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A Sex Comparison of Ambulatory Mechanics Relevant to Osteoarthritis in Individuals With and Without Asymptomatic Varus Knee Alignment

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The prevalence of medial knee osteoarthritis is greater in females and is associated with varus knee alignment. During gait, medial knee osteoarthritis has been linked to numerous alterations. Interestingly, there has been no research exploring sex differences during walking in healthy individuals with and without varus alignment. Therefore, the gait mechanics of 30 asymptomatic individuals with varus knees (15 females) and 30 normally-aligned controls (15 females) were recorded. Gait parameters associated with medial knee osteoarthritis were analyzed with two-factor analyses of variance. In result, varus males exhibited the greatest peak knee adduction moments, while normal females showed the greatest peak hip adduction angles and pelvic drop excursions. By sex, females exhibited greater peak hip adduction angles and moments and greater pelvic drop excursion, but lesser peak knee adduction angles. By alignment type, varus subjects exhibited greater peak knee adduction angles and moments, midstance knee flexion angles and excursion, and eversion angles and lateral ground reaction forces, but lesser peak hip adduction angles. In conclusion, females generally presented with proximal mechanics related to greater hip adduction, whereas males presented with more knee adduction. Varus subjects demonstrated a number of alterations associated with medial knee osteoarthritis. The differential sex effects were far less conclusive.

Keywords: gait, malalignment, varum

The etiology of idiopathic knee osteoarthritis (OA) is not well understood. While the occurrence of knee OA is more common in women, potential mechanical mechanisms explaining this sex difference in the onset of disease remain elusive.[1,2] In contrast, studies have identified knee malalignment as a prominent mechanical risk factor for incident knee OA, specifically varus knee structure leading to medial compartment OA via elevated articular cartilage contact stresses.[3–5] The construct that mechanical loading can lead to cartilage degradation implicates an ambulatory component to the disease initiation process.[6]

Kinematic and kinetic alterations to level walking due to medial knee OA are multijoint and multiplanar.[7] The most hallmark findings include elevated knee adduction angles and moments and decreased knee flexion angles and moments.[8–10] In a gait study investigating gender differences in knee OA patients compared with controls, OA patients generally showed elevated knee adduction, but females with OA were the subgroup demonstrating the most profound decreases in knee flexion.[11] The authors also determined that anthropometrics, stride characteristics (speed, stride length, and stance time), pain, stiffness, physical function, and disease severity did not significantly influence this interaction between gender and disease.

While studying individuals with medial knee OA is necessary to understand the progressive nature of the disease, evaluating populations at risk for developing OA is critical for identifying preventative measures. One such at-risk population is the varus-aligned individual. In a healthy, predominantly male cohort with varus malalignment, elevated peak knee adduction angles and moments, greater rearfoot eversion, and early stance lateral ground reaction forces were observed when compared with normally-aligned control subjects.[12] Interestingly, this cohort also exhibited increased midstance knee flexion angle and moment. Due to the uneven gender disparity in the study sample, however, these findings should not be generalized to females.

Based on the existing literature, females are more prone to knee OA, while knee malalignment also predisposes individuals to disease. Ambulatory mechanics have been found to reveal these differences. However, no studies have directly examined the influence that sex and varus structure may have on each other during locomotion. Therefore, the purpose of our cross-sectional gait analysis study was to examine the interaction between sex (male, female) and knee alignment type (normal, varus) on the ambulatory mechanics of otherwise healthy subjects. Based on the existing literature for these risk factors, we hypothesized that females with varus knees would exhibit gait characteristics most consistent with OA gait.

Methods

Sixty healthy subjects were recruited for this study and evenly split into four groups by sex and alignment type: male varus, female varus, male normal, and female normal. Subjects were recruited through online and paper postings at a university setting. All screening and testing occurred within a single session. Participants had to be between 18–35 years old, and have no history in the previous year of spinal or lower quarter pain or injury. Any history of ligamentous, meniscal, chondral, or bony pathology or surgery was

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cause for exclusion. To provide evidence that subjects were healthy and high functioning, they completed the Sports and Recreational Activities subscale of the Knee Injury and Osteoarthritis Outcome Score Knee Survey (KOOS-SR).[13] The KOOS-SR uses a five point Likert scale to score the difficulty experienced during the previous week with squatting, running, jumping, twisting or pivoting, and kneeling. The anchor points are 0 and 4, such that a score of 0 indicates no difficulty and 4 indicates extreme difficulty. Subjects were excluded with a score greater than 2/20.

Group assignment as either normal or varus was conducted using a caliper-inclinometer measurement of tibial mechanical axis with respect to vertical (Acuangle, Isomed, Portland, OR). Two previous studies have found this measure to be a valid alternative to the full limb radiograph for assessing frontal plane knee alignment.[14,15] Subjects were instructed to stand with their feet together, their weight evenly distributed, and their knees in full extension. The proximal caliper arm was positioned over the tibial tuberosity and the distal arm over the neck of the talus. With the device positioned in the subject's frontal plane, the angle from vertical was then recorded to the nearest degree. Values greater than or equal to 10° from vertical qualified for the varus groups. This cut point was 1.5 standard deviations from the mean from an in-house database of 50 healthy individuals (7.3° ± 1.8°). Only values between 6°–9° qualified for the normal groups, as this was the approximate range of one standard deviation above and below the database mean.

Subjects meeting these criteria were invited to participate in the study. Informed consent was obtained per university human subjects policies. Height in meters and weight in kilograms were recorded. Preparations for three-dimensional motion capture of level walking then commenced. The more malaligned limb was used for the varus subjects, and the more normally-aligned limb was used for the normal subjects. In the event of symmetrical limb values, a side was chosen at random. Anatomical reflective markers were positioned over the following landmarks: the iliac crests, the greater trochanters, the femoral condyles, the tibial plateaus, the malleoli, the first and fifth metatarsal heads, and the distal shoe (Nike Air Pegasus; Nike, Beaverton, OR). Tracking markers were placed over the anterior superior iliac spines and the L5-S1 interspinous space. Three individual tracking markers were placed on the proximal, distal, and lateral aspects of the rearfoot. A shell-mounted cluster of four markers was placed on the distal posterolateral thigh, as well as the posterolateral shank.

Once the subjects were appropriately prepared, data capture commenced. A standing calibration trial was collected, followed by a hip motion trial to derive a functional hip joint center.[16] These two trials were used to establish the segment coordinate systems for the pelvis, thigh, shank, and foot.[17] The anatomical markers were then removed for the walking trials. Video data were captured using an eight-camera Vicon motion analysis system (VICON, Oxford Metrics, UK) sampling at 120 Hz. Force plate data (BERTEC Corp., Worthington, OH) were captured at 1080 Hz. Subjects traversed a 23-m walkway at 1.46 m/s (± 2.5%). Walking velocity was monitored using the L5/S1 marker velocity along the line of progression, extracted from an immediate posttrial marker reconstruction. At least five usable trials were collected, such that walking velocity was acceptable, footstrikes on the plate were clean, and no more than minimal marker tracking difficulties were observed postcapture.

Postprocessing was initiated with marker labeling and gap filling in Vicon Nexus software. Individual stance-phases were exported in C3D format for processing in Visual 3D (C-Motion Inc, Rockville, MD). The segments were modeled as frustra of right cones, with segment origins located at the midpoint of the proximal segment end. Inertial properties were applied per previous literature.[18] To derive joint angle data, an X-Y-Z Cardan rotation sequence was chosen. External joint moments were calculated about the proximal end of the distal segment and normalized to body mass and height. Ground reaction forces were normalized to body mass. Custom software was written to extract discrete variables from the array data from the five trials (Labview 8.2, National Instruments, Austin, TX).

The variables of interest were discrete gait parameters identified in the literature to be relevant for or affected by knee OA.[6,7,10] The joint angle variables were: knee flexion at footstrike, peak knee flexion during midstance, knee flexion excursion from footstrike to midstance, peak knee adduction, peak knee internal rotation, peak hip extension, peak hip adduction, peak rearfoot eversion, and contralateral pelvic drop during early stance. The kinetic variables were: peak hip extension and adduction moments, peak knee adduction moment, peak knee flexion moments during early midstance, and peak lateral ground reaction forces during early stance.

Means and standard deviations were calculated for all variables. Descriptive group data were assessed using single-factor analyses of variance. For the variables of interest, two-factor (sex [male, female] by alignment type [varus, normal]) analyses of variance were conducted to identify interactions, main effects, and possible simple effects. The predetermined alpha level was .05. All analyses were performed using SPSS version 17 (SPSS Inc, Chicago, IL).

Results

The four groups were not different by age or KOOS-SR score (Table 1). However, body mass index was greatest in the normally-aligned males. For tibial axis relative to vertical, the pooled varus subjects were more inclined than the normal subjects by approximately 3°, with the normally-aligned females slightly more vertically oriented than their male counterparts by approximately 1°.

Statistical interactions between sex and alignment type were observed for three variables of interest: peak knee adduction moment ($P = .044$), peak hip adduction angle ($P = .045$), and pelvic drop excursion ($P = .022$) (Table 2). For peak knee adduction moment, the interaction was largely driven by a larger difference between the varus and normal males ($P \leq .001$) than the females ($P = .003$). At the hip, the normally-aligned females exhibited greater peak adduction angle than their varus female counterparts by nearly 4° ($P \leq .001$), and their normally-aligned male counterparts by 5° ($P \leq .001$). Finally, in regards to pelvic drop excursion, normally-aligned females demonstrated greater pelvic drop motion than the varus females by 1° ($P = .013$), and the normally-aligned males by 2° ($P \leq .001$).

Four main effects for sex were observed. For the females, peak hip adduction moment was 22% greater ($P \leq .001$), as the hip adducted about 4° more ($P \leq .001$) than the males. Pelvic drop excursion ($P = .002$) was also greater in the females by approximately 1°. At the knee, peak adduction angle ($P \leq .001$) was generally greater in the males.

Eight main effects were seen for alignment type. Varus subjects demonstrated less peak hip adduction angle than normally-aligned subjects ($P = .001$), as well as less peak hip extension angle ($P = .024$). For the frontal plane of the knee, the peak adduction moment of the varus subjects was 35% greater ($P \leq .001$), and peak adduction angle was greater by approximately 5° ($P \leq .001$). In the knee's sagittal plane, the varus subjects underwent approximately 4° more of flexion excursion during early stance ($P = .010$) to achieve about

Table 1 Subject demographics for the 4 groups (N = 60) presented as means and standard deviations

	Varus Males	Varus Females	Normal Males	Normal Females
Age (years)	23.40 (3.56)	21.07 (2.52)	23.7 (4.98)	22.20 (2.68)
Body mass index (kg/m²)	23.32 (2.56)	21.24 (3.02)	26.07 (5.25)	21.84 (1.84)
KOOS-SR score (0-20)	0.33 (0.62)	0.53 (0.83)	0.21 (0.58)	0.40 (0.63)
Tibial mechanical axis (degrees)	11.47 (0.64)	10.67 (0.82)	7.79 (0.70)	6.60 (1.50)

Table 2 Group means and standard deviations for target variables[a] followed by *p* values for sex-by-alignment type interaction, sex main effect, and alignment type main effect

	Varus Males	Varus Females	Normal Males	Normal Females	Interaction *p* Value	Sex *p* Value	Alignment *p* Value
Pelvis (global)/hip							
Contralateral pelvic drop excursion	4.9 (0.9)	5.2 (1.8)	4.5 (1.7)	6.5 (1.0)	*.022*	*.002*	.219
Peak extension moment	0.632 (0.135)	0.690 (0.167)	0.670 (0.094)	0.771 (0.100)	.815	.138	.373
Peak adduction moment	0.568 (0.100)	0.653 (0.110)	0.556 (0.103)	0.720 (0.058)	.108	*< .001*	.256
Peak extension angle	19.0 (6.1)	17.2 (7.7)	20.0 (7.1)	24.9 (7.7)	.078	.416	*.024*
Peak adduction angle	8.3 (2.1)	10.9 (2.6)	9.4 (2.9)	14.9 (2.9)	*.045*	*< .001*	*.001*
Knee							
Peak flexion moment	0.385 (0.118)	0.362 (0.114)	0.344 (0.080)	0.320 (0.109)	.986	.413	.140
Flexion angle (footstrike)	–0.6 (3.5)	–1.9 (4.6)	–0.2 (2.4)	–0.3 (4.0)	.539	.505	.302
Flexion angle (midstance)	19.1 (5.1)	19.2 (5.0)	16.7 (4.3)	15.6 (5.7)	.656	.715	*.028*
Flexion excursion	19.7 (4.1)	21.1 (8.5)	16.9 (4.7)	15.9 (4.5)	.431	.910	*.010*
Peak adduction moment	0.412 (0.052)	0.368 (0.088)	0.278 (0.048)	0.300 (0.045)	*.044*	.480	*< .001*
Peak adduction angle	6.8 (2.9)	3.4 (3.5)	0.9 (2.3)	–1.2 (1.9)	.355	*< .001*	*< .001*
Peak internal rotation angle	12.4 (7.0)	14.7 (6.9)	11.7 (5.8)	12.1 (4.7)	.551	.402	.291
Rearfoot/ground reaction force							
Peak eversion angle	9.1 (2.3)	8.9 (1.9)	5.6 (1.7)	5.6 (2.5)	.866	.828	*< .001*
Peak lateral force (loading)	0.063 (0.031)	0.054 (0.019)	0.042 (0.021)	0.034 (0.017)	.935	.179	*.001*

[a] Angles/excursions in degrees, external moments in Nm·kg⁻¹m⁻¹, forces in N·kg⁻¹.

3° greater peak flexion angle at midstance (P = .028). Distally, the varus subjects demonstrated greater peak rearfoot eversion by approximately 3° ($P \leq .001$), along with eliciting 52% greater early stance lateral ground reaction forces (P = .001).

Discussion

The main purpose of this study was to investigate the interaction between two known risk factors for incident knee OA (sex and knee alignment) using gait parameters known to be affected by the onset of disease as the target variables. We recruited varus-aligned males, varus-aligned females, normally-aligned males, and normally-aligned females. Our primary hypothesis was that varus females would be the group with the gait patterns most consistent with OA gait. Underlying this main hypothesis were two secondary expectations. First, females would exhibit more parameters indicative of OA than males, due to their greater susceptibility to OA.[1] Likewise, we also expected that varus subjects would present with more OA gait features than the normally-aligned participants, particularly in the frontal plane, also due to their greater disease susceptibility.[12] Our primary hypothesis was largely unsupported, as varus females did not uniquely present with characteristics most consistent with OA gait in comparison with the other three groups. Our secondary expectations were partly supported, as the varus subjects indeed presented with numerous features consistent with medial OA gait. However, the sex differences were fewer. Females generally presented with proximal mechanics related to greater hip adduction, whereas males presented with more knee adduction. We interpreted these sex trends generally as not explicative for the female prevalence bias for knee OA.

An interaction effect between sex and alignment type was noted for knee adduction moment, and the pooled varus subjects exhibited 35% higher moments than the pooled normal subjects. This moment is of relevance to knee OA disease severity and progression, and is often speculated to be relevant for disease initiation.[9,12,19] In the current study, the varus males exhibited a 12% higher moment compared with the varus females, and a 43% higher moment compared with the average of the normal alignment groups. As tibial axis correlates to knee adduction moment, and tibial axis was slightly higher (~0.8 degrees) in the varus males than varus females on average, this outcome was not surprising.[20] However, in comparing the normal alignment groups, the females presented with greater knee adduction moments and lesser tibial angulation. This inconsistency by sex underscores our imperfect understanding of the relationship between frontal plane structural alignment, sex, and joint loading during walking. Our current findings suggest that varus-aligned individuals, particularly males, may prophylactically benefit from load-altering interventions. This speculative suggestion is based on the assumption that greater joint loading is indeed a risk factor for incident disease.

Proximally, the peak hip adduction angle and contralateral pelvic drop data both produced interactive effects between sex and alignment type. On average, females adducted their hip to a greater degree than males by approximately 3°, exhibited a greater accompanying adduction moment, and also underwent more pelvic drop by approximately 1°. As excessive hip adduction and contralateral pelvic drop have been tied to patellofemoral pain and anterior cruciate ligament injury, diagnoses more commonly seen in females, this gender bias is not surprising.[21–23] Further, it has been observed that the female pelvis is wider than the male pelvis when normalized to leg length, which would demand greater hip adduction to achieve the same base of support width.[24] Finally, females have been found to have weaker hip abductors than males, the muscles which would provide the internal torque to resist external hip adduction and pelvic drop torques.[25] By alignment type, the varus-aligned subjects did not adduct as much at the hip as the normally-aligned subjects by 2°–3°. This finding supports the concept that varus knee structure introduces an abduction bias at the hip that is maintained throughout stance. Indeed, less hip adduction has also been seen in subjects with medial knee OA compared with control subjects.[26] Finally, the interactions for hip adduction and pelvic drop motion were driven by the much greater peak values in the normally-aligned females. As excessive hip adduction and pelvic drop excursion are thought to be parameters related to pathologies such as patellofemoral pain and iliotibial band syndrome, varus knee structure may lessen the likelihood for those particular problems, especially in males.

Beyond the greater hip adduction-related mechanics in the females seen in this study, we observed greater dynamic varus angles in the males. Peak knee adduction angle was nearly 3° greater than the females overall. Interestingly, we did not see a similar sex effect for the adduction moment, despite that peak adduction angle has a moderate correlation to adduction moment ($r = .68$).[20] While the implications of greater knee adduction angles alone are less clear than that of a high moment, it is likely that the effect is deleterious if varus alignment is indeed progressive, as has been suggested in the literature.[27] Based on our data, the group most mechanically susceptible to incident medial knee OA would be the varus males, rather than the varus females, assuming no other risk factors are involved.

Overall, the effect of alignment type ($F = 8.706$) was more powerful than that of sex ($F = 4.338$) in this study, in that more gait variables related to knee OA were distinguished by the presence or absence of varus structure. At the knee, it is well documented that individuals with knee OA present with more extended, stiffer gait patterns.[28–31] Both corroborating and advancing the findings of an earlier study on predominantly varus males, we observed greater knee flexion motion and peak flexion during early stance in the sex-pooled varus subjects.[12] Interestingly, the varus females exhibited even greater flexion mechanics than the males. While we did not examine factors such as quadriceps morphology, strength, or activation patterns, these gait findings suggest some alteration to typical quadriceps muscle performance. Based on our current findings, such a study might hypothesize greater cross-sectional area, muscle force-producing ability, or activation patterns of the quadriceps in the presence of healthy, varus knees. Further, while these findings should continue to be cross-validated in other laboratories, we suggest that the reversal of this flexion bias may indicate the onset of symptomatic disease in a varus knee. Prospective analyses of individuals with varus knees continue to be warranted.

Proximally, we observed less late-stance hip extension in the varus subjects, regardless of sex. This finding is in contrast to previous data on mostly varus males, suggesting hip extension is not altered in the presence of healthy genu varum.[12] However, the current study assessed a larger sample with an equal gender distribution, lending greater credence to the current study. The finding of decreased hip extension is in line with studies on individuals with medial knee OA, where decreased hip extension mechanics have been noted.[7,26,29] While hip mobility impairments into extension have been noted as a correlate to disability in hip and knee OA,[32] more work is warranted on the relationship between varus knee structure, knee OA, and mobility losses into extension at the hip. In the current analyses, hip extension loss is the only sagittal plane alteration associated with varus knees.

Distally, increased rearfoot eversion and early-stance lateral ground reaction forces were observed. These findings support the observations seen in the previous study on predominantly varus males.[12] The greater eversion relative to the shank is due to the greater frontal plane inclination of the tibia at footstrike. Due to the pose of the foot at initial contact, more eversion is needed to achieve plantigrade foot contact during midstance. In regards to the increased peak lateral ground reaction force during loading in the varus subjects, this again supports previous work on healthy varus males[12] and is in line with data on patients with medial OA.[7] Taken together, the altered frontal plane rearfoot mechanics and mediolateral ground reaction forces seen in medial knee OA may be related to accompanying varus structure.

As with any study, limitations must be acknowledged. A key limitation is the cross-sectional design, which does not allow for causative inference. Prospective works evaluating gait mechanics in genu varum over time are needed. Of particular interest would be the natural history of the sagittal alterations at the hip and knee seen in the current study. It is conceivable that both decreases in hip extension in late stance and the reversal of the increased knee flexion mechanics during early stance could function as kinematic indicators of disease onset. A second limitation is the use of a clinical measure for tibial angulation as a threshold to assign participants into the normal and varus groups. Despite the clinical utility of inclinometry, future work should consider utilizing the gold standard full-limb radiograph for group assignment.

In summary, the influence of varus knee structure was explored across sexes in otherwise healthy participants, using gait parameters affected by knee OA as the variables of interest. Females generally presented with proximal mechanics related to greater hip adduction, whereas males presented with more knee adduction. Varus subjects demonstrated a number of alterations seen in medial knee OA. While varus structure clearly contributes to a number of gait alterations associated with medial knee OA, the contributions of sex type are not as explicative of established epidemiological patterns.

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