in the subgroup of women with BMI<23.0 kg/m² aged 50 years and older with knee osteoarthritis

	Level of knee pain (dependent variable)						EQ-5D (dependent variable)				
	Nonstandardized		Standard-ized beta	t	P-Value		Nonstandardized		Standard-ized beta	t	P-Value
	B	Standard error					B	Standard error			
BMI	−0.148	0.164	−0.067	−0.905	0.367	Age	−0.006	0.002	−0.277	−4.068	<0.001
Kellgren-Lawrence grade	1.556	0.354	0.328	4.399	<0.001	BMI	0.000	0.010	0.001	0.013	0.990
Weekly hours of walking	-0.066	0.049	-0.099	-1.361	0.175	Level of knee pain	−0.024	0.004	−0.379	−5.360	<0.001
Coefficient	1.142	3.776	-	0.302	0.763	Kellgren-Lawrence grade	−0.019	0.022	−0.063	−0.878	0.381
						Percentage change of weight	0.006	0.003	0.151	2.167	0.032
						Coefficient	1.418	0.264	-	5.369	<0.001

while weekly hours of vigorous-intensity activity ($P = 0.005$) was negatively associated with EQ-5D (Table 4). In the subgroup of women with BMI > 27.5 kg/m², age ($P = 0.031$) was the only significant factor associated with the level of knee pain, and age ($P = 0.028$), BMI ($P = 0.024$) and level of knee pain ($P = 0.002$) were the factors significantly associated with EQ-5D. Weekly hours of moderate-intensity activity ($P = 0.006$) was negatively associated with EQ-5D (Table 5).

For the correlation between activity and weight

Table 4. Multiple regression analysis in the subgroup of women with 23.0 kg/m² ≤ BMI ≤ 27.5 kg/m² aged 50 years and older with knee osteoarthritis

	Level of knee pain (dependent variable)						EQ-5D (dependent variable)				
	Nonstandardized		Standardized beta	t	*P*-Value		Nonstandardized		Standardized beta	t	*P*-Value
	B	Standard error					B	Standard error			
Age	0.026	0.022	0.069	1.169	0.244	Age	−0.003	0.001	−0.152	−2.753	0.006
Kellgren-Lawrence grade	1.145	0.269	0.249	4.256	<0.001	Level of knee pain	−0.017	0.003	−0.355	−6.561	<0.001
Percentage change of weight	0.118	0.043	0.152	2.712	0.007	Kellgren-Lawrence grade	−0.008	0.013	−0.035	−0.615	0.539
Coefficient	−2.930	1.446	-	−2.026	0.044	Weekly hours of vigorous activity	-0.006	0.002	-0.148	-2.847	0.005
						Weekly hours of walking	0.004	0.002	0.124	2.388	0.018
						Coefficient	1.113	0.067	-	16.599	<0.001

Table 5. Multiple regression analysis in the subgroup of women with BMI > 27.5 kg/m² aged 50 years and older with knee osteoarthritis

	Level of knee pain (dependent variable)						EQ-5D (dependent variable)				
	Nonstandardized		Standardized beta	t	*P*-Value		Nonstandardized		Standardized beta	t	*P*-Value
	B	Standard error					B	Standard error			
Age	0.094	0.043	0.217	2.186	0.031	Age	−0.004	0.002	−0.215	−2.234	0.028
Coefficient	−3.584	2.836	-	−1.264	0.209	BMI	-0.009	0.004	-0.212	-2.293	0.024
						Level of knee pain	−0.012	0.004	−0.294	−3.238	0.002
						Kellgren-Lawrence grade	−0.023	0.020	−0.107	−1.118	0.266
						Weekly hours of moderate activity	−0.011	0.004	−0.249	−2.803	0.006
						Coefficient	1.505	0.172	-	8.749	<0.001

change, weekly hours of walking was the only factor that was significantly correlated with percentage change of weight during the past year (r = 0.215, *P* = 0.032) in the subgroup of women with BMI > 27.5 kg/m². There was no significant correlation between activity and weight change in the other subgroups.

DISCUSSION

This study investigated the factors associated with level of knee pain and health-related quality of life (EQ-5D), focusing on self-reported weight change and activity in community-based women aged 50 years and older with knee osteoarthritis.

Important confounding factors were excluded from the data, such as presence of malignancy and osteoarthritis medication. We analyzed the data as subgroups stratified according to BMI classification for Asian population.[23] Weight change and activity showed different association with level knee pain and health-related quality of life according to BMI subgroups.

In our whole cohort, BMI showed no significant correlation with knee pain or health-related quality of life. This is contrary to clinical consensus and previous study results that obesity has an important factor in the development and progression of osteoarthritis in terms of mechanical loading and biochemical pathway affecting inflammatory processes related with lipid metabolism.[6,14,24,25] The authors considered that BMI is a critical factor in pain and health-related quality of life and stratified the whole cohort according to BMI, specifically designed for Asian population.[23]

In our study, contrary to previous studies,[24,25] weight change during a year did not show significant correlation with the level of knee pain for the whole group of women aged 50 years and older with knee osteoarthritis. The association of weight change with knee pain showed differences according to BMI ranges. Weight reduction was significantly associated with lower level of knee pain in women with BMI range of overweight ($23.0 \text{ kg/m}^2 \le \text{BMI} \le 27.5 \text{ kg/m}^2$). This result does not concur with previous studies that have shown that weight loss improved physical function and pain in overweight females with knee osteoarthritis.[24, 25] This difference may have

been due to differing exclusion criteria (malignancies and osteoarthritis medication), differing ethnicities, or the effect of combined intervention such as exercise and diet. Furthermore, weight loss alone might not decrease knee pain without appropriate exercise or concomitant intervention in obese patients with knee osteoarthritis. An interesting finding is that weight gain was positively associated with health-related quality of life (EQ-5D) in subgroup of women with a lower BMI (Table 3).

The amount of activity did not show any relationship with the level of knee pain in this community-based observational study, but it showed significant relationship with health- related quality of life. In the subgroup of women with $23.0 \text{ kg/m}^2 \le \text{BMI} \le 27.5 \text{ kg/m}^2$, EQ-5D showed significant positive association with weekly hours of walking and negative association with that of vigorous-intensity activity. In the subgroup of women with BMI $> 27.5 \text{ kg/m}^2$, weekly hours of moderate-intensity activity showed significant negative association with EQ-5D. Therefore, vigorous-intensity activity in overweight women and moderate-intensity activity in obese women might adversely affect the health-related quality of life in knee osteoarthritis. Further investigation is required to reveal the causal relationship between activity and quality of life controlling other important factors, especially diet intake.[26-28]

The amount of weight change and physical activity could be associated with the level of knee pain and health-related quality of life separately according to BMI ranges. Our study results sug-

gested that weight reduction via walking exercise could reduce knee pain and improve health-related quality of life in the subgroup of Asian overweight women with knee osteoarthritis. However, the specific type of physical activity could impede the patients' health-related quality of life depending on the BMI ranges. Therefore, more sophisticated intervention might be required regarding physical activity and weight loss according to ethnicity and BMI ranges in women with knee osteoarthritis. Future studies with strictly designed diet and physical activity are required to elucidate the relationships among weight loss, knee pain, and health-related quality of life.

There are some limitations to this study. First, this study was essentially a cross-sectional study depending on a health-related questionnaire and specific examination. Therefore, causal relationships between independent and dependent variables are not certain. A further, longitudinal study with the relevant hypothesis is required to verify the causality of the variables. Second, we excluded confounding factors such as presence of malignancy and osteoarthritis medication because these variables could significantly affect the level of knee pain. However, this exclusion might not reflect the usual clinical situation, although the study setting could evaluate the factors affecting knee pain more precisely in a community-based population without any medical intervention for knee osteoarthritis. Third, self-reported weight change over the past year was used in our study, which is yet to be validated.[29,30] This may have caused unknown bias.

The effect of weight change on knee pain could be different according to BMI ranges. Walking activity could improve the quality of life and a weight reduction could decrease knee pain in overweight Asian women with knee osteoarthritis. However, a longitudinal research is required to reveal the causal relationship among the factors, strictly controlling diet and physical activity.

The effect of weight change on knee pain could be different according to BMI ranges. Walking activity could improve the quality of life and a weight reduction could decrease knee pain in overweight Asian women with knee osteoarthritis. However, a longitudinal research is required to reveal the causal relationship among the factors, strictly controlling diet and physical activity.

ACKNOWLEDGEMENTS

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