Sex Differences in Knee Joint Loading: Cross-Sectional Study in Geriatric Population

Du Hyun Ro, Dong Yeon Lee, Giho Moon, Sahnghoon Lee, Sang Gyo Seo, Seong Hwan Kim, In Woong Park, Myung Chul Lee

Department of Orthopaedic Surgery, Seoul National University Hospital, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 110-744, South Korea

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ABSTRACT: This study investigated sex differences in knee biomechanics and investigated determinants for difference in a geriatric population. Age-matched healthy volunteers (42 males and 42 females, average age 65 years) without knee OA were included in the study. Subjects underwent physical examination on their knee and standing full-limb radiography for anthropometric measurements. Linear, kinetic, and kinematic parameters were compared using a three-dimensional, 12-camera motion capture system. Gait parameters were evaluated and determinants for sex difference were evaluated with multiple regression analysis. Females had a higher peak knee adduction moment (KAM) during gait ($p = 0.004$). Females had relatively wider pelvis and narrower step width (both $p < 0.001$). However, coronal knee alignment was not significantly different between the sexes. Multiple regression analysis revealed that coronal alignment ($b = 0.014$, $p < 0.001$), step width ($b = -0.010$, $p = 0.011$), and pelvic width/height ratio ($b = 1.703$, $p = 0.046$) were significant determinants of peak KAM. Because coronal alignment was not different between the sexes, narrow step width and high pelvic width/height ratio of female were the main contributors to higher peak KAM in females. Sex differences in knee biomechanics were present in the geriatric population. Increased mechanical loading on the female knee, which was associated with narrow step width and wide pelvis, may play an important role in future development and progression of OA. © 2016 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res

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Knee osteoarthritis (OA) is among the most common and disabling medical conditions of the elderly.[1] The prevalence of symptomatic knee OA is an estimated 12.1% in adults older than 60 years, and nearly one in two individuals develop OA within their lifetime.[2,3] Advanced age and female sex are well-known non-modifiable risk factors of knee OA.[4,5] Prospective MRI studies show that women lose more cartilage at a faster rate than men after age 40 years,[6,7] and prevalence of knee OA is 2–3 times higher in older females than in age-matched males.[4,5]

Although, the effect of age and sex on presence of OA is well-established, the reasons for these discrepancies are unclear. Hormonal imbalance, such as reduced estrogen levels after menopause, is a popular theory among rheumatologists,[8] but current evidence is insufficient to support this.[8,9] Conversely, few have investigated biomechanical difference between the sexes, even though the difference in OA prevalence between the sexes is particularly prominent at the knee joint.[4,5] The risk of OA is two times higher in the female knee joint than in the male knee joint, but this discrepancy is not apparent in the hip or ankle joint.[4,5] This may indicate unique biomechanical features of the female knee joint, rather than systemic effect of hormones, may be responsible for the development of knee OA.

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Correspondence to: Myung Chul Lee (T: +82-2-2072-3212; F: +82-2-764-2718; E-mail: leemc@snu.ac.kr)

Unique features of female skeletal dimension and knee mechanics have been described in the literature.[10–15] Females have a wider, anteriorly tilted pelvis and greater valgus alignment than men, which is related to a unique gait pattern of increased up-and-down motion at the pelvis and narrower step width.[13,14] Acetabular orientation, increased anteversion, and abduction angle of female pelvis are also unique features of female.[16,17]

However, literature to support the relationship between skeletal dimensions and knee biomechanics is scarce.[13,14] We hypothesized that in a geriatric population, females would show greater knee joint loading relative to age-matched males, which would be associated with anthropometric features of females, and that these biomechanical differences of the knee joint would partially explain the female predisposition of knee OA. Therefore, this study aimed to determine (i) sex differences in knee joint loading in a geriatric population; and (ii) and to investigate determinants for such difference.

METHODS

Cross-sectional study performed for geriatric volunteers without the evidence of osteoarthritis (level of evidence: diagnostic test level II).

Study Subjects

This study was approved by the institutional review board at our institution, and informed consent was obtained from all subjects prior to participation. A total of 49 males and 50 age-matched females healthy geriatric volunteers were investigated. Medical records of the subjects were obtained, and participants underwent a physical examination and standing full-limb radiography of the knee. Volunteers were excluded if they had (i) difficulty or pain when walking more than five blocks; (ii) concurrent knee pain; (iii) evidence of radiographic osteoarthritis of the knee, hip, or ankle (grades 1–4 OA by

Kellegren–Lawrence [KL] scale); (iv) any prior surgery on the bones in the lower extremity; (v) neuromuscular involvement in the lower extremities; (vi) spine problem that limited activities of daily living; and (vii) mechanical axis on standing full-limb radiography greater than 5° of valgus or varus. This left 42 females and 42 males volunteers without knee OA who were included in the analysis. Average height, weight, and BMI of the female subjects were 153.6 cm, 57.8 kg, and 24.5 kg/m^2, respectively and 167.8 cm, 69.8 kg, and 24.8 kg/m^2 of the male subjects. Average age was 64.5 years in both sex groups and ranged from 60 to 69 years old (Table 1).

Data Collection

Gait Analysis Protocol

Gait data were collected from the Human Motion Analysis Lab at our institution. Participants were asked to perform 5 min of easy walking to warm up. After warming up, subjects had reflective markers from the Helen Hayes marker set placed at the following landmarks by a single operator with 17 years of experience (this operator also processed the data). Subjects were asked to walk at their usual speed along a 9-m track. Motion (kinematic) data were collected at a sample rate of 120 Hz using 12 couple-charged device (CCD) cameras with a three-dimensional optical motion capture system (Motion Analysis, Santa Rosa). Eva Real-Time software (Motion Analysis) and Microsoft Excel 2010 (Microsoft, Redmond) were used for real-time motion capture, post-processing, and marker data tracking. Average of three representative strides from five or six separate trials were used for analysis from each session. Linear gait data, namely walking speed (cm/sec), cadence (steps/min), stride length (cm), step width (cm), stance phase (% cycle), and swing phase (% cycle) were obtained. Step width was measured as the distance between ankle centers on the coronal plane during the foot strike of each foot averaged across all foot strike events. Ground reaction force (kinetic) data of each plane was normalized to height and weight (%BW*Ht). Sagittal data included pelvic tilt (orientation of the pelvis with respect to the femur), hip flexion (flexion angle with respect to the pelvis), knee flexion, ankle flexion, hip extension moment, knee extension moment, and ankle plantar flexion moment. Coronal data included pelvic obliquity (obliquity of the pelvic segment with respect to the horizontal line), hip adduction, knee varus, hip abduction moment, knee adduction moment (KAM), and ankle varus moment.

Table 1. Population Characteristics and Anthropometric Data of Study Subjects

	Female ($n = 42$) Mean (SD)	Male ($n = 42$) Mean (SD)	p
Age (years)	64.5 (2.7)	64.5 (2.8)	0.937
Height (cm)	153.6 (5.1)	167.8 (5.9)	**<0.001**
Weight (kg)	57.8 (7.5)	69.8 (8.3)	**<0.001**
BMI (kg/m^2)	24.5 (3.0)	24.8 (2.5)	0.654
Mechanical axis	Varus 1.69 (1.76)	Varus 1.88 (1.65)	0.615
Pelvic width (cm)	29.6 (1.64)	29.3 (1.06)	0.309
ANCOVA F value[a]	41.19 (d.f. = 1)		**<0.001**
Estimated value	30.60	28.20	**<0.001**
Pelvic width/height ratio	0.193 (0.009)	0.175 (0.005)	**<0.001**
Leg length (cm)	84.5 (4.3)	93.1 (3.7)	**<0.001**
ANCOVA F value[a]	155.49 (d.f. = 1)		**<0.001**
Estimated value	88.70	88.90	0.827

d.f., Degree of freedom; SD, standard deviation. Bold face indicates statistical significance.
[a]ANCOVA tests were done with height as the covariate, and sex as the fixed factor. Comparisons between continuous data was done by independent t-test.

Radiographic Assessment

The entire radiographic evaluation was independently performed by two authors who were fellowship-trained in arthroplasty and were blinded to other information of the study subjects. The inter-observer reliability for radiologic assessment was satisfactory (Cronbach's α value of 0.85–0.94). Thus, assessments taken from a single investigator (DHR) were used in the analyses. Mechanical axis was measured using standing full-limb radiography. It was defined as an angle formed by a line drawn from the center of the femoral head to the center of knee joint and a line drawn from the center of knee joint to the center of the ankle joint.

Leg length was measured from anterior–superior iliac spine to the medial malleolus of the ipsilateral leg. Pelvic width was measured as the widest point on AP radiography. All radiographic images were digitally acquired using a picture archiving and communication system (PACS) (Maroview 5.4, Infinitt, Seoul, Korea). Assessments were carried out using the PACS software while controlling the magnification.

Statistical Analysis

To calculate sample size, we assumed that 15% difference of KAM would be significant and set male's KAM values at 3.8 ± 0.9 (%BW*HT).[16] With α-error 0.05 and β-error 0.2, sample size was calculated to be 41 subjects in each sex groups. Considering exclusion criteria, we first included 50 subjects in each group. Sample size was determined with G*Power3® (Erdfelder et al., 1996).[17]

To find sex differences in knee joint loading, we first divided each volunteer's kinetic and kinematic data according to a standard gait cycle, namely initial double limb support (IDS), single limb support (SLS), terminal double limb support (TDS), and swing (SW) phase. Mean value of each gait cycle (i.e., IDS, SLS, TDS, and SW) was then compared with student t-tests. Peak value data were extracted and comparisons were made using student t-tests. Data from the right leg were used for statistical analysis.

Our gait data analysis included multiple comparisons, which include four gait trial segments $\times$ 13 measures $\times$ 1 quantity (mean) + 3 peak values (peak KAM, peak KEM, peak varus) + 6 linear gait measures. Hence, p-values were adjusted using Hochberg method in order to correct for multiple testing.[18] Adjusted p values <0.05 were considered statistically significant.

Basic characteristics and anthropometric differences were compared with student t-tests. ANCOVA, with height as a covariate and sex as the fixed factor, was used to analyze differences in leg length, speed, stride length, step width, and pelvic width.

Pearson's correlation coefficients were used to investigate the association between anthropometric data and gait parameters, linear regression analysis, and plotted scattergrams were used to investigate their relative contributions to knee joint loading. In regression, factors with a p-value

<0.20 in the univariate analysis were assessed subsequently with multivariate analysis using the stepwise method.

All statistical analyses were performed using SPSS® 19.0.1 for Windows® (SPSS Inc, Chicago, IL), and p-values <0.05 were considered significant.

RESULTS

Anthropometrics

Females were shorter and weighed less ($p < 0.001$), although BMI was similar between the sexes ($p = 0.654$) (Table 1). The mechanical axis on radiography was also similar, with both sexes showing slight varus alignment (female: varus 1.69°, male: varus 1.88°, $p = 0.615$). Pelvic width was similar but was wider in females when normalized to height ($p < 0.001$). Leg length was shorter in females ($p < 0.001$) and it was due to their shorter height (after normalization, $p = 0.827$).

Gait Data

Linear Data

Distribution of stance/swing phase was similar between the sexes ($p = 0.995$, Table 2). Despite the shorter stature of women, gait speed was similar to males ($p = 0.995$) due to the higher cadence in females. Female walked 5.1 steps more than male in a minute (female: 114.8 steps/min, male: 109.7 steps/min, $p = 0.038$). Stride length was shorter in females but it was due to their shorter stature. Despite the wider pelvis in females, step width was constantly narrower and was independent of short stature (female: 8.4 cm, male 11.6 cm, $p < 0.001$).

Kinematics and Kinetics

Sex differences in knee joint loading are presented in Figure 1. Knee adduction moment which reflects medial compartment loading, was increased in female at SLS phase ($p = 0.003$). Peak KAM was also higher in females (female: 2.76 (%BW*Ht), male: 2.18 (%BW*Ht), $p = 0.004$). However, coronal knee alignment during those phases (i.e., dynamic alignment) was not different (Fig. 1b). Peak knee joint varus during the stance phase was 5.70° in females and 5.78° in males ($p = 0.995$). Knee extension moment and knee flexion angle were similar between sexes (Fig. 1c and d). Hip adduction angle was higher and hip adduction moment was increased in females (Fig. 1e and f). Pelvic obliquity (coronal motion) was also increased in females ($p = 0.005$) (Fig. 1g).

Table 2. Linear Gait Data

	Female ($n = 42$)	Male ($n = 42$)	
	Mean (SD)	Mean (SD)	p
Stance phase (%)	60.6	61.0	0.995
Swing phase (%)	39.4	39.0	0.995
Cadence (steps/min)	114.8 (7.1)	109.7 (6.2)	**0.038**
Speed (cm/min)	111.2 (8.2)	113.8 (8.7)	0.995
ANCOVA F value[a]	0.002 (d.f. = 1)		0.965
Estimated value	111.2	113.7	0.416
Stride length (cm)	115.7 (7.2)	124.0 (7.2)	**<0.001**
ANCOVA F value[a]	7.960 (d.f. = 1)		**0.006**
Estimated value	118.5	121.3	0.258
Step width (cm)	8.4 (1.9)	11.6 (2.3)	**<0.001**
ANCOVA F value[a]	0 (d.f. = 1)		0.983
Estimated value	8.4	11.6	**<0.001**

d.f., Degree of freedom; SD, standard deviation. Bold face indicates statistical significance.
[a]ANCOVA tests were done with height as the covariate, and sex as the fixed factor. Comparisons between continuous data was done by independent t-test.

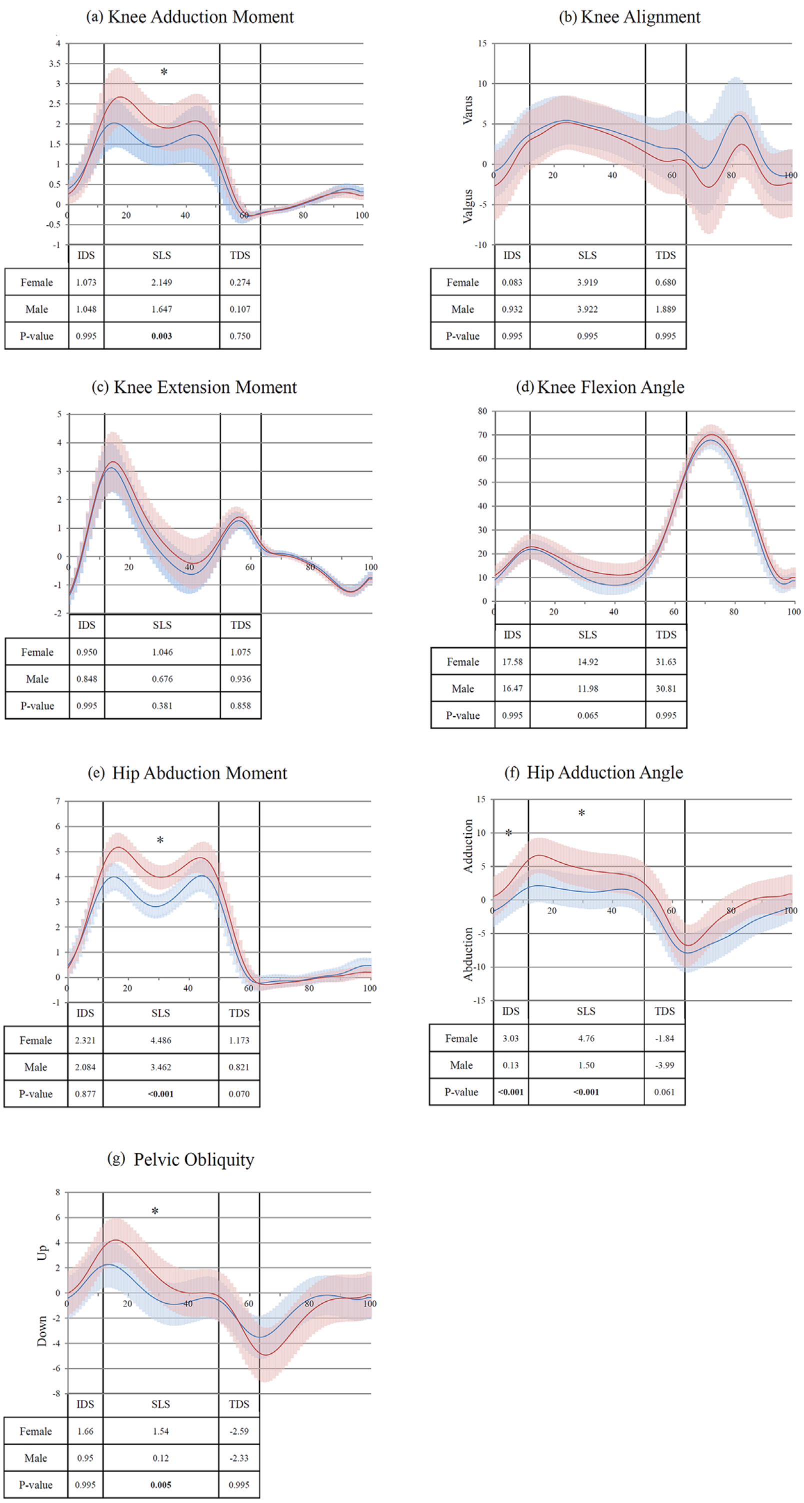
Factors Associated With Higher KAM in Females

We investigated factors associated with increased KAM in female. Peak KAM was significantly associated with step width ($r = -0.509$, $p < 0.001$), pelvic width/height ratio ($r = 0.412$, $p < 0.001$), peak knee varus during stance phase ($r = 0.546$, $p < 0.001$), and radiographic measurement of the mechanical axis ($r = 0.418$, $p < 0.001$). However, cadence, speed, pelvic width, stride length, coronal pelvis, and hip motion were not associated with peak KAM. Multiple regression analysis was performed to investigate the relative contributions of factors to medial knee joint loading. Factors with a p-value <0.20 in the univariate analysis included, namely, step width, pelvic width/height ratio, and peak knee varus during stance phase. Our model showed that peak knee varus ($b = 0.101$ [95%CI 0.06–0.14], $p < 0.001$), step width ($b = -0.072$ [95%CI −0.12 to 0.0.02, $p = 0.008$), and pelvic width/height ratio ($b = 17.68$ [95%CI 6.41–28.94], $p = 0.003$) were significant predictors of peak KAM. The model had an adjusted R^2 of 0.477. As the peak knee varus was not different between the sexes, narrow step width, and high pelvic width/height ratio in females were likely the main contributors to higher peak KAM in females (Fig. 2a–c).

DISCUSSION

The objective of this study was to investigate sex differences in knee joint loading in geriatric population and to find factors associated with this sex difference. In this study, we demonstrated increased loading in the female knee joint that was associated with narrower step width and wider pelvis.

Female predominance of knee joint OA is well described in the literature, as epidemiologic studies have shown that females have approximately a twofold greater risk of developing knee joint OA relative to males.[4,5] In particular, females ≥55 years tend to have increased rates of knee OA as well as more severe knee OA.[4–7] Although the effect of sex on knee joint OA is established in the literature, biomechanical explanations for this discrepancy are lacking. In addition, previous investigations of biomechanical factors have been performed mainly on the young healthy population. Cho et al. has shown that anthropometric characteristics of females influenced the gait pattern,[14] and



(a) Knee Adduction Moment

	IDS	SLS	TDS
Female	1.073	2.149	0.274
Male	1.048	1.647	0.107
P-value	0.995	**0.003**	0.750

(b) Knee Alignment

	IDS	SLS	TDS
Female	0.083	3.919	0.680
Male	0.932	3.922	1.889
P-value	0.995	0.995	0.995

(c) Knee Extension Moment

	IDS	SLS	TDS
Female	0.950	1.046	1.075
Male	0.848	0.676	0.936
P-value	0.995	0.381	0.858

(d) Knee Flexion Angle

	IDS	SLS	TDS
Female	17.58	14.92	31.63
Male	16.47	11.98	30.81
P-value	0.995	0.065	0.995

(e) Hip Abduction Moment

	IDS	SLS	TDS
Female	2.321	4.486	1.173
Male	2.084	3.462	0.821
P-value	0.877	**<0.001**	0.070

(f) Hip Adduction Angle

	IDS	SLS	TDS
Female	3.03	4.76	-1.84
Male	0.13	1.50	-3.99
P-value	**<0.001**	**<0.001**	0.061

(g) Pelvic Obliquity

	IDS	SLS	TDS
Female	1.66	1.54	-2.59
Male	0.95	0.12	-2.33
P-value	0.995	**0.005**	0.995

Figure 1. Kinetic and kinematic data stratified by sex. Red curve represents females; blue curve represents males. Shaded region represents ± one standard deviation. Mean data of each sex at initial double limb support phase (IDS), single limb support phase (SLS), and terminal double limb support phase (TDS) are described in the table. Asterisks in the graph and bold face type in the table indicates statistical significance. a) Knee adduction moment during the SLS and TDS phases was significantly higher in females; b) Knee alignment throughout the whole gait sequence was not statistically different between sexes; c) Knee extension moment during both the SLS and TDS phases was higher in females; d) Knee flexion angle during the SLS phase was higher in females; e) Hip adduction moment during the whole gait sequence was higher in females; f) Hip adduction angle during the whole gait sequence was significantly higher in females; g) Coronal pelvic motion and pelvic obliquity during the SLS phase was higher in women.

Kerrigan et al. compared knee joint torque during gait in both sexes.[13] They both concluded knee joint loading was not significantly different between both sexes. However, as gait changes with age, studies on the young, healthy population may have profound limitations for investigating biomechanical contributions to the development of OA in older individuals.[2,3,19,20] Therefore, cross-sectional study in a geriatric population is necessary to investigate the biomechanical contribution to the female predisposition to knee OA. We investigated geriatric volunteers without knee joint OA, as evidenced by both radiologic and clinical, and who could walk at least five blocks without pain or discomfort. To the best of our knowledge, this was the first report that demonstrated increased joint loading in geriatric females without knee OA.

Our data showed that geriatric females had 27% higher peak KAM and 30% higher average KAM in the

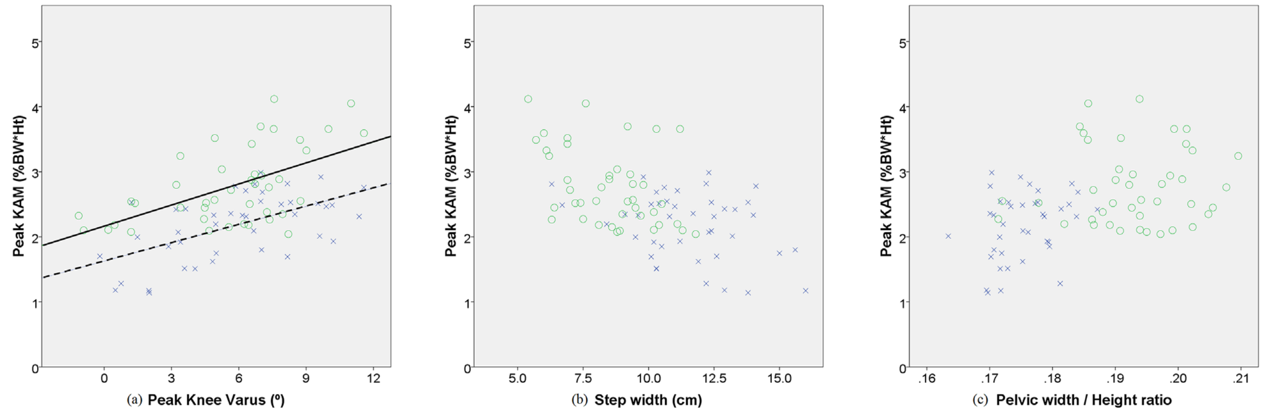


Figure 2. Scatter plot of peak KAM and associated variables. Female data were marked with "o," and male data was marked with "x." a) Scatter plot of peak KAM versus peak knee varus. Straight line indicates female trend line, and dotted line indicates male trend line. Females showed higher trend line than males, which was attributed to narrower step width and wider pelvis in females (b and c); b) Scatter plot of peak KAM versus step width. Females showed narrower step width and higher peak KAM; c) Scatter plot of peak KAM versus pelvic width/height ratio. Females showed wider pelvic width and higher peak KAM.

stance phase, indicating the female knee joint has substantially higher medial knee joint loading during gait.[21] Because KAM is also associated with arthritis progression and future loss in cartilage volume,[16,22,23] our results support the idea that biomechanical differences of the knee joint contribute to increased knee OA in females. Miyazaki et al. reported in their prospective 6-year follow-up study that the risk of knee OA was 6.46 times higher with a 1%BW*Ht increase in adduction moment.[22] Our female group showed 0.58%BW*Ht increase in peak KAM relative to male counterparts.

KAM is calculated as the product of the coronal plane GRF vector and the perpendicular distance from the vector to the knee joint center and is the best predictor of lower extremity alignment.[24,25] Varus alignment increases the moment arm, which increases KAM. Our result confirmed previous studies that show KAM as the best predictor of lower extremity alignment and that dynamic alignment was a more accurate predictor of KAM than X-ray measurements of static alignment.[24,25]

Despite substantial effect of alignment on KAM, lower extremity alignment was not different between both sexes, indicating the increased KAM in females cannot be explained by differences in alignment. Females had a wider pelvis and narrower step width than males, and our data showed that both of these variables increased KAM in females. We speculate that the wider pelvis increases the lever arm of the body center of mass (COM), which shifts the GRF more medially and causes an increase in KAM due to the greater perpendicular distance from the GRF to the center of the knee joint (Fig. 3). Narrow step width

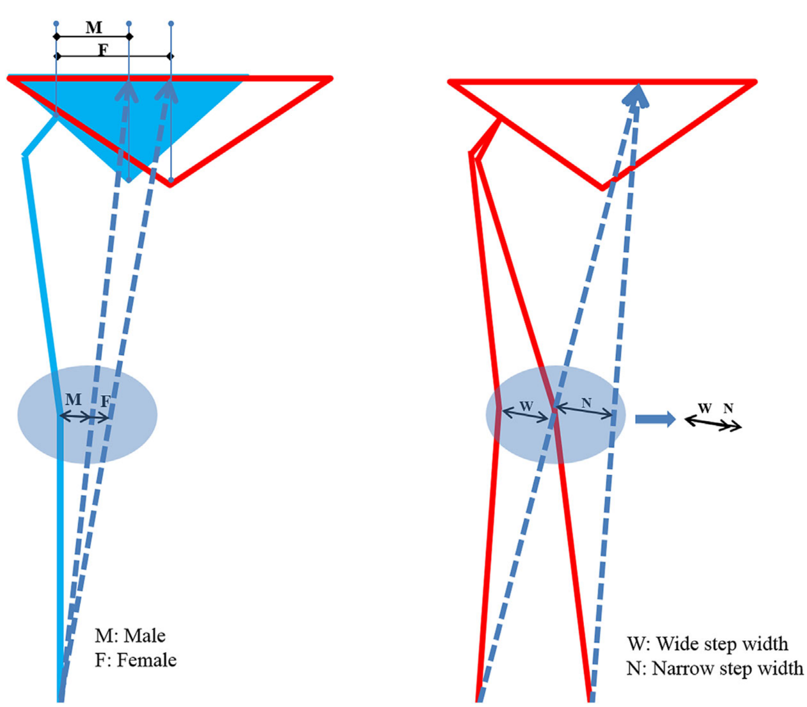


Figure 3. Schematic representations of KAM change according to the pelvic width and step width. Double arrow represents KAM, which is calculated as the product of the coronal plane ground reaction force (GRF) vector and the perpendicular distance from the vector to the knee joint center. Dotted line represents GRF. Left figure represents relatively narrow pelvis of male versus wider pelvis of female. KAM was increased in female. Right figure represents wide versus narrow step width at single limb stance phase. KAM was increased in wide pelvis.

also shifts the GRF vector more medially to the knee joint. Our results supports previous research that narrow step width increases KAM.[26]

Narrow step width was a unique characteristic of the female gait, although the reasons for this are unclear. Wider step width requires more power from the abductors, and on average, females have weaker abductor muscles and increased lever arm of body COM relative to males.[27,28] Thus, we speculate that the weaker abductor muscles in female may contribute to the narrower step width because these muscles would not have to work as hard. However, the narrow step width increases knee joint loading and may contribute to development of OA, which in turn may lead to a wider step width to decrease knee pain in their old age.

Our result should be considered in future research in knee OA. As geriatric female knee have increased loading in their knee, cartilages are more vulnerable to injury and subsequent progression of OA. When performing TKA, our biomechanical results should be also considered. Wider pelvis and narrow step width of female could result higher medial joint loading than male even after TKA. Gait retraining or specifically designed implant could be investigated in near future.

This study has some limitations. First, due to the cross-sectional nature of this study, we could not establish a causal relationship between increased KAM and knee OA in females. However, several prospective studies have indicated this causal relationship.[16,22,23] Miyazaki et al. first reported that baseline KAM predicts radiographic OA progression, as the risk of knee OA increased 6.46 times with a 1%Ht*BW increase.[22] Causal relationship has been supported by later prospective studies with a similar design.[16,23] Although our study design did not show the causal relationship, evidence from currently published literature strongly suggests the association.[16,22,23] However, further prospective longitudinal studies should be conducted to draw a more definite conclusion. Another limitation of our study is that we could not assess baseline cartilage status and meniscus status because we did not perform MRI scan in all patients. However, our participants likely represented a normal population without OA, as we excluded individuals with radiographic or clinical evidence of OA or possible OA. Furthermore, range of motion, KAM, gait speed, and cadence were characteristic of the normal population, further indicating our study subjects did not have OA. Third, a considerable amount of variance in our multivariate model remained unexplained. This indicates that other unknown factors, such as acetabular orientation or muscle function may have been related to the differences.[16,17] In the near future, we plan to improve our research by integrating such data.

In conclusion, this study showed sex differences in knee biomechanics in a geriatric population. Increased mechanical loading at the female knee, which was associated with narrower step width and wider pelvis, may play an important role in the development and progression of OA.

AUTHORS' CONTRIBUTIONS

DHR participated in data collection, performed data analysis, and interpretation, conception and design of the study, and drafted the manuscript. DYL participated in data collection, data analysis, and data interpretation. GM participated in data analysis and interpretation. SL coordinated all suggestions and edits. SGS participated in data collection and analysis. SHK participated in data analysis and interpretation. IWP participated in data analysis and collection. MCL participated conception and design of the study and data interpretation. All authors participated in reviewing and editing the manuscript, and approved the final manuscript.

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REFERENCES

1. Guccione AA, Felson DT, Anderson JJ, et al. 1994. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health 84:351–358.
2. Dillon CF, Rasch EK, Gu Q, et al. 2006. Prevalence of knee osteoarthritis in the United States: arthritis data from the third national health and nutrition examination survey 1991–94. J Rheumatol 33:2271–2279.
3. Murphy L, Schwartz TA, Helmick CG, et al. 2008. Lifetime risk of symptomatic knee osteoarthritis. Arthritis Rheum 59:1207–1213.
4. Prieto-Alhambra D, Judge A, Javaid MK, et al. 2014. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. Ann Rheum Dis 73: 1659–1664.
5. Srikanth VK, Fryer JL, Zhai G, et al. 2005. A meta-analysis of sex differences prevalence, incidence and severity of osteoarthritis. Osteoarthritis Cartilage 13:769–781.
6. Hanna FS, Teichtahl AJ, Wluka AE, et al. 2009. Women have increased rates of cartilage loss and progression of cartilage defects at the knee than men: a gender study of adults without clinical knee osteoarthritis. Menopause 16:666–670.
7. Ding C, Cicuttini F, Blizzard L, et al. 2007. A longitudinal study of the effect of sex and age on rate of change in knee cartilage volume in adults. Rheumatology (Oxford) 46:273–279.
8. Roman-Blas JA, Castaneda S, Largo R, et al. 2009. Osteoarthritis associated with estrogen deficiency. Arthritis Res Ther 11:241.
9. Nevitt MC, Felson DT, Williams EN, et al. 2001. The effect of estrogen plus progestin on knee symptoms and related disability in postmenopausal women: the Heart and Estrogen/Progestin Replacement Study, a randomized, double-blind, placebo-controlled trial. Arthritis Rheum 44:811–818.

10. Horton MG, Hall TL. 1989. Quadriceps femoris muscle angle: normal values and relationships with gender and selected skeletal measures. Phys Ther 69:897–901.
11. Simoneau GG, Hoenig KJ, Lepley JE, et al. 1998. Influence of hip position and gender on active hip internal and external rotation. J Orthop Sports Phys Ther 28:158–164.
12. Kerrigan DC, Todd MK, Della Croce U. 1998. Gender differences in joint biomechanics during walking: normative study in young adults. Am J Phys Med Rehabil 77:2–7.
13. Kerrigan DC, Riley PO, Nieto TJ, et al. 2000. Knee joint torques: a comparison between women and men during barefoot walking. Arch Phys Med Rehabil 81:1162–1165.
14. Cho SH, Park JM, Kwon OY. 2004. Gender differences in three dimensional gait analysis data from 98 healthy Korean adults. Clin Biomech (Bristol, Avon) 19:145–152.
15. McKean KA, Landry SC, Hubley-Kozey CL, et al. 2007. Gender differences exist in osteoarthritic gait. Clin Biomech (Bristol, Avon) 22:400–409.
16. Bennell KL, Bowles KA, Wang Y, et al. 2011. Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. Ann Rheum Dis 70:1770–1774.
17. Faul F, Erdfelder E, Lang AG, et al. 2007. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. Behav Res Methods 39:175–191.
18. Hochberg Y. 1988. A sharper Bonferroni procedure for multiple tests of significance. Biometrika 75:800–802.
19. Ko SU, Hausdorff JM, Ferrucci L. 2010. Age-associated differences in the gait pattern changes of older adults during fast-speed and fatigue conditions: results from the Baltimore longitudinal study of ageing. Age Ageing 39:688–694.
20. Callisaya ML, Blizzard L, Schmidt MD, et al. 2010. Ageing and gait variability—a population-based study of older people. Age Ageing 39:191–197.
21. Birmingham TB, Hunt MA, Jones IC, et al. 2007. Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. Arthritis Rheum 57:1012–1017.
22. Miyazaki T, Wada M, Kawahara H, et al. 2002. Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. Ann Rheum Dis 61:617–622.
23. Chehab EF, Favre J, Erhart-Hledik JC, et al. 2014. Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis. Osteoarthritis Cartilage 22:1833–1839.
24. Schmitz A, Noehren B. 2014. What predicts the first peak of the knee adduction moment? Knee 21:1077–1083.
25. Barrios JA, Royer TD, Davis IS. 2012. Dynamic versus radiographic alignment in relation to medial knee loading in symptomatic osteoarthritis. J Appl Biomech 28:551–559.
26. Brindle RA, Milner CE, Zhang S, et al. 2014. Changing step width alters lower extremity biomechanics during running. Gait Posture 39:124–128.
27. Kubinski SN, McQueen CA, Sittloh KA, et al. 2014. Walking with wider steps increases stance phase gluteus medius activity. Gait Posture 41:130–135.
28. Kim JW, Kwon Y, Chung HY, et al. 2011. Age-sex differences in the hip abductor muscle properties. Geriatr Gerontol Int 11:333–340.