Original Article

Relationship between severity of knee osteoarthritis and radiography findings of lower limbs: A cross-sectional study from the TOEI survey

Mitsuru Hanada*, Hironobu Hoshino, Hiroshi Koyama, Yukihiro Matsuyama

Department of Orthopaedic Surgery, Hamamatsu University School of Medicine, Hamamatsu, 431-3192, Japan

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ABSTRACT

Objective: This study aimed to compare radiographic parameters among radiographic severity of the medial knee osteoarthritis and between men and women in a rural Japanese population.

Methods: We measure nine radiographic parameters of the whole lower extremity in participants with neutral or varus alignment.

Results: Age and body mass index were related to the knee osteoarthritis severity. The knee osteoarthritis depended on not only varus alignment in the whole leg, but also varus deformity of proximal tibial condyle and the tibial plateau inclination, especially in women.

Conclusion: We must consider the difference of tibial condyle morphology and tibial plateau inclination before onset of the knee osteoarthritis.

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1. Introduction

Knee osteoarthritis is a complex degenerative disease that involves advancing age, hereditary disease, and post traumatic changes. The number of patients with knee osteoarthritis is increasing. In Japan, the number of patients with knee osteoarthritis is also increasing because of the aging society.^{1,2} Yoshimura et al. reported that radiographic knee osteoarthritis was observed in 42% of men and 62% of women over 40 years in Japan.² Several mechanical factors have been identified as having a significant influence on knee osteoarthritis, such as body height and weight, range of knee motion, knee alignment, bone mineral density, lower extremity muscle strength, varus thrust during gait, and knee adduction moment.^{3–10} Malalignment of the lower extremity is often observed in progressive knee osteoarthritis. A common pattern is varus alignment of the whole leg with a local osteoarthritic change in the medial compartment of the knee or valgus alignment with a local osteoarthritic change in the lateral compartment. This is often seen in Japanese women who have varus alignment.^{11,12} Varus malalignment of the lower extremity is considered responsible for the progression of medial knee

osteoarthritis.^{12–15} Thus, medial compartment knee osteoarthritis and varus deformity of the lower limbs are mutually detrimental to each other. Although the association between knee osteoarthritis and malalignment is well known, their pathogenic relationship is unclear.

We hypothesized that knee osteoarthritis is associated with the malalignment of the whole leg, the morphology of femur and tibia, and inclination of joint surfaces. Several factors cause varus deformity of the lower limbs, such as the alignment between the femur and tibia, gradient of the lower limb joints (knee and ankle), and difference of the morphology of the femoral and tibial condyles. However, it is unclear how these factors are associated with knee osteoarthritis, or how they may be used as indexes of knee osteoarthritis progression. Thus, we have conducted an epidemiological study every two years since 2012 regarding alignment focusing on whole spine and whole leg radiographs in Toei town of North-Shitara district in the Aichi Prefecture (TOEI Study) as a part of residents health screening.

In this study, we investigated the relationship between severity of knee osteoarthritis, participant's backgrounds (age, body height, and weight), and the several radiographic parameters concerning the alignment of the whole leg, inclination of the knee and ankle joints, and morphology of femur and tibia as a cross-sectional study in a large epidemiological cohort.

* Corresponding author at: Department of Orthopaedic Surgery, Hamamatsu University School of Medicine, 1-20-1 Handayama, Higashi-ku, Hamamatsu, 431-3192, Japan.

E-mail addresses: mitsuruhanada@gmail.com (M. Hanada), hoshi@hama-med.ac.jp (H. Hoshino), hiromania27@hotmail.com (H. Koyama), spine-yu@hama-med.ac.jp (Y. Matsuyama).

2. Methods

The TOEI Study was a cohort study evaluating the alignment of the whole spine and whole leg, conducted in 2012 with residents aged over 40 years as the subjects. Since then, the same survey has been performed every two years. In 2014, 608 people (237 men, 371 women) participated in this survey for the whole leg with particular attention to knee osteoarthritis. All subjects underwent radiography of the whole leg while standing, which included from the hip to ankle joints. People who had a history of trauma and who underwent surgical treatment in the lower extremity, including internal fixation or total hip or knee arthroplasty, were excluded. People with severe hip osteoarthritis, ankle osteoarthritis, and lateral compartment osteoarthritis of the knee were also excluded, in addition to patients with lower limbs whose hip joint and ankle joint were not completely included in the radiograph and that showed valgus alignment. The severity of knee osteoarthritis was based on the Kellgren-Lawrence (KL) classification.¹⁶ Grades KL-0 and KL-I were regarded as normal or having doubtful osteophytes, so they were included in normal group (Group N). KL-II, which had definite osteophytes and possible narrowing of joint space, was defined as the early osteoarthritis group (Group E). We defined KL-III and KL-IV, which had definite or severe narrowing of joint space, as the advanced osteoarthritis group (Group A). All radiographs were interpreted and graded by a single orthopedic surgeon. The participants whose severity groups in the right knee osteoarthritis were different from that in the left knee were excluded. Finally, 391 persons (170 men, 221 women) were included in this study. The radiographic data of their right lower extremity were used in this study.

2.1. Measurement of alignment parameters in whole lower leg in radiograph

In reference to a report by Cooke,¹⁷ we measured nine parameters for the alignment of the lower leg as follows, the hip-knee-ankle lateral angle (HKA), the femorotibial angle (FTA), the femoral neck and shaft angle (FNSA), the femoral condylar-hip angle (CH), the tibial plateau-ankle angle (PA), the inclination angle of the femoral condyles from the horizontal plane (FCI), the inclination angle of the tibial plateau from the horizontal plane (TPI), the femoral condylar-tibial plateau angle (CP) which was defined as the angle between the femoral and tibial joint surface line, and the inclination angle of the talus from the horizontal plane (TI) (Fig. 1a–i). The inclination angles from horizontal line and FNSA were our unique parameters. One orthopedic surgeon measured all indexes in all radiographs. Ideally, if the mechanical axis passed through the knee center, HKA was defined as 0°. In varus deformity, HKA becomes a negative value. As FCI, TPI, and KJA were defined, varus tilt for the knee was indicated in negative degrees, and valgus tilt was indicated in positive degrees. TI became a negative value when the ankle joint slanted lower to the medial side.

For the evaluation of intraclass correlation coefficients (ICC), the same 30 radiographs were measured three times after an interval of two weeks. ICC of HKA and FTA were 0.95 and 0.94, respectively. ICC of CH and PA were 0.89 and 0.93, respectively. Therefore, we considered that the reproducibility was fairly consistent in all parameters.

2.2. Statistical analysis

We compared the radiographic parameters and clinical findings between Groups N, E, and A, and compared these parameters within each Group between men and women. In addition, we evaluated the relationship between all radiographic parameters. In

Fig. 1. Radiographic parameters in a lower limb.

a: the hip-knee-ankle lateral angle (HKA), b: the femorotibial angle (FTA), the femoral neck and shaft angle (FNSA), c: the femoral condylar-hip angle (CH), the tibial plateau-ankle angle (PA), the femoral condylar-tibial plateau angle (CP) which was defined as the angle between the femoral and tibial joint surface line, d: the inclination angle of the femoral condyles from the horizontal plane (FCI), e: the inclination angle of the tibial plateau from the horizontal plane (TPI), f: and the inclination angle of the talus from the horizontal plane (TI).

the nine radiograph parameters, comparisons between each Group were performed using the Welch's *t*-test, and comparisons between men and women were also performed using the Welch's *t*-test. Correlations between each radiographic parameter were analyzed using the Pearson's correlation coefficient test. SPSS version 21 (IBM Corporation, Armonk, New York, USA) was used for all statistical analyses. A *p*-value of 0.05 was considered statistically significant.

Table 1

Basic data of the participants.

		Group N	Group E	Group A	
Number of lower limbs (men/women)		287 (139/148)	36 (13/23)	68 (18/50)	
Age (years)	men	70.5 ± 9.9	75.9 ± 8.2	76.9 ± 6.2	* ‡‡
	women	69.0 ± 8.2	72.4 ± 6.8	77.3 ± 6.4	* ‡‡ ‡‡
Body height (cm)	men	162.4 ± 6.5	163.9 ± 6.9	158.0 ± 4.9	† ‡‡
	women	150.3 ± 6.1	151.9 ± 6.2	147.5 ± 6.6	† ‡‡
Body weight (kg)	men	60.4 ± 10.0	59.7 ± 10.4	58.1 ± 8.2	NS
	women	47.7 ± 6.9	50.8 ± 6.5	52.2 ± 8.1	* ‡‡
Body mass index (kg/m ²)	men	22.8 ± 3.1	22.2 ± 3.1	23.2 ± 2.6	NS
	women	21.1 ± 2.9	22.0 ± 2.3	23.9 ± 2.7	†† ‡‡

mean value ± SD.

*: $p < 0.05$, **: $p < 0.01$ (Group N vs Group E).†: $p < 0.05$, ††: $p < 0.01$ (Group E vs Group A).‡: $p < 0.05$, ‡‡: $p < 0.01$ (Group N vs Group A).

NS: no significance.

3. Results

Basic data regarding age, sex, body height, weight, and body mass index (BMI) for all Groups are shown in Table 1. In men, there were significant differences in age between Group N and Groups E and A. ($p < 0.05$, < 0.01 , respectively). In women, there were significant differences in age between every Group ($p < 0.05$, < 0.01 , < 0.01 , respectively). Participants' ages tended to be older if OA stages were more severe. Although there was no significant difference in body weight and BMI in men between every Group, there were significant differences in body height, weight, and BMI in women. Body height in Group A was significantly smaller and body weight in Group A was heavier than that in Group N and/or Group E.

Table 2 shows the values of radiographic parameters in each Group and the difference between men and women participants. In both sexes, HKA and FTA in Group A were significantly greater than those in Groups N and E ($p < 0.01$, < 0.01 , respectively). Although a difference existed between men and women in Group N, the difference was minimal ($< 1^\circ$). FNSA showed significant differences between Group N and Group A in women and between men and women in Group N. CH and TI were independent of knee OA

severity, although there were significant differences between men and women in all Groups. PA in Group A was greater than that in Groups N and E, and there was significant difference between men and women in Group N. FCI in Group A was significantly less than that in Groups N and E, and there were significant differences between men and women in all Groups. TPI in Group A was greater than that in Group N, and there were significant differences between men and women in Groups N and E. Although there was significant difference of KJA only between Group N and Group A in men, there were significant differences of KJA between every Group in women.

Table 3 shows the correlation between all radiographic parameters. HKA was associated with FTA, PA, and KJA. KJA was associated with FCI and TPI.

4. Discussion

We conducted a study including radiograph examinations focusing on the alignment of the whole spine and leg from 2012.^{18–20} This is the first report examining the relationship between the deformity of the knee and alignment of the whole lower limbs in our cohort study. We believed that a relationship existed between knee osteoarthritis located in the medial compartment and varus deformity of whole lower extremity, and in addition, that the severity of knee osteoarthritis was related to the age. Previously in Japan, Shiozaki et al. reported that aging was one of the risk factors for knee osteoarthritis.^{12,21} In this study, participants in Group A with KL-III and IV were older than those in Group N with KL-0 and I and in Group E with KL-II. Our results were similar to their study in this respect. However, in this study, there were no significant differences of body weight and BMI between each group in men. In women, body weight and BMI with knee osteoarthritis were significantly higher than in those without knee osteoarthritis or with the mild form. Higano et al. reported that advanced knee osteoarthritis had a significantly higher odds ratio compared to early osteoarthritis regarding high BMI in women.²² However, they did not investigate men. Shiozaki et al. reported that a high BMI was strongly related to osteoarthritis of the knees in women, but not in men.¹² In this study, BMI in men was also not related to the severity of knee osteoarthritis. We consider that the pathophysiologic process underlying the progression to severe knee osteoarthritis may differ between men and women.

In recent years, Brouwer et al. in the Rotterdam study reported that varus alignment had an approximately twofold higher risk for the onset of medial knee osteoarthritis compared to normal alignment and clarified the relationship between malalignment and onset of knee osteoarthritis.²³ Several reports have suggested that malalignment of the lower extremity has an influence on

Table 2

The values of radiographic parameters in each Group.

		Group N	Group E	Group A	
HKA	male	181.9 ± 2.6	182.6 ± 3.2	186.6 ± 4.5	†† ‡‡
	female	182.2 ± 2.6	183.6 ± 3.5	187.3 ± 4.8	†† ‡‡
FTA	male	177.2 ± 3.1	178.2 ± 3.4	182.4 ± 4.1	†† ‡‡
	female	176.3 ± 3.0 §§	177.7 ± 3.5	182.7 ± 5.7	†† ‡‡
FNSA	male	132.6 ± 5.0	132.4 ± 6.0	134.9 ± 7.0	NS
	female	130.2 ± 5.2 §§	130.0 ± 5.9	132.3 ± 5.4	†
CH	male	94.2 ± 2.5	94.0 ± 2.5	94.3 ± 2.7	NS
	female	91.5 ± 2.8 §§	91.5 ± 3.2 §	92.0 ± 2.4 §§	NS
PA	male	83.9 ± 2.4	84.3 ± 3.0	82.1 ± 2.3	† ‡‡
	female	85.3 ± 2.4 §§	85.3 ± 2.6	83.3 ± 3.3	†† ‡‡
FCI	male	−4.1 ± 2.7	−3.9 ± 2.4	−5.4 ± 2.8	NS
	female	−0.9 ± 3.0 §§	−1.0 ± 3.4 §§	−3.1 ± 2.6 §§	† ‡‡
TPI	male	−4.0 ± 2.5	−2.9 ± 2.2	−2.5 ± 4.2	†
	female	−1.9 ± 2.8 §§	−0.6 ± 3.4 §	−0.5 ± 3.1	* ‡‡
KJA	male	−0.1 ± 1.7	−1.0 ± 2.4	−2.9 ± 3.7	†‡
	female	1.0 ± 2.2 §§	−0.4 ± 1.5	−2.6 ± 2.7	** †† ‡‡
TI	male	−7.4 ± 5.3	−6.0 ± 6.1	−6.2 ± 7.5	NS
	female	−1.1 ± 6.0 §§	−0.9 ± 5.3 §	0.5 ± 5.6 §§	NS

mean ± SD.

*: $p < 0.05$, **: $p < 0.01$ (Group N vs Group E).†: $p < 0.05$, ††: $p < 0.01$ (Group E vs Group A).‡: $p < 0.05$, ‡‡: $p < 0.01$ (Group N vs Group A).§: $p < 0.05$, §§: $p < 0.01$ (men vs women in each Group).

NS: no significance.

Table 3

The correlation between KL grade and each radiographic index. A: men, B: women.

A		HKA	FTA	FNSA	CH	PA	FCI	TPI	KJA	TI
HKA	R		0.917	−0.089	0.389	0.549	−0.082	0.244	−0.394	0.231
	P		<0.01	0.259	<0.01	<0.01	0.290	<0.01	<0.01	<0.01
FTA	R			0.143	0.182	0.697	−0.193	0.079	−0.327	0.133
	P			0.064	−0.018	<0.01	0.018	0.306	<0.01	0.084
FNSA	R				−0.340	0.181	−0.217	−0.178	−0.043	−0.121
	P				<0.01	−0.018	<0.01	0.020	0.579	<0.01
CH	R					−0.220	0.685	0.426	0.299	0.341
	P					<0.01	<0.01	<0.01	<0.01	0.017
PA	R						−0.431	−0.494	0.087	−0.183
	P						<0.01	<0.01	0.260	0.017
FCI	R							0.657	0.396	0.301
	P							<0.01	<0.01	<0.01
TPI	R								−0.433	0.430
	P								<0.01	<0.01
KJA	R									−0.163
	P									0.033

B		HKA	FTA	FNSA	MDFA	MPTA	DFI	PTI	KJA	AJI
HKA	R		0.466	0.013	−0.330	−0.613	−0.132	0.299	−0.483	0.320
	P		<0.01	0.849	<0.01	<0.01	0.049	<0.01	<0.01	<0.01
FTA	R			0.086	−0.083	−0.382	−0.161	0.014	−0.198	0.089
	P			0.203	0.219	<0.01	0.017	0.840	<0.01	0.186
FNSA	R				0.271	−0.137	−0.228	−0.094	−0.154	−0.099
	P				<0.01	0.043	<0.01	0.163	0.022	0.144
MDFA	R					−0.193	−0.745	−0.452	−0.344	−0.382
	P					<0.01	<0.01	<0.01	<0.01	<0.01
MPTA	R						0.474	0.436	0.054	0.025
	P						<0.01	<0.01	0.429	0.713
DFI	R							0.605	0.464	0.265
	P							<0.01	<0.01	<0.01
PTI	R								−0.425	0.362
	P								<0.01	<0.01
KJA	R									−0.101
	P									0.132

R: Pearson's correlation coefficient.

knee osteoarthritis.^{10,12–15,21,23} In this study, FTA and HKA in people with severe radiographic knee osteoarthritis were varus compared to those in people with normal and mild knee osteoarthritis. However, Hunter et al. reported in a Framingham Osteoarthritis Study that malalignment may be a marker for the severity and progression of knee osteoarthritis but is not predictive of the onset of the disease.²⁴ Therefore, it remains unclear whether malalignment of the lower extremity is a cause or consequence of knee osteoarthritis.

Cooke et al. reported that the valgus degree of the femoral condyle with varus knee osteoarthritis was lesser in patients compared to healthy adults in Canada.²⁵ Our results, which show that knee osteoarthritis was not associated with the deformity of the distal femoral condyle but with the proximal tibial condyle, might be different from their result. A probable cause for this was that lower limbs with valgus alignment were excluded in this study. Thus, healthy participants with valgus alignment of the lower limbs whose HKA was over 0° were not included. They might have a more significantly valgus femoral condyle. However, Higano et al. clarified that varus alignment of the proximal tibial plateau already exists before the onset of knee osteoarthritis in advanced osteoarthritis and varus alignment because the proximal tibia influences the morphologic alterations of proximal medial tibia.²² This influence might be due to racial differences. Although Higano et al. used radiographs only around the knee joint and not the whole leg,²² in this study we evaluated the deformities of the distal femoral condyle and proximal tibial plateau using radiographs of the whole leg in the standing position. In our survey, TPI was

preserved until KL-II in Group E, and PA in Group A was greater (varus for the knee) than for those in Group N and E. However, CH did not differ between all groups. FCI differed in only Group A in women. Therefore, proximal tibial condyle deformity and tibial plateau inclination might be crucial for development of medial knee osteoarthritis compared to distal femoral condyle deformity in the Japanese. TI was also preserved even in Group A. Thus, TI may not be influenced by the presence of knee osteoarthritis as much.

Nonetheless, Aoda et al.²⁶ and Omori et al.²⁷ reported that lateral thrust is one of the predictors of varus knee osteoarthritis in the Japanese. FTA and HKA as static parameters of knee alignment may have less influence on medial knee osteoarthritis than dynamic mechanical factors, such as lateral thrust. However, their method for evaluating lateral thrust comprised clinical findings during gait. Consequently, a precise procedure for evaluating lateral thrust quantitatively may be necessary. Similar to their findings, the results of our study indicate that severe knee osteoarthritis might not depend on femoral condyle deformity but on femoral condyle inclination.

Regarding the difference between severe knee osteoarthritis and non-osteoarthritis in the femur, CH was not related to severity of knee osteoarthritis and FCI was related to knee osteoarthritis in women only. In contrast, PA and TPI differed between all groups in both men and women. In conclusion, we considered that a difference of the tibial side, such as PA and TPI, could be significantly associated with progression of knee osteoarthritis.

There were several limitations to this study. First, the study had a cross-sectional design, and it remains unclear whether malalignment of the lower extremity, knee inclination, and the change in the morphology of the proximal tibial condyle are a cause or a consequence of knee osteoarthritis. Second, the number of subjects with knee osteoarthritis, especially Group A, was small compared to persons in Group N. Third, we had no clinical findings regarding, for example, range of knee motion and knee pain. As whole leg radiographs were taken in a natural position in each participant, we did not consider rotational alignment in leg position, which may affect all radiographic parameters examined in this study.

In this study, we showed that varus alignment of lower limbs, varus deformity of the proximal tibial condyle, and varus inclination of tibial plateau were associated with medial knee osteoarthritis severity. Therefore, we must consider not only the varus alignment of the lower limbs but also the morphology of the proximal tibial condyle and joint surface inclination of the distal femur before the onset of knee osteoarthritis. However, the alteration in tibial condyle morphology and tibial plateau inclination may pre-exist and predispose to knee osteoarthritis, and it is possible that these alterations occur as knee osteoarthritis progresses. A longitudinal analysis including a greater number of advanced knee osteoarthritis cases may be considered for further research.

Contributions

MH participated in the design of the study, measured the data, contributed to statistical analyses, made interpretation of results, and drafted the manuscript.

HH, HK, and YM acquired the data, made interpretation of the results, and revised the manuscript.

All authors have approved the final version for submission.

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Conflict of interest

None.

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