Factors Predicting Health-related Quality of Life in Knee Osteoarthritis Among Community-dwelling Women in Japan: The Hizen-Oshima Study

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Knee osteoarthritis is the most common chronic joint disorder in elderly people. However, a population-based, longitudinal study on health-related quality of life in knee osteoarthritis has not been conducted in Japan. We studied 333 women aged 50 years and older at baseline, with 8 to 9 years of follow-up. Anteroposterior weight-bearing knee radiographs were obtained at baseline and graded according to the Kellgren-Lawrence criteria. Definite osteoarthritis was defined as Kellgren-Lawrence grade 2 or higher in at least 1 joint. At baseline, all participants were asked if they had knee pain and comorbidities (heart disease, lung disease, stroke, or diabetes mellitus). Height (m), weight (kg), and chair stand time were measured.

At follow-up, quality of life in knee osteoarthritis was evaluated using the Japanese Knee Osteoarthritis Measure score. Multiple linear regression analysis showed that age, knee osteoarthritis, knee pain, comorbidity, and increasing chair stand time were independently related to subsequent health-related quality of life. These findings suggest that treating knee osteoarthritis and comorbidities, managing pain, and optimizing lower extremity muscle strength may be effective targets for intervention.
Musculoskeletal conditions have made an enormous and growing public health impact worldwide. The United Nations, the World Health Organization (WHO), governments, and professional and patients’ organizations therefore declared 2000 to 2010 the Bone and Joint Decade, with the aim of determining the burden of musculoskeletal diseases and improving the health-related quality of life of people with musculoskeletal conditions. Knee osteoarthritis is the most common chronic joint disorder in elderly people. A recent Japanese epidemiological study showed that the prevalence of radiographic knee osteoarthritis was 42.6% in men and 64.2% in women in the ≥40-year age group, and that the estimated number of patients with knee osteoarthritis was approximately 25 million in the total population of 128 million people.

The use of outcome measures has been spreading in clinical medicine. The Japanese Knee Osteoarthritis Measure (JKOM) was created as an outcome measure for patients with knee osteoarthritis. This measure was developed to assess patient-based, health-related quality of life that reflects Japanese social and cultural backgrounds, and it has been proven to have sufficient reliability and validity by means of statistical evaluation and comparison with the Western Ontario and McMaster Universities Arthritis Index (WOMAC), disease-specific measures for osteoarthritis of the hip and knee, and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). So far, the JKOM has been mainly used in hospital-based patients, but not in community-dwelling people.

Factors relating to limitations in activities in knee osteoarthritis have been studied frequently in cross-sectional studies. However, longitudinal studies found limited evidence; radiographic osteoarthritis, pain, muscle strength, comorbidities, and obesity were reported to be predictive factors for subsequent limitations in activities in knee osteoarthritis. Furthermore, to the best of our knowledge, there has been no research on quality of life in knee osteoarthritis in Japan.

The objective of this longitudinal epidemiologic study was to identify the factors that predict the health-related quality of life in knee osteoarthritis using JKOM, focusing on radiographic osteoarthritis, pain, muscle strength (assessed by chair stand ability), comorbidities, and obesity among community-dwelling women in Japan.

Materials and Methods

Patients

The Hizen-Oshima Study is a prospective, population-based cohort study of osteoporosis and osteoarthritis. Details of the Hizen-Oshima study have been previously published. Briefly, all women aged 40 years and older in Oshima, a town in Nagasaki Prefecture in Japan, were invited to participate. The town of Oshima has a population of approximately 5800 (2850 men, 2950 women), including approximately 2000 women aged 40 years or older. Despite having a shipyard in the town, Oshima is a mainly rural area. The baseline examination of each patient was performed at the Oshima Health Center between 1998 and 1999. A total of 586 women (approximately 30% of the eligible women) participated in the study. All participants were noninstitutionalized, living independently at baseline, and were able to ambulate independently (with or without a cane). All patients gave their written, informed consent before participation.

In 2008, a follow-up mail survey on quality of life in knee osteoarthritis was conducted. Of the 586 participants in the baseline survey, 495 were alive, 46 were dead, and 45 had moved to a different municipality. The questionnaire was mailed to the women who were known to be alive, and 392 women responded. Mean ages of nonresponders and responders were 67.3 ± 10.3 and 62.8 ± 8.9 years, respectively; the mean age was significantly higher in nonresponders than in responders (P < .0001). This study was approved by the local and institutional ethics committees.

Knee Radiographs at Baseline

Anteroposterior weight-bearing knee radiographs were obtained at baseline and graded according to the criteria described by Kellgren and Lawrence. Radiographs were obtained with the patients’ knees in full extension. Definite osteoarthritis was defined as Kellgren-Lawrence grade 2 or higher in at least 1 joint.

Measurements at Baseline

All patients were asked if they had knee pain on most days during the previous month and if they had any comorbidities (heart disease, lung disease, stroke, or diabetes mellitus). Height (m) and weight (kg) were measured with light clothing and without shoes, and body mass index (BMI) was calculated as weight (kg)/height² (m²). Chair stand time was measured as the time it took (average of 2 trials) to stand up from a standard chair 5 times; the patients were asked not to use their arms for assistance.

Clinical Manifestations at Follow-up

The JKOM score was used to evaluate quality of life in knee osteoarthritis. The JKOM is a patient-based, self-answered evaluation score that includes 25 items in 4 subcategories (pain and stiffness, activities of daily living, social activities, and general health condition), with 100 points as the maximum score. The JKOM is higher in patients with more pain and physical disabilities, and this evaluation modality is considered to have sufficient reliability and validity for studies of the clinical outcomes of Japanese people with knee osteoarthritis. Treatment status of knee osteoarthritis was not available in this study.

Statistical Analysis

Women missing some variables (n = 28) or aged younger than 50 years (n = 31)
were excluded from the analysis, leaving 333 women for data analysis (Figure). The follow-up rate was 56.8% (333/586). The chi-square test was used to compare categorical variables. For comparisons of means among multiple groups, a general linear modeling method (analysis of variance) and Tukey’s method for multiple comparisons were used. Multiple linear regression analysis was used to explore the effects of knee osteoarthritis, knee pain, comorbidity, and obesity on JKOM score, adjusting for age and follow-up time. All statistical analyses were performed using SAS software, version 9.1.3 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Mean follow-up time was 9.2±0.4 years (range, 8.4-9.7 years). Table 1 summarizes some of the patients’ baseline characteristics. Mean age was 64.2±7.4 years. Approximately 30% of women had knee osteoarthritis, and 33% had knee pain during the previous month. The prevalence of comorbidities and obesity was 23.1% and 30.6%, respectively.

Table 2 shows the JKOM scores at follow-up by selected baseline variables. The JKOM score increased with advancing age (P<.0001). The JKOM score was significantly higher with comorbidity than without comorbidity (P<.0001). The score was also significantly higher in obese women than in nonobese women (p=.0058). The score increased with increasing chair stand time (P<.0001).

The JKOM score at follow-up was compared by baseline knee osteoarthritis and/or knee pain status: group A (neither knee osteoarthritis nor pain), group B (pain only), group C (knee osteoarthritis only), and group D (knee osteoarthritis and pain) (Table 3). Group C and group D had significantly higher JKOM scores than group A. The JKOM score of group D was higher than that of group B or group C. No significant difference in the score was found between group B and group C.

Multiple linear regression analysis showed that age, knee osteoarthritis, knee pain, comorbidity, and increasing chair stand time were independently related to increased JKOM score (Table 4). Obesity was not related to the JKOM score.

DISCUSSION

In the present study, age, knee osteoarthritis, knee pain, comorbidities, and increasing chair stand time at baseline were independently related to subsequent health-related quality of life, measured by the JKOM. To the best of our knowledge,
this is the first epidemiologic study that applied the JKOM to community-dwelling people in Japan.

A cross-sectional study showed the relationship between knee osteoarthritis and functional disability in the Framingham cohort.\textsuperscript{22} Jordan et al\textsuperscript{6} reported that, in performance of lower-extremity tasks such as walking outside or climbing, there were associations with moderate/severe radiographic knee osteoarthritis independent of knee pain. In the epidemiologic follow-up study of the National Health and Nutrition Examination Survey I (NHANES I), patients with radiographic knee osteoarthritis were more likely than patients without knee osteoarthritis to report difficulty with physical functioning 10 years later.\textsuperscript{11} The present result using the JKOM was identical, suggesting that knee osteoarthritis has an independent association with subsequent physical disability.

Table 2

<table>
<thead>
<tr>
<th>Comorbidity\textsuperscript{a}</th>
<th>No.</th>
<th>Mean JKOM Score</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>256</td>
<td>39.8±17.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Yes</td>
<td>77</td>
<td>52.0±23.1</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>231</td>
<td>40.6±18.6</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>102</td>
<td>47.0±20.3</td>
<td>.0058</td>
</tr>
<tr>
<td>Chair stand time (5 times), s</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Q1 (4.7-7.3)</td>
<td>73</td>
<td>35.6±14.2</td>
<td></td>
</tr>
<tr>
<td>Q2 (7.4-8.4)</td>
<td>80</td>
<td>41.3±16.8</td>
<td></td>
</tr>
<tr>
<td>Q3 (8.5-9.9)</td>
<td>85</td>
<td>39.6±13.1</td>
<td></td>
</tr>
<tr>
<td>Q4 (10.0-23.1)</td>
<td>95</td>
<td>51.6±25.4</td>
<td>&lt;.0001  (for trend)</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Presence of heart disease, lung disease, stroke, or diabetes mellitus.

Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean JKOM Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: neither knee OA nor pain</td>
<td>36.2±13.9</td>
</tr>
<tr>
<td>B: knee pain only</td>
<td>41.5±15.6</td>
</tr>
<tr>
<td>C: knee OA only</td>
<td>44.2±20.4\textsuperscript{a}</td>
</tr>
<tr>
<td>D: knee OA and pain</td>
<td>61.4±23.0\textsuperscript{a,b,c}</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Presence of heart disease, lung disease, stroke, or diabetes mellitus.

Table 4

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>Standard Error</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>0.66</td>
<td>0.14</td>
</tr>
<tr>
<td>Follow-up, y</td>
<td>0.34</td>
<td>2.34</td>
</tr>
<tr>
<td>Knee OA, yes/no</td>
<td>8.00</td>
<td>2.04</td>
</tr>
<tr>
<td>Knee pain, yes/no</td>
<td>8.12</td>
<td>1.96</td>
</tr>
<tr>
<td>Chair stand time (5 times), s</td>
<td>1.10</td>
<td>0.40</td>
</tr>
<tr>
<td>Comorbidity, yes/no\textsuperscript{a}</td>
<td>6.22</td>
<td>2.14</td>
</tr>
<tr>
<td>Obesity, yes/no</td>
<td>2.23</td>
<td>1.93</td>
</tr>
</tbody>
</table>

\textsuperscript{a}Presence of heart disease, lung disease, stroke, or diabetes mellitus.
factor in the physical function limitation of knee osteoarthritis.24 The mechanism by which pain contributes to disability in knee osteoarthritis has been demonstrated to result from pain causing avoidance of activity, leading to muscle weakness and disability.7

Lin et al24 reported that poor chair stand performance was associated with disability assessed by WOMAC. Several studies demonstrated that chair stand performance was significantly correlated with lower extremity muscle strength.16,17 The correlation between quadriceps muscle strength and chair stand time indicates the importance of good muscle function in the lower extremities.25 Quadriceps weakness is also reported to be associated with knee pain and disability.8,26

Comorbid conditions, common in patients with osteoarthritis, may contribute to disability.7 The epidemiologic follow-up study of NHANES I suggested that the presence of coexistent chronic disease may increase the amount of long-term disability from knee osteoarthritis.12 A recent cross-sectional study reported that comorbidity severity was associated with more limitations in activities in elderly patients with hip or knee osteoarthritis.10 Unfortunately, information on its severity was not available in this study. Further studies that include comorbidity severity are needed.

Previous studies have demonstrated that obesity is associated with limitations in activity, physical function, and quality of life in osteoarthritis.5,9,27 Sharma et al24 found a longitudinal relationship between greater BMI at baseline and poor WOMAC function outcome over 3 years. In the present study, obese women had a higher JKOM score (poor quality of life) than nonobese women on univariate analysis, but obesity was not related to the JKOM score on multiple regression analysis. In the present study, obese women had more knee osteoarthritis (44.1% vs 27.3%; P= .003) and comorbidity (29.4% vs 20.4%; P=.07) than nonobese women. These confounding variables may in part explain the disappearance of the significance of obesity on multiple regression analysis.

This study had several limitations. First, although our study design was similar to the epidemiologic follow-up studies of NHANES I,11,12 there was no measure of disease state at follow-up and no measure of the JKOM score (disability or quality of life) at baseline. Thus, changes in disease, disability, or quality of life status with time could not be detected. Since osteoarthritis does not tend to regress, and the proportion of the sample in the defined disease categories will increase over time, it is likely that the present findings underestimate the association between knee osteoarthritis and subsequent disability or quality of life. Further study is needed to examine the changes in disease, disability, and quality of life status with time. Second, nonresponders were older than responders. Some women may have not responded because they were functionally limited by their age-related medical conditions. The nonresponse of these women would weaken the association of disease and disability or quality of life in our results. Third, other factors such as socioeconomic status, social support, and mental health that may modify the disease-disability or quality of life were not available.12,24,28 Fourth, the present patients were women; thus, the results of the present study cannot be generalized to men with knee osteoarthritis.

**CONCLUSION**

The findings of the present study outline the clinical and public health impact of knee osteoarthritis, knee pain, comorbidities, and increasing chair stand time on subsequent knee osteoarthritis-specific, health-related quality of life among community-dwelling Japanese women. It would be important to understand the knee osteoarthritis-related factors affecting subsequent quality of life, because with increased life expectancy, the number of older persons having knee osteoarthritis will increase markedly over the next several decades. These data suggest that treating knee osteoarthritis and comorbidity, managing pain, and optimizing lower extremity muscle strength may be effective targets for intervention.

**REFERENCES**

12. Ettenger WH, Davis MA, Neuhau JS, Mallon KP. Long-term physical functioning in per-


