Osteoarthritis and Cartilage Open 6 (2024) 100454

Contents lists available at ScienceDirect

Osteoarthritis and Cartilage Open

journal homepage: www.elsevier.com/journals/osteoarthritis-and-cartilage-open/2665-9131

Ten-year trends in values of joint space width and osteophyte area of knee joints: Comparison of the baseline and fourth ROAD study surveys

Banri Kitamura [a,b], Toshiko Iidaka [b], Chiaki Horii [c], Shigeyuki Muraki [b], Hiroyuki Oka [d], Hiroshi Kawaguchi [e], Kozo Nakamura [f], Toru Akune [g], Yuta Otsuka [a], Takayuki Izumo [a], Takao Tanaka [a], Tomohiro Rogi [a], Hiroshi Shibata [a], Sakae Tanaka [c], Noriko Yoshimura [b,*]

[a] Institute for Health Care Science, Suntory Wellness Limited, 8-1-1 Seikadai, Seika-cho, Soraku-gun, Kyoto 619-0284, Japan
[b] Department of Preventive Medicine for Locomotive Organ Disorders, 22nd Century Medical & Research Center, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
[c] Department of Orthopaedic Surgery, Sensory and Motor System Medicine, Graduate School of Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
[d] Department of Medical Research and Management for Musculoskeletal Pain, 22nd Century Medical and Research Center, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
[e] Department of Orthopaedic Surgery, Tokyo Neurological Center, 4-1-17 Toranomon, Minato-ku, Tokyo 105-0001, Japan
[f] Towa Hospital, 4-7-10 Towa, Adachi-ku, Tokyo 120-0003, Japan
[g] National Rehabilitation Center for Persons with Disabilities, 4-1 Namiki, Tokorozawa-shi, Saitama 359-0042, Japan

ARTICLE INFO

Handling Editor: Professor H Madry

Keywords:
Osteoarthritis
Knee
Computer-aided diagnosis
Joint space width
Osteophyte

ABSTRACT

Objective: Considering the joint space width and osteophyte area (OPA) of the knee joints of Japanese adults, this study elucidated the ten-year trends in medial minimum joint space width (mJSW) and OPA using data of two independent cohorts from a population-based cohort study.
Methods: The baseline survey of the Research on Osteoarthritis/Osteoporosis Against Disability study was conducted from 2005 to 2007; 2975 participants (1041 men, 1934 women) completed all knee osteoarthritis (OA) examinations. The fourth survey was performed from 2015 to 2016; distinct 2445 participants (764 men, 1681 women) completed identical examinations. The medial mJSW and medial tibial OPA were measured bilaterally using an automated system.
Results: The mean medial mJSW (standard deviation) was 3.22 (0.96) mm and 2.65 (0.95) mm at baseline and 3.81 (1.20) mm and 3.13 (1.15) mm in the fourth survey for men and women, respectively. The mean medial mJSW in the fourth survey was significantly greater in both men and women in all age groups than at baseline ($p < 0.01$). The mean OPAs in men aged 40–49 and 60–69 years and women aged 40–49, 50–59, 60–69, and 70–79 years were significantly smaller in the fourth survey ($p < 0.05$). The trend in mJSW remained the same even after adjusting for confounding factors in the multivariate analysis, but the trend in OPA was weakened.
Conclusions: A significant improvement in the medial mJSW within 10 years could decrease the incidence and progression of knee OA and prevent the risk of walking disability.

1. Introduction

Japan is becoming a super-aging society with an increasing number of people requiring long-term care and support [1]. According to the 2022 Comprehensive Survey of Living Conditions (Ministry of Health, Labour and Welfare), joint disease is the fifth leading cause of care requirement and the first leading cause of support requirement [2], which shows osteoarthritis (OA) influences the need for long-term care and support significantly. Specifically, knee OA directly affects the walking ability of older adults, deteriorating their quality of life [3]. Therefore, knee OA is a

* Corresponding author. Department of Preventive Medicine for Locomotive Organ Disorders, 22nd Century Medical & Research Center, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.
E-mail addresses: banri_kitamura@outlook.com (B. Kitamura), iidaka-kgw@umin.ac.jp (T. Iidaka), harukabc@gmail.com (C. Horii), smuraki@muraki-seikei.com (S. Muraki), taigis54@yahoo.co.jp (H. Oka), kawaguchi0126@gmail.com (H. Kawaguchi), kozo-nakamura-62@jcom.home.ne.jp (K. Nakamura), akunetoru@rehab.go.jp (T. Akune), yuta_otsuka@suntory.co.jp (Y. Otsuka), takayuki_izumo@suntory.co.jp (T. Izumo), takao_tanaka@suntory.co.jp (T. Tanaka), tomohiro_rogi@suntory.co.jp (T. Rogi), hiroshi_shibata@suntory.co.jp (H. Shibata), tanakas-ort@h.u-tokyo.ac.jp (S. Tanaka), noripu2yoshi@gmail.com (N. Yoshimura).

https://doi.org/10.1016/j.ocarto.2024.100454
Received 15 June 2023; Accepted 26 February 2024

major public health problem, considering chronic pain and disability in elderly individuals.

Knee OA causes degeneration of the articular cartilage, narrowing of the joint space, and formation of osteophytes with aging, causing arthralgia and movement disorders. The Kellgren–Lawrence (KL) classification is the gold standard for assessing knee OA on radiography [4]. While radiographic imaging and KL classification are widely used convenient methods, categorical evaluation and detection of small changes over time are difficult. For the quantitative and objective evaluation of knee OA, we developed the knee OA computer-aided diagnosis (KOACAD) system using the baseline data of population-based cohort entitled the Research on Osteoarthritis/Osteoporosis Against Disability (ROAD) study [5,6]. KOACAD is a fully automated system that quantifies the major features of knee OA on standard radiographs with good reproducibility and reliability; it measures the minimum joint space width (mJSW) in medial compartments and osteophyte area (OPA) at the medial tibia using digitized knee radiographs. As mentioned, The reference values for mJSW and OPA based on sex and age or the KL grade strata in Japan using the KOACAD system were published previously using ROAD study data from the 2005–2007 survey. Associations between KOACAD parameters and lifestyle-related diseases, nutrient intake, or occupational actiities are also elucidated in previous cross-sectional studies [7–9].

Although the aging population is rapidly increasing in Japan, recent studies have reported the rejuvenation of the physical functions of Japanese people. Suzuki et al. compared the physical constitution and physical function of the elderly in 2007 and 2017 and observed the rejuvenation phenomenon among the new generation of Japanese older adults [10]. Moreover, the prevalence rates of osteoporosis and hip OA have decreased, based on the results of the baseline survey and the fourth survey conducted 10 years after the ROAD study [11,12]. In light of these findings, we hypothesized that a similar decreasing trend may exist in the components of the knee joint, such as mJSW and OPA. In the present study, radiographic measurements of the knee joint were performed using X-ray films from the fourth ROAD survey in 2015–2016 and investigated the 10-year trends in the Medial mJSW [mm] and OPA values.

2. Methods

2.1. Participants

We recruited participants from the ROAD study, which is a national, prospective study of OA comprising population-based cohorts from several Japanese communities. Details regarding the cohort profiles are described previously [6,13] and we provided only a brief summary.

Between 2005 and 2007, a baseline database, including the clinical and genetic information of 3040 residents was created. Participants with available data in the resident registration records of three communities with different characteristics were recruited for the study. The first community, Itabashi, Tokyo, is situated in an urban region; a total of 1350 participants (≥60 years) were recruited from this community. The second community, Hidakagawa, Wakayama, is situated in a mountainous region; a total of 864 participants (≥40 years) were recruited from this region. The third community, Taiji, Wakayama, is situated in a coastal region. A total of 826 patients (≥40 years) were recruited from this region.

The fourth ROAD study was conducted in 2015–2016 and served as a 10-year follow-up of the baseline survey. Its findings will be used as the new baseline in the next 10 years. Therefore, similar to the methods used in the original study, individuals were invited to participate in the present study. Among the three chosen regions, with the collaboration of town hall authorities, information about the ROAD study examinations was advertised in the town hall's public relations publication, and residents aged >40 years (60 years in Itabashi) were invited to participate. Besides publication, individuals who participated in the baseline, second, and third ROAD study surveys were invited via letters. The following inclusion criteria of the baseline survey were utilized: ability to (1) visit the clinic where the survey was performed, (2) provide self-reported data, and (3) understand and sign an informed consent form. No other exclusion criteria were used. Eventually, 2893 individuals (895 men and 1998 women; mean age, 68.9 years) participated in the fourth survey. Among them, 1666 individuals (525 men and 1141 women) participated in the baseline and fourth surveys. The other 1227 individuals (370 men and 857 women) were the new participants in the fourth survey. Accordingly, the baseline and fourth surveys were two independent cohorts of subjects enrolled ten years apart.

The study was approved by the ethics committees of the University of Tokyo (approval numbers 1264 and 1326), Wakayama Medical University (No. 373), and the Tokyo Metropolitan Institute of Gerontology (approval number 5). Written informed consent was provided by all participants.

2.2. Questionnaire, interview, and anthropometric measurements

Participants completed a 400-item interviewer-administered questionnaire on lifestyle characteristics, including occupation, smoking habits, alcohol consumption, family history, medical history, physical activity, reproductive variables, and previous knee injury history. Height and weight were measured, and BMI was calculated as weight (kg)/height^2 (m^2).

2.3. Radiographic assessment

All participants underwent radiographic examination of both knees using an anteroposterior (AP) view with weight bearing and foot-map positioning. Fluoroscopic guidance with a horizontal AP radiography beam was used to visualize the joint space; images were downloaded as Digital Imaging and Communications in Medicine format files.

The KOACAD system [5] was programmed to measure mJSW in the medial compartments and OPA at the medial tibia using digitized knee radiographs. Initially, radiographic magnification was corrected based on the image size of a rectangular metal plate. To determine the region of interest including the tibiofemoral joint space, a vertical neighborhood difference filter was used to identify points with high absolute values for a difference of scales. The center of all points was calculated, and the region of interest was chosen. Within the ROI, the outline of the femoral condyle was designated as the upper rim of the joint space. The two ends were determined; vertical lines from the ends were considered the outside rims of the joint space. Outlines of the anterior and posterior margins of the tibial plateau were drawn like that of the femoral condyle; the middle line between the two outlines was designated as the lower rim of the joint space (Fig. 1A). A straight regression line for the lower rim outline was then drawn, and intersections of the lower rim outline and the regression line were designated as the inside rims. The mm was determined as the minimum vertical distance in the medial joint space area surrounded by the upper, lower, inside, and outside rims (Fig. 1B). To measure the OPA, the medial and lateral outlines of the femur and tibia were drawn, and inflection points for these outlines were calculated. The medial outline of the tibia from the inflection point was drawn upwards to the joint level, and the area that was medially prominent over the smoothly extended outline was designated the OPA (Fig. 1C).

In a previous study, the KOACAD system was applied to the Digital Imaging and Communications in Medicine data of the baseline survey by an experienced orthopedist who developed this system (H.O.), and there was strong reliability for this measurement [6]. Herein, the KOACAD system was applied to the fourth survey data by another observer (B.K.), and values for mm and OPA based on sex and age in Japan (2015–2016) were calculated. For the evaluation of intraobserver reliability for this measurement, the mm and OPA on 100 randomly selected knee radiographs from the fourth survey were measured by the same observer (B.K.) at >1 week after the initial measurements; intraobserver reliabilities

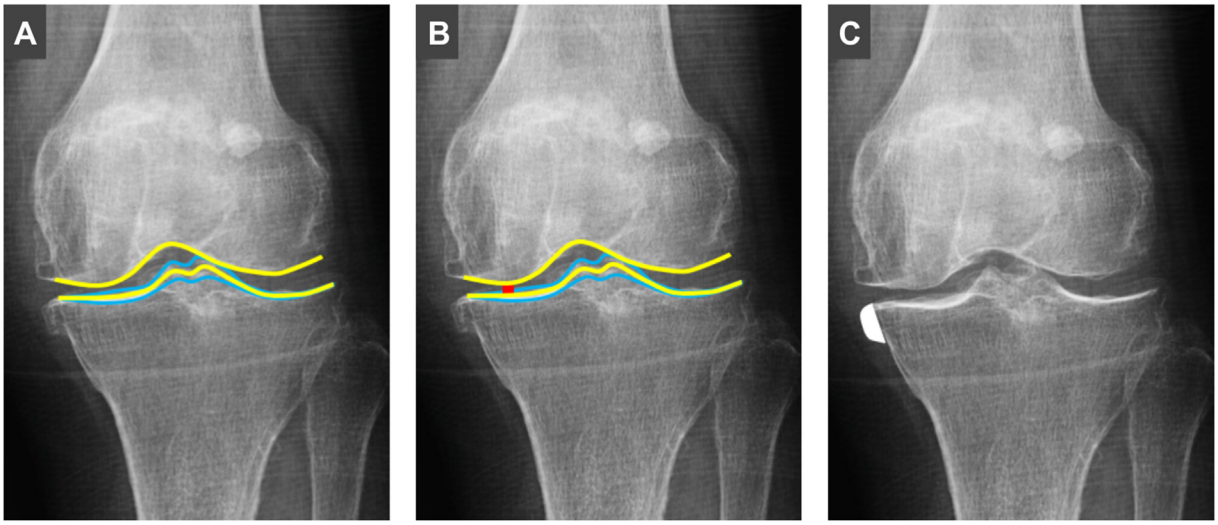

Fig. 1. Schema of image processing by the knee osteoarthritis computer-aided diagnosis (KOACAD) system. (**A**) Outlines of the femoral condyle (upper yellow line) and anterior and posterior margins of the tibial plateau (blue lines). The middle line (lower yellow line) between these two outlines represents the lower rim of the joint space. (**B**) Medial minimum joint space widths (red line) as minimum vertical distances in medial joint space areas. (**C**) Osteophyte area (white area) is determined as the medial prominence over the smoothly extended outline of the tibia.

based on intraclass coefficients of correlation were adequate for assessment (0.90 and 0.90, respectively). Mm and OPA values were compared between the corresponding age-stratified groups from the baseline and fourth surveys. Interobserver reliability was evaluated to confirm the reliability of observations by two observers (H.O. and B.K.). The mm and OPA on 180 randomly selected knee radiographs from the baseline survey were also measured by two observers to determine the interobserver reliability using ICCs, which were also considered adequate for assessment (0.84 and 0.85, respectively).

2.4. Statistical analysis

Descriptive statistics are presented as means and standard deviations, unless otherwise specified. Differences in mean age, height, weight, and BMI between men and women were examined using the *t*-test. Differences in age, height, weight, and BMI among communities (urban, mountainous, and coastal regions) were determined using one-way analysis of variance and Tukey's honestly significant difference post hoc comparisons. Differences in the proportions of current smokers and current drinkers between men and women and among communities were determined using the chi-squared test.

For radiographic measurements from baseline and fourth surveys, means and standard deviations were calculated for each knee. The *t*-test was used to compare the mean values of the mm and OPA between men and women, and one-way analysis of variance and Tukey's honestly significant difference post hoc comparisons were used to compare these values among groups stratified by age and sex. Differences in the mean values of radiographic measurements between the corresponding age-stratified groups from baseline and fourth surveys were examined using the *t*-test. Statistical analyses for the baseline survey were performed using STATA statistical software (STATA, College Station, TX, USA), and those for the fourth survey were performed using JMP® 15 (SAS Institute Inc., Cary, NC, USA), and STATA statistical software.

3. Results

3.1. Participants' characteristics

The results of the baseline survey have been reported previously [6]. Of the 2893 participants in the fourth survey, 431 (14.9%) did not undergo plain radiography, whereas 17 (0.59%) underwent bilateral TKA; thus, these participants were excluded. The remaining 2445 participants (84.5%) (764 men, 1681 women; mean age, 68.8 years; range, 18–97 years) were included in this study. A summary of the participants' characteristics is shown in Table 1.

Regarding the participants in the fourth survey, although no significant difference in the mean age between men and women was observed, men had significantly higher body height, weight, BMI, and number of current smokers and current drinkers than women ($p < 0.01$). Age, height, weight, and proportions of current smokers and current drinkers were significantly different among residents of the three communities ($p < 0.01$) —coastal residents were significantly younger and had higher body height and weight than those of residents of the other two communities; urban residents were significantly older and had lower body height and weight than those of residents of the other two communities. BMI was comparable among residents of all three communities. The proportions of current smokers and current drinkers were lower in urban residents than in coastal and mountainous residents.

3.2. Radiographic measurements of the knee joint classified by sex and age from the fourth survey

The number of knee joints assessed in the baseline and fourth surveys is shown in Table 2. Among the knees included in this study, those that had undergone TKA and UKA were excluded. The mean values of the mm and OPA of the knees from the baseline and fourth surveys classified by sex are presented in Table 2. In both surveys, the mean value of the mm was significantly greater in men than in women ($p < 0.05$), whereas the mean value of OPA was significantly lower in men than in women ($p < 0.05$).

Table 2 shows the mean values of the mm and OPA of the knees from the baseline and fourth surveys classified by age.

Considering men in the baseline survey, the mm was significantly smaller in participants in their 60s than in those in their <40s, as well as in participants in their 70s and ≥80s than in those in their <70s ($p < 0.05$). The OPA was significantly greater in participants in their 70s than in those in their 50s ($p < 0.05$). Among women, the mm was significantly smaller in participants in their 60s than in those in their <60s, in participants in their 70s than in those in their <70s, and in participants in their ≥80s than in those in their <80s ($p < 0.05$). The OPA was significantly greater in participants in their 70s than in those in their <70s, as well as in participants in their ≥80s than in those in their <80s ($p < 0.05$).

Regarding men in the fourth survey, the mm was significantly smaller in participants in their 50s and 60s than in those in their <50s, in participants in their 70s than in those in their <70s, and in participants in

Table 1
Summary characteristics of subjects.

Characteristics	Baseline survey			Fourth survey				
	Overall	Men	Women	Overall	Men	Women	*p value* men vs. women	*p value* among communities
Number of subjects	2975	1041	1934	2445	764	1681		
Community								
Urban	1290 (43.4%)	448 (43.0%)	842 (43.5%)	561 (22.9%)	133 (17.4%)	428 (25.5%)		
Mountainous	862 (29.0%)	318 (30.1%)	544 (28.1%)	845 (34.6%)	294 (38.5%)	551 (32.8%)		
Coastal	823 (27.7%)	275 (26.4%)	548 (28.3%)	1039 (42.5%)	337 (44.1%)	702 (41.8%)		
Age [years]	70.2 (11.1)	71.0 (10.7)	69.8 (11.3)	68.8 (13.6)	68.4 (14.3)	69.0 (13.4)	0.30	<0.01
Height [cm]	154.2 (8.9)	162.5 (6.7)	149.8 (6.5)	155.9 (9.5)	165.5 (7.0)	151.5 (6.9)	<0.01	<0.01
Weight [kg]	54.9 (10.3)	61.3 (10.0)	51.5 (8.6)	55.4 (11.4)	64.0 (11.3)	51.4 (9.0)	<0.01	<0.01
Body mass index [kg/m^2]	23.0 (3.3)	23.2 (3.0)	22.9 (3.5)	22.7 (3.5)	23.3 (3.3)	22.4 (3.5)	<0.01	0.08
Current smokers	11.7%	25.7%	3.5%	7.7%	19.0%	2.6%	<0.01	<0.01
Current drinkers	40.0%	64.2%	25.9%	39.8%	67.0%	27.6%	<0.01	<0.01

Data are the mean (standard deviation).
t-test for comparison of age, height, weight and BMI between men and women.
One-way analysis of variance (ANOVA) for comparison of age, height, weight, and BMI among communities.
Chi-squared test for comparison of current smokers and current drinkers between men and women and among communities.

Table 2
Measurement values of KOACAD classified by age and sex.

	Baseline survey			Fourth survey		
Age strata [years]	Number of knees	Medial mJSW [mm]	OPA [mm^2]	Number of knees	Medial mJSW [mm]	OPA [mm^2]
Overall	5950	2.85 (0.99)	2.83 (8.40)	4877	3.34 (1.21)	2.36 (7.41)
Men						
<40	28	4.12 (0.92)	0	50	4.70 (0.80)	0.09 (0.66)
40–49	82	3.67 (0.75)	0.40 (1.98)	118	4.59 (0.94)	0.02 (0.18)
50–59	214	3.63 (0.75)	0.30 (1.51)	218	4.07 (1.02)^{ab}	0.23 (1.36)
60–69	334	3.37 (0.93)^{a}	0.96 (3.60)	421	4.02 (0.97)^{ab}	0.22 (1.43)
70–79	1052	3.13 (0.96)^{abcd}	1.35 (4.68)^{c}	314	3.75 (1.25)^{abcd}	1.01 (4.05)^{d}
>80	372	2.94 (0.98)^{abcd}	1.31 (4.06)	404	3.16 (1.24)^{abcde}	1.81 (5.68)^{abcde}
Total	2082	3.22 (0.96)	1.12 (4.07)	1525	3.81 (1.20)	0.78 (3.64)
Women						
<40	62	3.37 (0.61)	0.18 (1.25)	68	3.82 (0.71)	0
40–49	210	3.22 (0.64)	0.46 (2.09)	246	3.76 (0.79)	0.11 (0.85)
50–59	418	3.03 (0.78)	0.96 (2.87)	474	3.52 (0.94)^{b}	0.56 (2.54)
60–69	762	2.80 (0.98)^{abc}	2.33 (6.39)	835	3.35 (1.03)^{ab}	1.41 (4.53)
70–79	1764	2.52 (0.92)^{abcd}	4.60 (11.2)^{abcd}	877	3.08 (1.14)^{abcd}	3.55 (8.37)^{abcd}
>80	652	2.32 (0.95)^{abcde}	6.39 (12.70)^{abcde}	852	2.52 (1.20)^{abcde}	6.69 (12.87)^{abcde}
Total	3868	2.65 (0.95)$^{\#}$	3.76 (9.87)$^{\#}$	3352	3.13 (1.15)$^{\#}$	3.07 (8.50)$^{\#}$

Data are the mean (standard deviation).
mJSW, minimum joint space width; OPA, osteophyte area.
[a] Significantly different from those of group <40 years ($p < 0.05$).
[b] Significantly different from those of group in their 40s ($p < 0.05$).
[c] Significantly different from those of group in their 50s ($p < 0.05$).
[d] Significantly different from those of group in their 60s ($p < 0.05$).
[e] Significantly different from those of group in their 70s ($p < 0.05$).
[#] Significantly different from those of men ($p < 0.05$).
One-way analysis of variance (ANOVA) and Tukey's honestly significant difference (HSD) post hoc comparisons for comparison among age-stratified groups.
t-test for comparison between total men and women.

their ≥80s than in those in their <80s ($p < 0.05$). The OPA was significantly greater in participants in their 70s than in those in their 60s, as well as in participants in their ≥80s than in those in their <80s ($p < 0.05$). Among women, the mm was significantly smaller in participants in their 50s than in those in their 40s, in participants in their 60s than in those in their <50s, in participants in their 70s than in those in their <70s, and in participants in their ≥80s than in those in their <80s ($p < 0.05$). The OPA was significantly greater in participants in their 70s than in those in their <70s, as well as in participants in their ≥80s than in those in their <80s ($p < 0.05$).

3.3. Comparison between the baseline and fourth surveys

The mm in men in the baseline and fourth surveys was 3.22 (0.96) mm and 3.81 (1.20) mm, respectively, with a significant difference ($p < 0.01$) (Table 2). In women, the mm in the baseline and fourth surveys was 2.65 (0.95) mm and 3.13 (1.15) mm, respectively, with a significant difference ($p < 0.01$). The mean values of the mm in men and women classified according to age from the baseline and fourth surveys are shown in Fig. 2. The mm in both men and women in the fourth survey was significantly greater than that in participants of corresponding ages in the baseline survey ($p < 0.01$).

The OPA in men in the baseline and fourth surveys was 1.12 (4.07) mm^2 and 0.78 (3.64) mm^2, respectively (Table 2), with a significant difference ($p < 0.05$). The OPA in women in the baseline and fourth surveys was 3.76 (9.78) mm^2 and 3.07 (8.50) mm^2, respectively, with a significant difference ($p < 0.01$). Fig. 3 shows the mean values of the OPA among men and women classified by age from the baseline and fourth surveys. In men, the OPA of participants in their 40s and 60s in the fourth survey was significantly smaller than that of participants of

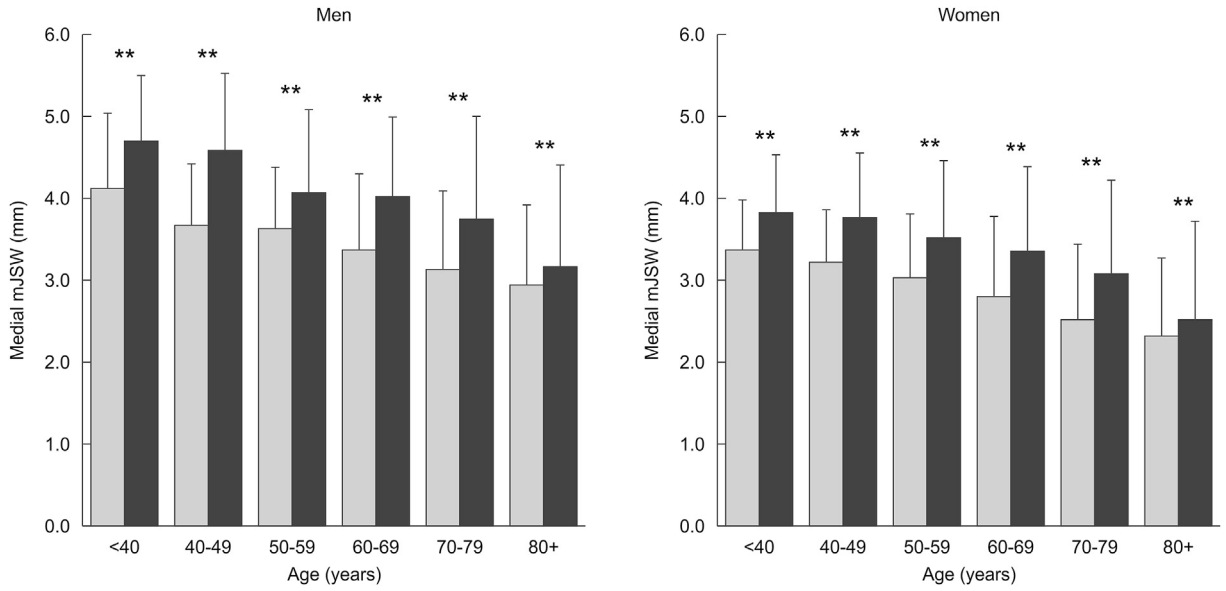

Fig. 2. Mean value ± standard deviation of the medial mJSW in men and women classified by age between 2005 and 2007 (gray bar) and between 2015 and 2016 (black bar). **Significantly different between the corresponding age-stratified groups using the *t*-test. ($p < 0.01$).

corresponding ages in the baseline survey ($p < 0.05$). In women, the OPA of participants in their 40s–70s in the fourth survey was significantly smaller than that of participants of corresponding ages in the baseline survey ($p < 0.05$).

To determine the trend of changes in the values of knee OA components within 10 years, we conducted a multivariate analysis. First, we analyzed the data with mJSW values as the objective variable; participation in the baseline or fourth survey as the explanatory variable; and sex, age, BMI, region (urban, mountainous, or seaside), smoking status (current smoker or non-smoker), and drinking status (current drinker or non-drinker) as adjusting variables. Results showed that the values of mJSW in the fourth survey were significantly greater than those in the baseline survey (beta = 0.205, $R^2 = 0.2195$, $p < 0.0001$), but no significant difference was observed in the OPA values between the baseline and fourth surveys (beta = 0.09, $R^2 = 0.0969$, $p = 0.73$).

4. Discussion

We measured mms and OPAs of the knee joints assessed using the KOACAD system in the baseline and fourth surveys of the ROAD study, which were two independent cohorts of subjects enrolled ten years apart. To our knowledge, this is the first large-scale population-based study that examines the trends in mJSW and OPA over a 10-year period in the Japanese population. Compared with the corresponding age group, the mean mm in the fourth survey was significantly greater in both men and women in all age groups ($p < 0.01$). This trend in the mJSW values was maintained even after adjusting for confounding factors in the multivariate analysis, while the trend in the OPA values showed an inconsistent pattern.

Regarding the reasons of the increase in mJSW over the past 10 years, we have considered the following three reasons. The first reason is the

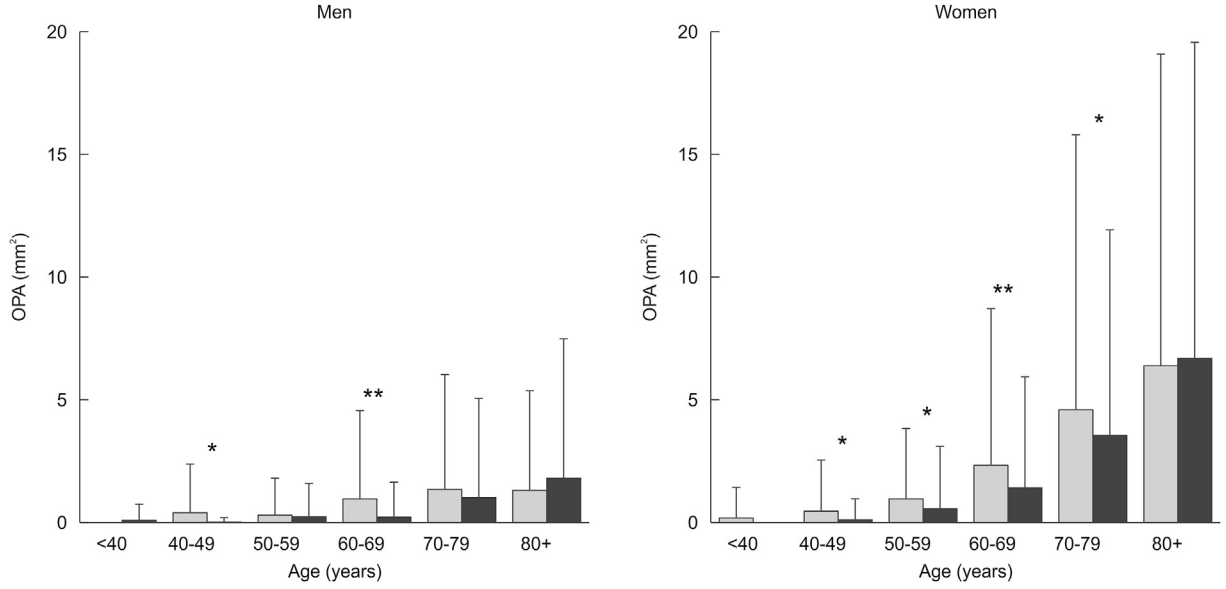

Fig. 3. Mean value ± standard deviation of the OPA in men and women classified by age between 2005 and 2007 (gray bar) and between 2015 and 2016 (black bar). *Significantly different between the corresponding age-stratified groups using the *t*-test. ($p < 0.05$). **Significantly different between the corresponding age-stratified groups using the *t*-test. ($p < 0.01$).

increase in anthropometric height among Japanese individuals. According to the National Health and Nutrition Survey of Japan, the height of both men and women in their 40s, 50s, 60s, and 70s significantly increased between 2005 and 2015 across corresponding age groups ($p < 0.01$) [14,15] To the best of our knowledge, there are no reports on the association between height and mJSW. However, from the data of the Osteoarthritis Initiative (OAI) study, mJSWs of knees with KL grade 0 were reported as 5.12 (0.77) mm for men and 4.40 (0.70) mm for women [16], which were greater than our previous findings, i.e., 3.70 (0.77) mm for men and 3.26 (0.65) mm for women [7]. The average heights of men and women from the United States (from where the OAI population was recruited) and Japan were 175.3 cm and 161.3 cm, and 167.5 cm and 154.2 cm, respectively [15,17]. Therefore, the difference in mJSW between OAI data and our Japanese data might result from the difference in height. In asymptomatic community-based adults, increased knee height measures were associated with a reduced risk of medial tibial cartilage defects [18]. Therefore, increased heights of Japanese men and women may have positively affected their knees, increased the mJSW. Considering women in their 50s and 60s, BMI significantly decreased between 2005 and 2015, because their heights increased while their weights were comparable. BMI significantly influences knee OA; a decrease in BMI in women may also positively affect their knees.

The second reason is the improvement in muscle strength among Japanese adults. T. Suzuki et al. compared grip strength of Japanese elderly between 2007 and 2017 and reported increased grip strength at ≥75 years of age in men and ≥70 years of age in women [10]. Grip strength shows an association with quadriceps strength and reflects a common underlying construct with knee extension strength among healthy adults [19,20]. Quadriceps were significantly impaired in participants with knee OA, as compared with age-matched controls, and muscle strength (especially that of the quadriceps) was a major determinant of both performance-based and self-reported physical function [21]. Greater quadriceps strength was protective against cartilage loss at the lateral compartment of the patellofemoral joint [22]. Thus, greater quadriceps strength may protect the knee joint cartilage against loss, and increase the mJSW among the Japanese elderly. The quadriceps muscle strength was measured in the fourth ROAD study, but not in the baseline study. Therefore, the direct impact of the quadriceps cannot be conclusively stated in this comparative study. However, in the future, we believe we can clarify the influence of quadriceps muscle strength on the values of mJSW at the knee joints.

The third reason is the improvement in nutritional status among Japanese individuals. According to the 1971 National Nutrition Survey of Japan, daily intake of vitamins B2 and C increased from 0.79 mg to 0.91 mg and from 73 mg to 108 mg, respectively, between 1961 and 1971 [23]; in contrast, they did not increase between 2005 and 2015 [14,15]. People aged approximately 60 years in 2005 and 2015 were in their adolescence in 1961 and 1971, respectively; thus, their nutritional status during 1961 and 1971 significantly affected our study results. We previously reported that vitamins B2 and C were positively associated with mJSW and negatively associated with OPA from a cross-sectional analysis of the baseline survey of the ROAD study [8]. Therefore, the condition of the knee joints might have improved in the Japanese elderly because of better nutritional status, including vitamin B2 or C consumption. The daily intake of animal protein increased from 25.3 g to 34.7 g between 1961 and 1971, which might have improved muscle strength and positively affected the knee joints of the Japanese elderly.

This study has several limitations. First, although the ROAD study included a large number of participants, they all participated voluntarily and were recruited from only three areas, and we also included participants who lived independently rather than those living in institutional settings. To determine any selection bias in the ROAD study, anthropometric measurements and lifestyle variables, such as frequencies of smoking and alcohol drinking, were compared between participants and the general Japanese population. Data regarding the general population in Japan were obtained from the 2005 or 2015 National Health and Nutrition Survey conducted by the Ministry of Health, Labour and Welfare, Japan [14,15]. Considering the baseline survey, BMIs were compared between the participants and the Japanese population in 2005; men aged 70–74 years in the baseline survey had a significantly smaller body built than men of this age group in the overall Japanese population ($p < 0.05$). The proportion of current smokers and current drinkers in the general Japanese population was compared with that in the baseline survey population; both proportions were significantly higher in the general Japanese population than in the baseline survey population. Considering the fourth survey, BMIs were also compared between the participants and the Japanese population in 2015, and men aged 50–59 years and 60–69 years had significantly greater and smaller body built, respectively, than men of corresponding age groups in the overall Japanese population ($p < 0.05$ and $p < 0.01$). Women aged 30–39 years in the fourth survey had a significantly smaller body built than women of this age group in the overall Japanese population ($p < 0.05$). The proportion of current smokers and drinkers in the general Japanese population was also compared with that of the fourth survey population; both proportions were significantly higher in the former. Although our study participants' BMIs did not differ significantly from those of the general Japanese population for most age groups, the former were healthier considering smoking and drinking.

Second, the fourth survey included both first-time participants and those who had participated in multiple surveys; including the latter could affect the measurements. Of the participants in the fourth survey, 25.1%, 14.2%, 12.7%, and 48.0% were first-, second-, third-, and fourth-time participants in the ROAD study, respectively. The first-, second-, third-, and fourth-time participants had mean (SD) mm values of 3.47 (1.13) mm, 3.62 (1.10) mm, 3.30 (1.25) mm, and 3.19 (1.25) mm, and mean OPA values of 1.30 (4.61) mm^2, 1.12 (5.37) mm^2, 2.65 (8.91) mm^2, 3.30 (8.74) mm^2 respectively, with significant differences ($p < 0.05$). These differences were examined using multiple regression analysis after adjusting for age, BMI, and sex; no significant association was observed between the frequency of past survey participation and mJSW after adjustment ($p = 0.33$). This observation suggests that the mJSW obtained in the fourth survey was not affected by the frequency of past survey participation. On the contrary, significant negative associations were found between first-time participation in the fourth survey and OPA ($p < 0.05$); thus, first-time participants in the fourth survey have significantly small OPAs and healthier knee joints. The attenuation of the 10-year difference in OPA values may have been influenced by participation in past surveys.

In conclusion, a comparison of the baseline and fourth survey results of the ROAD study revealed that the mm increased between the corresponding age-stratified groups in the previous 10 years after adjusting the multivariate analysis for several confounding factors. Meanwhile, no significant difference was observed in the OPA values. Our findings indicate that the Japanese people demonstrate healthier or more rejuvenated knees. Therefore, it is possible to maintain the quality of life and extend the healthy-life expectancy of this population in the future. The ROAD study will be continued in the future, and further investigations should elucidate the 10-year changes within the same group of participants and the mechanisms contributing to the trend in the knee health of Japanese people.

Author Contributions

Conceptualization: B.K., T.I. (Toshiko Iidaka), Y.O., T.I. (Takayuki Izumo), T.T., T.R., H.S., and N.Y.; data curation: B.K.; formal analysis: B.K.; funding acquisition: H.O., S.T. and N.Y.; investigation: T.I. (Toshiko Iidaka), C.H., and N.Y; methodology: S.M., H.O., H.K., K.N., T.A., S.T., and N.Y.; supervision: N.Y.; writing: original draft, B.K.; writing: review & editing, Y.O., T.I. (Takayuki Izumo), T.T., T.R., H.S., and N.Y. All authors have read and agreed to the published version of the manuscript.

Role of the funding sources

This work was supported by Grant-in-Aid funding from the Ministry of Health, Labour and Welfare: 19FA1401 (Director, Sakae Tanaka), 19FA0701 (Director, Hiroyuki Oka), and 19FA1901 (Director, Estuo Chosa). The study was also supported by Scientific Research grants 19H03895, and Challenging Exploratory Research grants 18K18447 to Noriko Yoshimura. The study was partly supported by grants from the Japan Agency for Medical Research and Development (17dk0110028h0001, Director, Noriko Yoshimura; 17gk0210007h0003, Director, Sakae Tanaka). Further, the study was partly supported by grants from the Mitsui Sumitomo Insurance Welfare Foundation (2016, Director, Noriko Yoshimura), and Japan Dairy Association (2017, Director, Noriko Yoshimura). The funding agencies had no role in the study design, collection, analysis and interpretation of data; in the writing of the manuscript; and in the decision to submit the manuscript for publication.

Data statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the ethics committees of the University of Tokyo (approval numbers 1264 and 1326) and the Tokyo Metropolitan Institute of Gerontology (approval number 5).

Patient consent

Written informed consent was provided by all participants.

Declaration of competing interest

Six of the authors (B.K., Y.O., T.I. [Takayuki Izumo], T.T., T.R. and H.S.) are salaried employees of Suntory Wellness Limited. All other authors have no conflicts of interest. B.K., Y.O., T.I. (Takayuki Izumo), T.T., T.R., and H.S. contributed to interpret the data, revise and approve the manuscript with other authors as well. However, this study was not related to any products of the company.

Acknowledgments

The authors are grateful to all of participants and investigators for their support and cooperation. We would like to thank Editage (www.editage.com) for English language editing.

References

[1] Cabinet Office, Government of Japan, The Annual Report on the Ageing Society Japan, 2021. https://www8.cao.go.jp/kourei/english/annualreport/2021/pdf/2021.pdf. (Accessed 10 November 2023).
[2] Ministry of Health, Labor and Welfare, Japan, Comprehensive Survey of Living Conditions, 2022, https://www.mhlw.go.jp/toukei/saikin/hw/k-tyosa/k-tyosa22/dl/06.pdf. (Accessed 10 November 2023).
[3] M. Vitaloni, A. Botto-van Bemden, R.M. Sciortino Contreras, D. Scotton, M. Bibas, M. Quintero, et al., Global management of patients with knee osteoarthritis begins with quality of life assessment: a systematic review, BMC Muscoskel. Disord. 20 (2019) 493, https://doi.org/10.1186/s12891-019-2895-3.
[4] J.H. Kellgren, J.S. Lawrence, Radiological assessment of osteo-arthrosis, Ann. Rheum. Dis. 16 (1957) 494–502, https://doi.org/10.1136/ard.16.4.494.
[5] H. Oka, S. Muraki, T. Akune, A. Mabuchi, T. Suzuki, H. Yoshida, et al., Fully automatic quantification of knee osteoarthritis severity on plain radiographs, Osteoarthritis Cartilage 16 (2008) 1300–1306, https://doi.org/10.1016/j.joca.2008.03.011.
[6] N. Yoshimura, S. Muraki, H. Oka, A. Mabuchi, Y. En-Yo, M. Yoshida, et al., Prevalence of knee osteoarthritis, lumbar spondylosis and osteoporosis in Japanese men and women: the research on osteoarthritis/osteoporosis against disability study, J. Bone Miner. Metabol. 27 (2009) 620–628, https://doi.org/10.1007/s00774-009-0080-8.
[7] H. Oka, S. Muraki, T. Akune, K. Nakamura, H. Kawaguchi, N. Yoshimura, Normal and threshold values of radiographic parameters for knee osteoarthritis using a computer-assisted measuring system (KOACAD): the ROAD study, J. Orthop. Sci. 15 (2010) 781–789, https://doi.org/10.1007/s00776-010-1545-2.
[8] S. Muraki, T. Akune, Y. En-yo, M. Yoshida, S. Tanaka, H. Kawaguchi, et al., Association of dietary intake with joint space narrowing and osteophytosis at the knee in Japanese men and women: the ROAD study, Mod. Rheumatol. 24 (2014) 236–242, https://doi.org/10.3109/14397595.2013.854055.
[9] S. Muraki, H. Oka, T. Akune, Y. En-yo, M. Yoshida, K. Nakamura, et al., Association of occupational activity with joint space narrowing and osteophytosis in the medial compartment of the knee: the ROAD study (OAC5914R2), Osteoarthritis Cartilage 19 (2011) 840–846, https://doi.org/10.1016/j.joca.2011.03.008.
[10] T. Suzuki, Y. Nishita, S. Jeong, H. Shimada, R. Otsuka, K. Kondo, et al., Are Japanese older adults rejuvenating? Changes in health-related measures among older community dwellers in the last decade, Rejuvenation Res. 24 (2021) 37–48, https://doi.org/10.1089/rej.2019.2291.
[11] N. Yoshimura, T. Iidaka, C. Horii, S. Muraki, H. Oka, H. Kawaguchi, et al., Trends in osteoporosis prevalence over a 10-year period in Japan: the ROAD study 2005–2015, J. Bone Miner. Metabol. 40 (5) (2022) 829–838, https://doi.org/10.1007/s00774-022-01352-4.
[12] T. Iidaka, C. Horii, S. Muraki, H. Oka, H. Kawaguchi, K. Nakamura, et al., Trends in prevalence of hip osteoarthritis over a 10-year period in Japan: the ROAD study 2005–2015, Osteoarthr Cartil Open 4 (3) (2022) 100285, https://doi.org/10.1016/j.ocarto.2022.100285.
[13] N. Yoshimura, S. Muraki, H. Oka, H. Kawaguchi, K. Nakamura, T. Akune, Cohort profile: research on osteoarthritis/osteoporosis against disability (ROAD) study, Int. J. Epidemiol. 39 (2010) 988–995, https://doi.org/10.1093/ije/dyp276.
[14] Ministry of Health, Labor and Welfare, Japan, The National Health and Nutrition Survey Japan, 2005, https://www.mhlw.go.jp/bunya/kenkou/eiyou07/dl/01-01a.pdf. (Accessed 10 November 2023).
[15] Ministry of Health, Labor and Welfare, Japan, The National Health and Nutrition Survey Japan, 2015, https://www.mhlw.go.jp/bunya/kenkou/eiyou/dl/h27-houkoku-04.pdf. (Accessed 10 November 2023), https://www.mhlw.go.jp/bunya/kenkou/eiyou/dl/h27-houkoku-05.pdf.
[16] C. Ratzlaff, E.L. Ashbeck, A. Guermazi, F.W. Roemer, J. Duryea, C.K. Kwoh, A quantitative metric for knee osteoarthritis: reference values of joint space loss, Osteoarthritis Cartilage 26 (2018) 1215–1224, https://doi.org/10.1016/j.joca.2018.05.014.
[17] US Department of Health and Human Services, Anthropometric Reference Data for Children and Adults: United States, 2015-2018, 2021. https://stacks.cdc.gov/view/cdc/100478. (Accessed 10 November 2023).
[18] A.J. Teichtahl, A.E. Wluka, B.J. Strauss, Y. Wang, P. Berry, M. Davies-Tuck, et al., The associations between body and knee height measurements and knee joint structure in an asymptomatic cohort, BMC Muscoskel. Disord. 13 (2012) 19, https://doi.org/10.1186/1471-2474-13-19.
[19] R.W. Bohannon, S.R. Magasi, D.J. Bubela, Y.C. Wang, R.C. Gershon, Grip and knee extension muscle strength reflect a common construct among adults, Muscle Nerve 46 (2012) 555–558, https://doi.org/10.1002/mus.23350.
[20] O.Y.A. Chan, A.H. van Houwelingen, J. Gussekloo, J.W. Blom, den Elzen Wpj, Comparison of quadriceps strength and handgrip strength in their association with health outcomes in older adults in primary care, Dordrecht, Netherlands, Age 36 (2014) 9714, https://doi.org/10.1007/s11357-014-9714-4.
[21] A.H. Alnahdi, J.A. Zeni, L. Snyder-Mackler, Muscle impairments in patients with knee osteoarthritis, Sport Health 4 (2012) 284–292, https://doi.org/10.1177/1941738112445726.
[22] S. Amin, K. Baker, J. Niu, M. Clancy, J. Goggins, A. Guermazi, et al., Quadriceps strength and the risk of cartilage loss and symptom progression in knee osteoarthritis, Arthritis Rheum. 60 (2009) 189–198, https://doi.org/10.1002/art.24182.
[23] Ministry of Health, Labor and Welfare, Japan, The National Nutrition Survey Japan, 1971, https://www.nibiohn.go.jp/eiken/chosa/kokumin_eiyou/doc_year/1969_71/196971_kek.pdf. (Accessed 10 November 2023).