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Original Article

Predictive symptoms associated with the development of radiographic knee osteoarthritis: a 10-year longitudinal study from the Iwaki cohort

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ABSTRACT

Purpose: This 10-year longitudinal cohort study aimed to investigate the annual rate of development of radiographic knee osteoarthritis (drKOA) and its predictive symptoms in the general Japanese population.
Methods: A total of 263 volunteers (154 women) from the Iwaki Health Promotion Project were followed up over 10 years. Standing anteroposterior knee radiographs were obtained and the Kellgren–Lawrence grade was evaluated. drKOA was defined as a change from grade 0 or 1 to ≥2 over 10 years. Knee symptoms were evaluated using the Knee injury and Osteoarthritis Outcome Score at baseline. Logistic regression analyses were performed to identify symptoms related to drKOA, and a predictive formula was created based on the associated symptoms.
Results: The overall incidence of drKOA was 52.9% (annual rate, 4.34%). Regression analysis revealed that predictive symptoms for drKOA were stiffness [$p = 0.033$; odds ratio (OR) = 1.89], frequent pain ($p = 0.024$; OR = 1.38), difficulty in ascending stairs, jumping, twisting, and kneeling ($p = 0.009$–0.046; OR = 1.71–2.78), and poor knee-related quality of life ($p < 0.001$–0.005; OR = 1.53–2.18). Furthermore, the prediction formula created using these predictive symptoms demonstrated an area under the curve of 0.663, a cutoff value of 97 out of 100 points, an OR of 2.99, $p < 0.001$, sensitivity of 0.676, and specificity of 0.589.
Conclusions: The annual incidence rate of drKOA was 4.34% in the general Japanese population. The identified symptoms would be useful to predict the drKOA and consider the etiology of the early phase of this disease.

1. Introduction

Knee osteoarthritis (KOA) is a common, progressive, and degenerative multifactorial joint disease characterized by chronic pain and disability [1]. The global prevalence of KOA was estimated to be over 650 million in 2020 [2], indicating an increasing health burden with notable implications for affected individuals, healthcare systems, and socioeconomic costs [1,3,4]. Regarding the prediction for the development of radiographic KOA (drKOA), previous studies have revealed age, female sex, obesity, previous knee injuries, and knee pain as risk factors [2,5–7]. Although proactive intervention before KOA progresses is important to avoid knee arthroplasty, predictive criteria or preventive interventions have not been established on the basis of these few risk factors [1,8].

Recently, the concept of early KOA was proposed, and evidence of this has accumulated [9,10]. Previous studies have revealed that bone marrow lesions, subchondral cysts, bone attrition, meniscal lesions, and synovitis are observed on magnetic resonance imaging (MRI) even in people without radiographic KOA (rKOA) [11–13]. These studies suggest that preventive interventions for KOA, such as weight loss, patient education, and exercise therapy, should be implemented before radiographic changes appear, and patients who will develop radiographic changes in the future must also be identified. From this view, it is beneficial to understand the symptoms that predict drKOA.

This study aimed to estimate the rate of drKOA and to identify its related symptoms in the general Japanese population using data from a 10-year longitudinal study. It was hypothesized that certain symptoms would predict drKOA and the aim was to develop a prospective knee symptom-based prediction formula.

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2. Materials and methods

2.1. Overview of the Iwaki Health Promotion Project

The Iwaki Health Promotion Project is a population-based health checkup study that has been conducted since 2005 to improve health conditions and the average life span in the Iwaki area of Hirosaki City, located in the Western Aomori Prefecture of Japan. Approximately 1200 adults aged ≥20 years undergo an annual medical checkup from various specialists (physicians, surgeons, orthopedists, gynecologists, psychiatrists, and urologists) from Hirosaki University Hospital, who investigate diseases and disorders across various fields [10,14]. The present study used 2008 (baseline) and 2018 (endpoint) data from that health checkup.

All participants provided written informed consent before participation, and the study was conducted in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine (Hirosaki, Aomori, Japan) (approval nos. 2008-025, May 29, 2008; and 2018-063, May 11, 2018).

2.2. Definition of development of radiographic knee osteoarthritis

All participants without contraindications underwent plain radiography of the anterior-posterior knee joints in the standing position during their general health checkups in 2008 and 2018. Three orthopedic surgeons classified the severity of rKOA into grades 0–4 based on the Kellgren–Lawrence (KL) grading system [15]. When the KL grade of the right and left knees differed, the higher grade was adopted, and the same knee was examined at the endpoint [16]. rKOA was defined as KL grade 2 or higher. drKOA was defined as a change from KL grade 0 or 1 to ≥2. In this study, accelerated drKOA was defined as a change from KL grade 0 or 1 to ≥3 or those who underwent total knee arthroplasty at the endpoint. For the assessment of KL grade for 624 knees in 2018, the inter-rater reliability of the two surgeons expressed as a κ coefficient was 0.649.

2.3. Participants

A total of 886 volunteers (325 men and 561 women) participated in the Iwaki Health Promotion Project health checkup program in 2008. Among them, 18 participants were excluded because of a history of rheumatoid arthritis, knee fracture, knee tumor, or knee surgery (e.g., total knee arthroplasty or meniscus repair). Furthermore, 237 participants with rKOA were excluded (Fig. 1). Among 289 participants who were followed-up for over 10 years, 26 participants without knee joint radiograph data were excluded. Finally, 263 participants (41.7%) who participated in the health checkup program and finished the remeasurement of knee radiography (10-year follow-up) were enrolled in the current study (Fig. 1).

At baseline, the mean ± standard deviation age of the 263 participants was 54.8 ± 9.9 years, and 154 (58.5%) were women.

2.4. Medical history and lifestyle habits

All of the participants completed questionnaires regarding their past medical history, lifestyle, fitness habits, occupational history, family history, and health-related quality of life (QoL). Participants who exercised at least 2 days per week were included in the fitness habit group. Only participants who had smoked or consumed alcohol at baseline were included in the smoking and alcohol consumption habit groups, whereas those who did so in the past were included in the non-habit groups.

2.5. Measurement of bone mineral density (BMD)

BMD was determined by unilateral calcaneus quantitative ultrasound using an Aloka-AOS-100NW device (Aloka, MedWrench, Tokyo, Japan) at baseline, similar to previous reports on the same cohort [17]. Based on the measured transmission index (TI) and speed of sound (SOS), the osteo sono assessment index (OSI) was calculated using the following formula: $OSI = TI \times SOS^2$. Because of the space of the survey area and shielding radiation exposure in 2008, the dual-energy X-ray absorptiometry method was not adopted for BMD measurement.

2.6. Evaluation of knee symptoms

Participants provided disease-specific information, including a description of their cervical, knee, and lower extremity symptoms. Knee symptoms were evaluated using the Knee injury and Osteoarthritis Outcome Score (KOOS) at baseline. The KOOS consists of 42 knee-related items, each scored from 0 to 4, with higher scores indicating worse conditions in each item. Summed scores on five subscales (symptoms, pain, activities of daily living, sports/recreation, and QoL) were converted to 100 points, where 0 represents total knee disability and 100 represents perfect knee health [18–20]. The score of each question in the KOOS was evaluated as a knee symptom.

2.7. Statistical analysis

First, sample size calculations were simulated to determine the number of moderating variables that should be included in the drKOA and KOOS in the Student's *t*-test. The annual rate of drKOA was referenced from two previous studies [6,16]. The necessary sample size for the drKOA group was 66 participants, with $\alpha = 0.05$ and power of 80%.

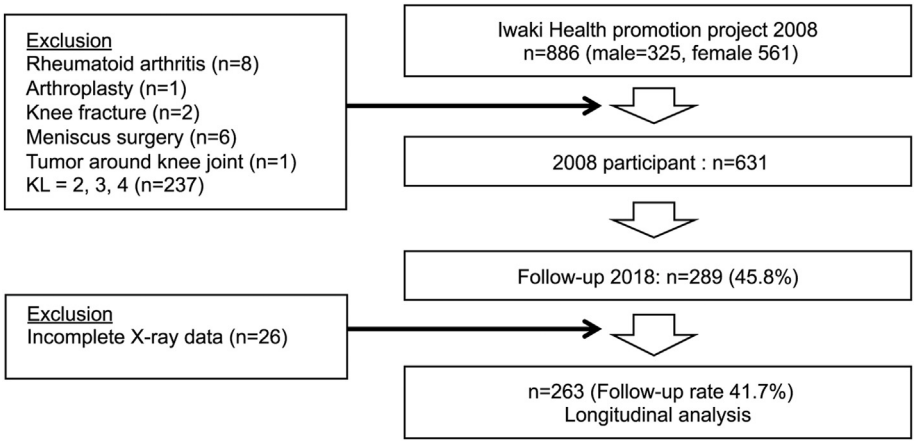

Fig. 1. Flowchart of participant enrolment for the study. KL = Kellgren–Lawrence.

Next, the annual rate of drKOA was calculated based on the cumulative incidence rate over 10 years. Additionally, the age- and sex-specific cumulative incidence rate of drKOA was calculated for the following age groups: 20–39, 40–49, 50–59, 60–69, and ≥70 years. The mean age, height, body weight, body mass index (BMI), KOOS subscales, and BMD were compared using the Mann–Whitney *U* test between the non-drKOA and drKOA groups at baseline. Differences in the prevalence of sex, smoking, alcohol consumption, and fitness habits between the non-rKOA and rKOA groups were analyzed using the χ^2 test.

To examine the relationship between drKOA and knee symptoms, crude logistic analyses were conducted with each KOOS item (42 items) as independent variables. Furthermore, on the basis of methods in the literature [21], the number of moderating variables was set within one-tenth of the number of participants with drKOA in the multiple logistic analysis. Then, the multiple regression analysis was performed with each KOOS item (42 items) as independent variables and age, sex, BMI, BMD, and lifestyle habits as moderating variables. KOOS items that were significantly correlated in these multiple regression analyses were defined as "predictive symptoms." In addition, the same regression analysis was performed with the dependent variable replaced by accelerated drKOA over a 10-year period. Using the identified predictive symptoms, a symptom-based prediction formula was created using a 100-point scale. Finally, receiver operating characteristic (ROC) curve analysis was performed to validate the accuracy of this formula in determining the cutoff value for predicting the drKOA. The Youden index (YI) [(sensitivity) + (specificity) – 1] was used to select candidates for the optimal cutoff values. Statistical tests were conducted using IBM SPSS Statistics Version 28.0 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$.

3. Results

3.1. Comparison of demographic characteristics of participants at baseline

There were 124 non-drKOA participants (mean age 50.8 years) and 139 drKOA participants (mean age 55.3 years) (Table 1). At baseline, participants in the rKOA group were older ($p < 0.001$), predominantly female, had a lower rate of smoking ($p = 0.012$) and alcohol consumption habits ($p = 0.015$), and had lower KOOS scores except for symptoms.

Table 1
Comparison of demographic characteristics between the development of radiographic knee osteoarthritis (drKOA) and non-drKOA groups.

Characteristic	Non-drKOA (KL grade 0 or 1; $n = 124$)	drKOA (KL grade ≥2; $n = 139$)	p value[a]
Age (years)	50.8 ± 9.5	55.3 ± 8.6	<0.001
Female sex	57 (46.0)	97 (69.8)	<0.001
BMI (kg/m^2)	22.3 ± 2.5	22.9 ± 2.93	0.136
OSI (×10^6)	2.71 ± 0.38	2.70 ± 0.39	0.435
Smoking habit	31 (25.0)	18 (12.9)	0.012
Alcohol consumption habit	69 (55.6)	57 (41.0)	0.015
Fitness habit	26 (21.0)	33 (23.7)	0.590
KOOS symptom	94.3 ± 8.9	83.2 ± 20.5	0.233
KOOS pain	94.9 ± 5.6	81.1 ± 20.4	<0.002
KOOS ADL	98.8 ± 5.3	91.1 ± 15.1	<0.002
KOOS sports and recreation	92.4 ± 15.3	77.4 ± 26.1	<0.001
KOOS QoL	87.5 ± 17.3	69.1 ± 26.1	<0.001

Data are presented as mean ± standard deviation or *n* (%).
ADL = activities of daily living; BMI = body mass index; drKOA = development of radiographic knee osteoarthritis; KL = Kellgren–Lawrence; KOOS = Knee injury and Osteoarthritis Outcome Score; OSI = osteo sono assessment index; QoL = quality of life.
[a] Data were compared using the Mann–Whitney *U* test and χ^2 test, with a *p* value of <0.05 considered statistically significant.

3.2. Rates of development of radiographic knee osteoarthritis over 10 years

Among 263 participants without rKOA, 1 patient underwent total knee arthroplasty, 20 participants developed KL grade 3 rKOA, and 118 participants developed KL grade 2 rKOA over the 10-year period. The cumulative rate of drKOA was 52.9% (139 of 263 participants), and the annual rate of drKOA was estimated to be 4.34%. Additionally, the cumulative rate of accelerated drKOA was 8.0% (21 of 263 participants), with an estimated annual rate of 0.77% (Table 2). By sex and age, the rate of drKOA was highest in the ≥70 years age group both for men and women (Fig. 2).

3.3. Predictive symptoms

Regression analysis identified nine predictive symptoms associated with drKOA from KOOS items (Table 3), as follows: (1) stiffness after sitting, lying, or resting later in the day; (2) frequent knee pain; (3) difficulty in ascending stairs; (4) difficulty in jumping; (5) difficulty in twisting/pivoting on the injured knee; (6) difficulty in kneeling; (7) frequent awareness of their knee problem; (8) lack of confidence in their knee; and (9) difficulty with their knee in general. Regarding accelerated drKOA, eight symptoms were identified, as follows: (1) experiencing frequent knee pain; (2) difficulty in running; (3) difficulty in jumping; (4) difficulty in twisting/pivoting on the injured knee; (5) difficulty in kneeling; (6) frequent awareness of their knee problem; (7) lack of confidence in their knee; and (8) difficulty with their knee in general (Table 4). The results of model coefficients omnibus tests were all $p < 0.05$ in the present multiple regression formula. On the other hand, the result of Hosmer–Lemeshow test was not necessarily $p < 0.05$.

3.4. Prediction formula and its accuracy

On the basis of these predictive symptoms, a prediction formula was created as a 100-point scale, as follows:

$$100 - (\text{average scores of 9 predictive symptoms})/4 \times 100 \text{ for drKOA; and}$$

$$100 - (\text{average scores of 8 predictive symptoms})/4 \times 100 \text{ for accelerated drKOA.}$$

ROC analysis revealed that the cutoff value predicting drKOA was 97 out of 100 points for this prediction formula: area under the curve (AUC) = 0.663; odds ratio (OR) = 2.99; $p < 0.001$; sensitivity 0.676; specificity 0.589; and YI = 0.265 (Fig. 3). Moreover, regarding accelerated drKOA, the cutoff value was calculated as 82 out of 100 points: AUC = 0.789; OR = 8.52; $p < 0.001$; sensitivity 0.667; specificity 0.810; and YI = 0.265 (Fig. 4). Below these cutoffs, 66% of drKOA and 23% of accelerated drKOA were accurately predicted using these formulae.

Table 2
Changes in Kellgren–Lawrence (KL) grade over 10 years.

KL grade	Baseline	Endpoint
Grade 0 or 1	263	124
Grade 2	0	118
Grade 3	0	20
Grade 4	0	0
Confirmed arthroplasty implant (TKA)	0	1
Ratio of drKOA (cumulative and annual rate)		139 (52.9%, 4.34%)
Rate of accelerated drKOA (cumulative and annual rate)		21 (8.0%, 0.77%)

Data for each KL grade and the development and progression rates of radiographic knee osteoarthritis (rKOA) are presented as numbers. rKOA is defined as a KL grade ≥2 on plain radiography of the posteroanterior knee joints in the standing position.
drKOA = development of radiographic knee osteoarthritis; KL = Kellgren–Lawrence; TKA = total knee arthroplasty.

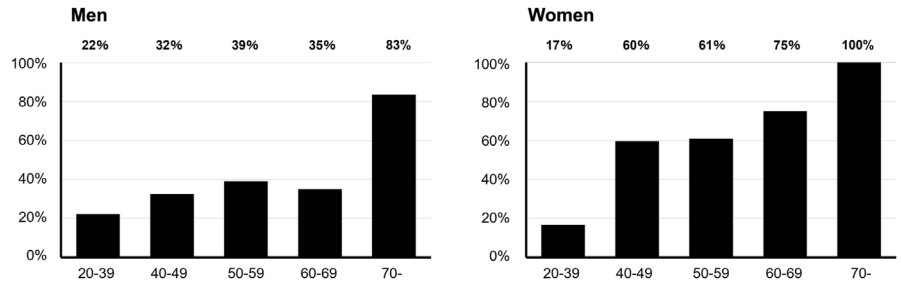

Fig. 2. Rate of development of radiographic knee osteoarthritis (drKOA) over 10 years in men and women. Black bars and numbers indicate the age- and sex-specific rates of drKOA. A total of 109 men and 154 women were followed-up.

Table 3
Symptoms associated with development of radiographic knee osteoarthritis.

KOOS item/question	Crude				Multiple (adjusted)			
	β	*p* value	OR	95% CI	β	*p* value	OR	95% CI
How severe is your knee stiffness after sitting, lying, or resting later in the day?	0.78	0.006	2.19	1.26–3.80	0.63	0.033	1.89	1.05–3.37
How often do you experience knee pain?	0.64	0.027	1.89	1.08–3.31	0.32	0.024	1.38	1.04–1.83
Difficulty in ascending stairs	1.40	0.002	4.04	1.67–9.79	1.20	0.026	2.78	1.13–6.81
Difficulty in jumping	0.85	<0.001	2.34	1.52–3.59	0.61	0.009	1.84	1.17–2.89
Difficulty in twisting/pivoting on the injured knee	0.75	0.002	2.13	1.33–3.39	0.61	0.016	1.84	1.12–3.01
Difficulty in kneeling	0.78	0.003	2.17	1.30–3.64	0.54	0.046	1.71	1.01–2.89
How often are you aware of your knee problem?	0.55	<0.001	1.73	1.29–2.31	0.43	0.005	1.53	1.14–2.07
How much are you troubled by a lack of confidence in your knee?	0.58	<0.001	1.78	1.29–2.47	0.54	0.002	1.71	1.21–2.41
In general, how much difficulty do you have with your knee?	0.90	<0.001	2.47	1.63–2.47	0.78	<0.001	2.18	1.42–3.37

Crude and multiple logistic regression analyses using the forced entry method were performed, with the development of radiographic knee osteoarthritis as the dependent variable.
Independent variables: KOOS items. Moderating variables: age, sex, body mass index, osteo sono assessment index, smoking, alcohol consumption, and fitness habit.
A p value of <0.05 was considered statistically significant (crude and multiple).
CI = confidence interval; KOOS = Knee injury and Osteoarthritis Outcome Score; OR = odds ratio.

Table 4
Symptoms associated with accelerated development of radiographic knee osteoarthritis.

KOOS item/question	Crude				Multiple (adjusted)			
	β	*p* value	OR	95% CI	β	*p* value	OR	95% CI
How often do you experience knee pain?	0.45	0.006	1.58	1.13–2.18	0.44	0.004	1.09	1.02–1.16
Difficulty in running	0.90	<00001	2.45	1.64–3.67	0.64	0.007	1.9	1.19–3.01
Difficulty in jumping	0.86	<0.001	2.36	1.58–3.54	0.58	0.014	1.78	1.12–2.83
Difficulty in twisting/pivoting on the injured knee	0.81	<0.001	2.27	1.52–3.38	0.66	0.002	1.94	1.18–2.96
Difficulty in kneeling	0.91	<0.001	2.48	1.55–4.00	0.75	0.003	2.12	1.30–3.47
How often are you aware of your knee problem?	0.70	<0.001	1.95	1.41–2.70	0.59	<0.001	1.8	1.27–2.55
How much are you troubled by a lack of confidence in your knee?	0.58	0.006	1.78	1.19–2.68	0.57	0.015	1.77	1.12–2.79
In general, how much difficulty do you have with your knee?	0.83	<0.001	2.28	1.41–3.71	0.73	0.005	2.08	1.24–3.46

Crude and multiple logistic regression analyses using the forced entry method were performed, with accelerated development of radiographic knee osteoarthritis as the dependent variable.
Independent variables: KOOS items. Moderating variables: age, sex, and body mass index.
A p value < 0.05 was considered statistically significant (crude and multiple).
CI = confidence interval; KOOS = Knee injury and Osteoarthritis Outcome Score; OR = odds ratio.

4. Discussion

The most important finding from a 10-year observational study was that the annual rate of drKOA was 4.34% in the general population. Furthermore, the current study identified predictive symptoms for drKOA, including stiffness, frequent pain, difficulty ascending stairs, jumping, twisting, and kneeling, and low knee-related QoL. These results would be useful for patients to understand and consider their future condition. Additionally, these symptoms would allow preventive treatments to be initiated.

Compared with previous systematic reviews, the prevalence of rKOA in this study was higher than in the USA, UK, and other Western countries, and was comparable with that in Japan [2], despite differences in diagnostic methods. The prevalence of rKOA in Japan is thought to be influenced by the unique lifestyle, which involves frequent bending and stretching of the knee, which is related to KOA [23–25], and the fact that the participants in this study comprised the general population of a rural area [2]. The high prevalence of rKOA was correlated with sex and age, with the prevalence gradually increasing with age [2,22,26].

General risk factors for these participants were validated using previously reported risk factors, including age, female sex, obesity, and lifestyle habits, which have been proven in previous longitudinal studies [3,27–30]. In the current cohort, age and female sex were predictors of drKOA, similar to previous systematic reviews and Japanese longitudinal studies [2,6,26,27].

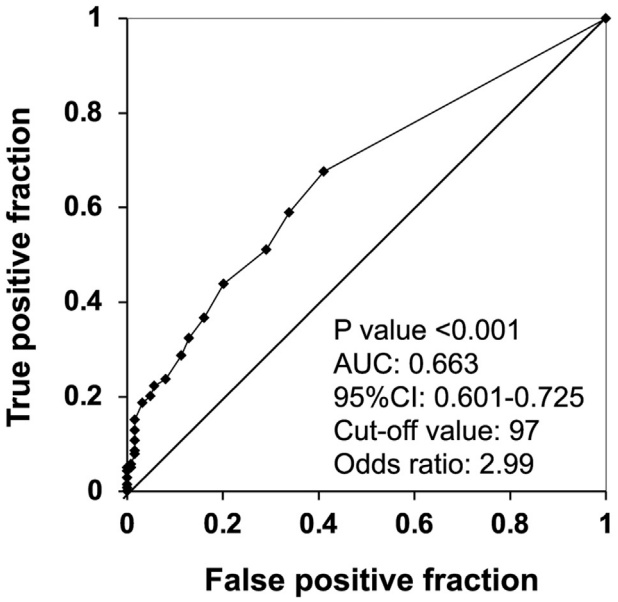

Fig. 3. Receiver operating characteristic curves for symptoms associated with the development of radiographic knee osteoarthritis. Knee symptoms were evaluated using the Knee injury and Osteoarthritis Outcome Score (KOOS). The questions included are those that showed significant differences in the multiple logistic analysis. AUC = area under the curve; CI = confidence interval.

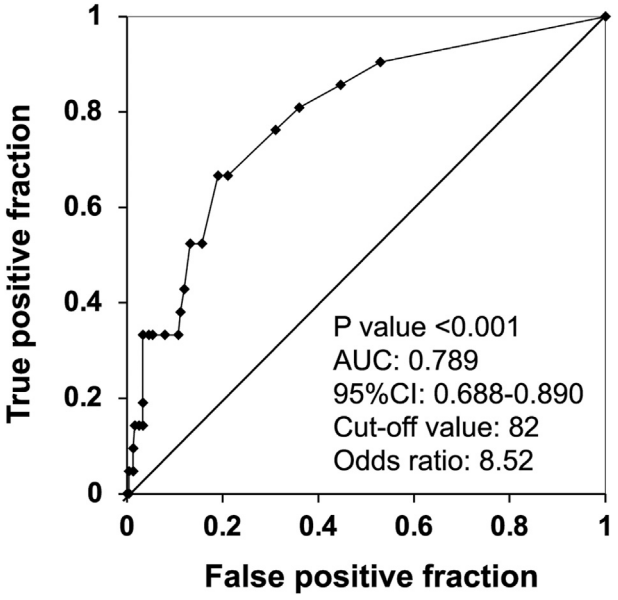

Fig. 4. Receiver operating characteristic curves for symptoms associated with the accelerated development of radiographic knee osteoarthritis. Knee symptoms were evaluated using the Knee injury and Osteoarthritis Outcome Score (KOOS). The questions included are those that showed significant differences in the multiple logistic analysis. AUC = area under the curve; CI = confidence interval.

This longitudinal study evaluated the relationship between KOOS items and drKOA. Knee symptoms at baseline assessed by the KOOS were associated with drKOA, suggesting that participants with an increasing KL grade may experience knee problems before structural changes appear on radiographs. In the present study, participants in the drKOA group experienced more severe stiffness later in the day and more frequent knee pain, consistent with the European Alliance of Associations for Rheumatology (EULAR) recommendations for the diagnosis of KOA [31], which seemed to be a precursor complaint for drKOA.

Regarding knee joint function and daily living, the drKOA group had difficulty ascending stairs, jumping, twisting their injured knees, and kneeling. Furthermore, participants with drKOA were more frequently aware of knee problems, lacked confidence in their knees, and had more severe knee difficulties. Regarding knee function, including stair use and KOA, some studies have reported that elevated KL grade and pain can decrease the ability to climb stairs [32,33], and pain probably first appears during weight-bearing activities involving bending of the knee, such as using stairs [34]. Although these reports did not mention knee activities other than stair use, stair climbing, jumping, twisting, and kneeling were identified as functional disturbances that predicted drKOA. In contrast, although there are differences in the evaluation methods, squatting was not a predictor of drKOA in this study [35,36].

Although a systematic review reported that there is no clear consensus on the quantitative assessment of knee-related QoL [37], some studies have suggested that older age, female sex, and higher BMI in patients with KOA are associated with a lower QoL [38,39]. It has been reported that activity-related pain causes a decline in QoL [40], and maintaining physical activity improves QoL [41]. Low KOOS QoL scores among participants with drKOA in this study reaffirmed the importance of assessing QoL in the prevention of drKOA.

According to the ROC analysis, the cutoff for symptoms associated with drKOA, which was converted to 100 points as in the KOOS formula [18,19], was less than 97 points. This result is satisfied when one of the nine risk symptoms deteriorates by two or more points or when two of the nine deteriorate by one or more points. The present prediction formula was useful due to the result of the model coefficients omnibus tests. Although the prediction accuracy was not high enough (AUC = 0.663), it was considered useful to evaluate these symptoms to identify individuals with predicted deterioration of the knee joint at an early stage and to trigger appropriate interventions, such as weight loss, patient education, and exercise, owing to the fact that once KOA develops there is no curative treatment and it causes irreversible degeneration [8]. In the future, the Hosmer–Lemeshow test are necessary to improve accuracy in the prediction of drKOA.

This study revealed that seven of the eight predictive symptoms for accelerated drKOA overlapped with those for drKOA. On that basis, the cutoff value of the formula based on the ROC curve was more accurate than that of the drKOA analysis. This result suggests that a score of less than 82 in the drKOA prediction formula indicates a higher likelihood of severe knee problems in the future. In addition, it would be worthwhile to investigate whether these predictive symptoms could identify high-risk groups for conventional accelerated osteoarthritis, even though the definitions of these conditions differ.

The present study has some limitations. First, image evaluation was limited to baseline and 10-year follow-up radiographs; accordingly, details of the timing of the drKOA were unknown. Recently, the concept of accelerated KOA has been introduced, suggesting that progression from no radiographic changes to progressive KOA occurs within 4 or 5 years [29,42]. In this study, some participants with accelerated drKOA may have been considered part of the so-called accelerated KOA. However, the strength of the results is that participants were found to have knee symptoms as early as 10 years prior, which may provide sufficient time for preventive intervention. Second, images other than knee joint radiographs could not be evaluated. Regarding MRI images in patients without rKOA, Katsuragi et al. [12] reported that the existence of osteophytes was a risk factor for drKOA. However, in the current study it was not possible to assess whether participants in the rKOA group had minute MRI findings at baseline. The number of participants in this study at baseline was more than 800, and it was considered impractical to perform an MRI on all participants because of time and cost issues. Third, the follow-up rate of the current study was low (41.7%). This may be because the participants who were unable to be followed-up for 10 years were older and had a higher prevalence of KOA; thus, health problems

may have contributed to their inability to participate in this health checkup. Voluntary participants joined this cohort each year, and it was not possible to randomly enroll them. Finally, the study sample comprised the general Japanese population in a rural area, and data regarding confounding factors were not available. It is important to recognize that recall bias may exist in terms of related or unrelated associations, including the KOOS. KOA is a multifactorial disease with many related factors; thus, it was not possible to include all the confounders in this analysis.

In conclusion, in this 10-year longitudinal cohort study, the rates of drKOA and accelerated drKOA were 52.9% and 8.0%, respectively, with annual rates of 4.34% and 0.77%. On the basis of the predictive symptoms related to drKOA (stiffness, frequent pain, difficulty in ascending stairs, jumping, twisting, and kneeling, and low knee-related QoL), a novel predictive formula was created, and its accuracy was moderate even without any radiographic abnormalities. This may allow for individuals with predicted deterioration of the knee joint to be identified at an earlier stage and thus allow for timely preventative measures to be implemented.

Ethics

This study was approved by the Ethics Committee of Hirosaki University Graduate School of Medicine (approval nos. 2008-025, May 29, 2008; and 2018-063, May 11, 2018) and was conducted in accordance with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All participants provided written informed consent before participation.

Author contributions

E. Sasaki was responsible for organization and co-ordination of the study and was the chief investigator responsible for data analysis. E. Sasaki, D.C., T.T., Y.K., Y.S., Y.T., E.T., and Y.I. developed this study design. All authors contributed to the writing of the final manuscript.

Data statement

The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Declaration of competing interest

The authors declare no competing interests.

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