

Cyclic variations in multiplanar knee laxity influence landing biomechanics.

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Abstract:

Purpose: Females vary substantially in their multiplanar cyclic knee laxity changes across the menstrual cycle. The biomechanical implications of these cyclic changes are relatively unknown. Our purpose was to first cluster females based on their cyclic changes in anterior knee laxity (AKL), genu recurvatum (GR), varus–valgus (VV), and internal–external (IER) rotation knee laxity across the menstrual cycle. We then compared changes in landing biomechanics from days of minimum to maximum laxity between female clusters and a group of males.

Methods: A total of 49 males and 71 females were measured for AKL, GR, VV, and IER and underwent biomechanical analysis of a double-leg drop jump (0.45 m) at two time points: day of minimum (T1) and maximum (T2) AKL in each female across her menstrual cycle (males matched in time). Cluster analysis identified four distinct patterns of multiplanar cyclic knee laxity changes from T1 to T2 (C1–C4). Males were classified as a separate group.

Results: When landing from a jump, female clusters who increased both sagittal and frontal plane laxity from T1 to T2 (C3, C4) had 3.7° to 5.2° greater net movement toward knee valgus from T1 to T2 compared with females who did not increase both sagittal and frontal plane laxity

(C1) ($P = 0.041$). Females who increased IER without increasing AKL from T1 to T2 (C2) had -3.7° to -8.1° greater net movement toward knee internal rotation when compared with females who increased both AKL and IER (C3, C4) or males who maintained similar laxity from T1 to T2.

Conclusions: Changes in knee joint kinematics across the menstrual cycle were dependent on both the absolute and the relative magnitude of multiplanar knee laxity changes. The combination of relatively greater knee valgus coupled with relatively greater external rotation in those with large multiplanar knee laxity changes (C4) suggests an increased susceptibility to high-risk knee joint positions on ground contact and early in the landing phase.

Keywords: menstrual cycle | ACL | anterior knee laxity | genu recurvatum | varus-valgus laxity | rotational laxity | sports medicine | exercise science | kinesiology

Articles:

Greater magnitudes of knee laxity (i.e., anterior knee laxity (AKL) [30,42,44], genu recurvatum (GR) [18,23,26,28,30], general joint laxity (which encompasses GR) [12,18,28,30,42], and internal rotation laxity [7]) have been reported in the contralateral knee of ACL patients compared with uninjured controls. Females have greater knee laxity than males (2,7,13,31,36,41,42), and this sex difference can be magnified at certain times of the female's menstrual cycle due to the cyclic increases in her knee joint laxity (33,34,36). Because the risk of ACL injury is not uniform across the female's menstrual cycle (4,40,43), there is a need to understand the implications of these cyclic knee laxity changes on weight bearing knee joint neuromechanics.

Studies investigating the effect of cyclic knee laxity changes across the menstrual cycle on knee joint neuromechanics have largely focused on AKL. Park et al. (27) compared AKL and knee joint biomechanics of common sport movements at three time points during the menstrual cycle in 26 women; a 1.3-mm increase in AKL was associated with 30% greater knee adduction moment impulse ($N \cdot m \cdot s^{-1}$) during the stance phase of a side-cutting maneuver and 20% greater peak adduction and external rotation moments and 45% greater external rotation moment impulse during a jump-and-stop task. Shultz et al. (38) reported an association between cyclic increases in AKL with cyclic increases in anterior translation of the tibia relative to the femur produced by transition of the knee from non-weight bearing to weight bearing; for every 1.00-mm increase in AKL across days of the menstrual cycle, there was a predicted 0.74-mm increase in anterior tibial translation. These findings suggest that cyclic increases in AKL as small as 1–2 mm can have clinically meaningful effects on knee joint neuromechanics.

More recently, cyclic increases in GR and varus–valgus (VV) and internal–external rotation (IER) knee laxity have been reported across the menstrual cycle, although the absolute magnitude of these cyclic changes and the proportional magnitude of cyclic changes that occur across different anatomical planes can vary substantially between females (33,36). This intersubject variability in multiplanar cyclic knee laxity changes may have important implications on knee joint biomechanics. To date, few studies have examined more than one laxity variable relative to ACL injury risk (e.g., AKL and GR) (18,26,42). However, among these few studies, their results imply that each type of laxity may contribute uniquely to ACL injury risk. The unique contributions of individual laxity values are also supported by studies which demonstrate that components of high-risk knee joint biomechanics (e.g., greater dynamic knee valgus, greater anterior tibial translation) often occurred in the same plane(s) of motion as greater magnitudes of knee laxity (35,37,38). Thus, studying cyclic changes in knee laxity within a single plane of motion may not fully describe how weight bearing knee joint biomechanics and ACL injury risk are ultimately affected by cyclic changes in knee laxity across the menstrual cycle.

Therefore, our purpose was to first cluster females based on the similarity of their cyclic changes in AKL, GR, VV, and IER (i.e., multiplanar knee laxity) between days of their menstrual cycle when AKL was at its minimum (T1) and maximum (T2). We then compared changes in landing neuromechanics from T1 to T2 between female clusters and a group of males. We expected female clusters with greater magnitudes of cyclic knee laxity changes during normal, ovulatory, menstrual cycles would demonstrate greater cyclic changes in their knee joint neuromechanics during landing. We further expected that the magnitude and direction of these neuromechanical changes would depend on both the absolute magnitude of cyclic knee laxity changes and the proportional magnitude of change across anatomical planes.

METHODS

The sample consisted of 74 females and 50 males (18–30 yr) who participated in a larger study examining the effects of hormone mediated knee joint laxity on weight bearing knee joint neuromechanics (38). Participants were recreationally active (2.5–10 h·wk⁻¹) for the past 3 months and nonsmokers, had a body mass index (weight / height²) ≤30 kg·m⁻², and had no history of knee ligament or cartilage injury. Females were nulliparous, with self-reported normal menstrual cycles lasting 26–32 d (±1 d month to month), and had not used exogenous hormones for at least 6 months. We chose to exclude subjects who smoked, who had recently used exogenous hormones, and who had a body mass index >30 kg·m⁻² (i.e., those categorized as obese) to limit the potential for abnormal hormone levels and menstrual cycle irregularities. All

participants provided informed consent approved by the university institutional review board. To identify T1 and T2 in females, AKL was measured each morning over two cycles on six consecutive days after menses onset (self-report) and 8–10 consecutive days after ovulation (CVS One Step Ovulation Predictor (sensitivity 20 mIU·mL⁻¹ luteinizing hormone, accuracy 99%); CVS Corp., Woonsocket, RI). In the following month (i.e., third cycle), males and females were measured for AKL, GR, VV, and IER and underwent biomechanical analysis of a double-leg drop jump landing (0.45 m height) on the estimated days of minimum (T1) and maximum (T2) AKL for each female (based on when minimum and maximum AKL were observed in the two tracking cycles). Males were matched in time with a female with similar baseline AKL (± 0.5 mm). The dominant leg (preferred stance leg when kicking a ball) was tested. Subjects were familiarized to all study procedures 2 wk before testing, and they refrained from physical activity on the day of testing until all measurements were obtained.

Procedures for measuring AKL and GR (33) and total VV and IER (39) and their associated measurement reliability have previously been reported. AKL represented the anterior displacement (mm) of the tibia relative to the femur produced by an anterior load of 133 N applied to the tibia with the knee flexed to $25^\circ \pm 5^\circ$ using the KT-2000™ knee arthrometer (Medmetric Corp., San Diego, CA). GR was measured in supine with a standard goniometer as the amount of knee hyperextension ($^\circ$) achieved during maximal knee extension. VV and IER were measured in the Vermont Knee Laxity Device with gravitational loads eliminated, and the knee flexed to 20° and non-weight bearing. Electromagnetic position sensors (Ascension Technology Corp., Burlington, VT) attached to the thigh and shank recorded total frontal and transverse plane rotational displacements of the tibia relative to the femur at 10 N·m varus-valgus and 5 N·m internal-external torques, respectively. Participants were instructed to fully relax their thigh muscles and sEMG monitored the thigh muscles during laxity testing to ensure the muscles were not active. Three measurements for each laxity variable were averaged for analysis. Using these methods, intraclass correlation coefficients and standard error of measurements [ICC_{2,k}(SEM)] for day-to-day repeat measurements were 0.97 (0.4 mm) for AKL, 0.97 (0.5 $^\circ$) for GR, 0.91 (0.9 $^\circ$) for VV, and 0.89 (2.8 $^\circ$) for IER (33,39).

Measurement procedures for knee joint neuromechanics during the initial landing phase of a double leg drop jump have also been previously reported (35). At each time point (T1 and T2), participants were first instrumented with sEMG electrodes (10-mm bipolar Ag–AgCl surface electrodes; Blue Sensor N-00-S; Ambu Products, Ølstykke, Denmark) placed at a location estimated to be midway between the motor point and the distal tendon of the lateral and medial quadriceps (LQ, MQ), the lateral and medial hamstrings (LH, MH), and the lateral and medial gastrocnemius (LG, MG) oriented perpendicular to the length of the muscle fibers (37). The reference electrode was attached over the flat portion of the anteromedial aspect of the tibia.

Absence of crosstalk between sampled muscles was visually confirmed during manual muscle testing using the scope mode of the data acquisition software. Peak muscle activation amplitudes (Myopac telemetric system; Run Technologies, Mission Viejo, CA; amplification of $1 \text{ mV} \cdot \text{V}^{-1}$, frequency bandwidth of 10–1000 Hz, common mode rejection ratio of 90 dB·min at 60 Hz, input resistance of $1 \text{ M}[\Omega]$, and an internal sampling rate of 8 kHz) were obtained during 3–5 s of maximal effort isometric contractions (MVIC) against a fixed resistance for knee extension, knee flexion and ankle plantarflexion with the knee positioned in 25° of flexion and while seated in an isokinetic dynamometer (Biodex System 3; Biodex Medical Systems, Inc., Shirley, NY). Electromagnetic position sensors (Motion Star; Ascension Technology Corp.) were then attached to the sacrum, the C7 spinous process, the anterior midshaft of the third metatarsal, the midshaft of the medial tibia, and the lateral aspect of the midshaft of the femur of the dominant limb. Joint centers were calculated using the methods of Leardini (21) (hip) and centroid (24) (knee and ankle). Once fully instrumented, participants completed five barefoot drop jumps from a 0.45-m platform placed 0.1 m behind the rear edge of the force plate (type 4060; Bertec Corp., Columbus, OH). Participants were instructed to drop off the platform and immediately perform a maximal vertical jump on landing, keeping their hands at ear level throughout the landing. Participants were provided no specific instructions on how to land. In addition to the familiarization session, three practice trials were allowed before data collection on each test day. Kinematic (100 Hz), sEMG, and kinetic (1000 Hz) data were simultaneously collected and synchronized using a foot contact threshold of 10 N to trigger data collection. Trials were repeated if the participant lost their balance, did not land symmetrically, let their hands drop below ear level, or failed to land back onto the force plate after the maximal vertical jump.

To analyze muscle activation amplitudes, sEMG signals for each muscle were band-pass-filtered from 10 to 350 Hz, using a fourth-order, zero-lag Butterworth filter (20) then processed using a centered RMS algorithm (100-ms time constant for MVIC trials, 25-ms time constant for the drop jump trials). sEMG data from the initial landing phase of the five drop landing trials were ensemble averaged, and the peak RMS amplitude obtained for each muscle during 150 ms immediate before (prelanding activation) and 150 ms after (postlanding activation) initial ground contact was normalized to its mean peak RMS amplitude during MVIC trials (%MVIC). The medial and lateral aspects of each muscle were averaged to represent a single representative value for each of the quadriceps, hamstring, and gastrocnemius muscles.

Knee motion data were linearly interpolated to force plate data and low-pass-filtered at 12 Hz using a fourth-order, zero-lag Butterworth filter. Knee motions were calculated using Euler angle definitions with a rotational sequence of Z' Y' X" (15). Kinetic (force plate) data were low-pass-filtered at 12 Hz using a fourth-order, zero-lag Butterworth filter (5), and intersegmental knee moment data were calculated using inverse dynamics and normalized to each participant's height

and body weight (expressed as N·m per body weight per height $\times 102$). Kinematic and kinetic data for the initial landing phase (initial contact to peak center of mass displacement) were then normalized to 99 points and averaged across the five drop jump trials to yield a single representative motion or moment curve for each variable and individual (6,10). The mean coefficient of variation for the duration of the five landing trials (initial foot contact to peak COM displacement) within each subject for T1 ($7.0\% \pm 4.4\%$) and T2 ($7.0\% \pm 4.5\%$) suggests that participants landed in a very similar manner across the five trials with respect to landing duration. Using these representative ensemble average curves, measurement consistency [ICC2,5(SEM)] for male kinematic and kinetic data obtained approximately 2 wk apart confirmed relatively stable biomechanical data across time when knee laxity is not expected to change: 0.82 (3.0°), 0.94 (3.4°), and 0.94 (2.9°) for initial, peak, and mean knee flexion–extension motions; 0.71 (2.2°), 0.80 (2.9°), and 0.80 (2.8°) for initial, peak, and mean knee valgus motions; 0.87 (2.9°), 0.88 (3.3°), and 0.88 (3.2°) for initial, peak, and mean knee internal rotation motions; 0.84 (0.70 N·m per body weight per height $\times 102$) and 0.89 (0.94 N·m per body weight per height $\times 102$) for mean and peak knee flexion moments; 0.87 (1.7 N·m per body weight per height $\times 102$) and 0.80 (2.2 N·m per body weight per height $\times 102$) for mean and peak knee varus moments; and 0.78 (0.93 N·m per body weight per height $\times 102$) and 0.84 (0.81 N·m per body weight per height $\times 102$) for mean and peak knee internal rotation moments.

Statistical analysis

The Ward hierarchical clustering and nonhierarchical clustering (k-means) analyses were used to identify patterns of multiplanar cyclic knee laxity changes based on the magnitude of change in each subjects' AKL, GR, VV, and IER from T1 to T2, and then each female was assigned to one of these clusters. Standardized scores were used to ensure that the magnitude of any one variable did not overwhelm the model (8). Once these clusters were identified, ANOVA followed by multiple pairwise comparisons (Bonferroni adjustment) examined difference in baseline knee laxity values (as measured at T1) and cyclic knee laxity values (measured as the change in value from T1 to T2) among the identified clusters and males. Males were included as a control group because their knee laxity was not expected to change over time.

Female clusters were then compared with each other, and the group of males on their pattern of change (i.e., from T1 to T2) in sagittal (KFE), frontal (KVV), and transverse (KIER) plane knee motions and moments during the initial phase of the drop landing using a 5 (cluster) \times 2 (time) \times 99 (% landing) multivariate repeated-measures ANOVA procedures (kinetics and kinematics analyzed separately). Significant multivariate results (conducted initially to control for type 1 error) were then followed by univariate tests and post hoc pairwise comparisons (no adjustment)

to identify differences within each variable. For interactions including %landing, we first computed the change in the knee motion or moment curve (T2 - T1) at each %landing and then used repeated-measures ANOVA with trend analysis to compare the pattern of change in motion/moments between clusters. This approach allowed us to observe not only differences between clusters (and T1 vs T2) in minima and peak values but also differences in the rate of change in knee motions and moments from initial to peak and approximately where these differences in motion patterns diverge/converge relative to the landing phase. Lastly, prelanding and postlanding muscle activation amplitudes were compared between clusters using 5 (cluster) \times 2 (time) \times 3 (muscle) repeated-measures ANOVA, followed by simple main effects testing for significant interactions. Analyses were performed using statistical software packages SAS (SAS Institute, Inc., Cary, NC) and PASW (SPSS, Inc., Chicago, IL) ([alpha] level $P < 0.05$). The study sample was powered based on the larger project (38), which was originally planned to examine only AKL. Because of the complexity and somewhat exploratory nature of the current study (i.e., clustering females on their multiplanar knee laxity and thus not knowing the sample size of each cluster a priori), a priori power analyses for this specific study were not conducted. However, these (and smaller) sample sizes have proven more than adequate to reveal meaningful differences in knee joint biomechanics as a result of intersubject differences in knee laxity values (35,37,38).

RESULTS

Three females did not complete the study and were excluded from the data analysis. One male subject was excluded because he exercised before his second test session, which increased his AKL by 2 mm.

Cluster analysis

The cluster analysis identified four distinct patterns of multiplanar cyclic knee laxity changes from T1 to T2 (Fig. 1). Table 1 lists descriptive statistics for baseline (T1) and cyclic (T2 - T1) knee laxity values stratified by cluster (males included for comparative purposes) and indicates where values between clusters were significantly different. Females in cluster 1 had no cyclic change in AKL or GR and decreased VV and IER from T1 to T2; they were labeled C1:[DELTA]-VV IER to denote their decrease in VV and IER. Females in cluster 2 had no cyclic change in AKL but had modest cyclic increases in GR, VV, and IER; they were labeled C2:[DELTA]+GR VV IER to denote their increase in GR, VV, and IER. Females in clusters 3 and 4 had comparable cyclic increases in AKL, GR, and VV. However, cluster 3 decreased IER ($-1.9^\circ \pm 5.3^\circ$) from T1 to T2, whereas cluster 4 increased IER a substantial amount from T1 to T2 ($19.1^\circ \pm 3.8^\circ$); they were labeled C3:[DELTA]+AKL GR VV/-IER and

C4:[DELTA]+ALL++IER, respectively, to likewise denote the magnitude and direction of their cyclic knee laxity changes.

Table 1 & Figure 1 are omitted from this formatted document.

Analysis of knee motion

Aggregate means \pm SD for knee motion and moments across the entire landing phase stratified by cluster and time are provided in Table 2. (See Supplemental Digital Content 1, <http://links.lww.com/MSS/A150> for graphic depiction of sagittal, frontal, and transverse plane knee motion and moment curves across the landing phase for T1, and their net change in values from T1 to T2, stratified by cluster.) The multivariate test examining sagittal, frontal, and transverse plane knee kinematics identified significant differences between clusters (main effect; $P = 0.032$), clusters by time ($P = 0.023$), clusters by %landing phase ($P < 0.01$), and clusters by time by %landing phase (three-way interaction; $P < 0.01$). Follow-up univariate tests for KVV motion revealed a significant cluster main effect ($P = 0.015$) and cluster by time interaction ($P = 0.041$). When examining the cluster-by-time interaction, the change in KVV from T1 to T2 in the two female clusters who increased both sagittal and frontal plane knee laxity (C3:[DELTA]+AKL GR VV/-IER; C4:[DELTA]+ALL++IER) was significantly different from the change in KVV from T1 to T2 in females with no cyclic increase in knee laxity (and who actually decreased their VV and IER from T1 to T2) (C1:[DELTA]-VV IER). That is, while observed changes in KVV from T1 to T2 within each cluster were relatively small [(i.e., significant but of similar magnitude to the measurement error for C1 ([DELTA]-2.4° \pm 3.9°) and C4 ([DELTA]2.8° \pm 1.5°) but not significantly different for C3 ([DELTA]1.3° \pm 4.6°)], the net differences between clusters indicate that C3 and C4 moved toward 3.7° and 5.2° greater relative valgus from T1 to T2 when compared with C1. Although males also had a 3.7° greater relative net change toward valgus from T1 to T2 compared with C1, the change within males was not significant, and the knee remained in slight varus at both time points (Table 2). Further, post hoc analysis of the main effect for cluster revealed that regardless of time point, absolute knee valgus angles were generally greater in the three clusters who experienced cyclic knee laxity increases (C2:[DELTA]+GR VV IER = 3.2° \pm 7.7°, C3:[DELTA]+AKL GR VV/-IER = 2.5° \pm 6.0°, and C4:[DELTA]+ALL++IER = 4.9° \pm 5.6°) compared with males (-1.0° \pm 5.4°) (all $P < 0.038$). However, knee valgus angles were not significantly different between males and the female cluster with no cyclic increase in knee laxity ($P = 0.054$).

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Follow-up univariate tests for KIER motion revealed significant cluster by time ($P = 0.025$) and cluster-by-time-by-%landing phase ($P = 0.048$) interactions. When interpreting the cluster by time interaction, the change in KIER from T1 to T2 in the female cluster with cyclic increases in all laxity variables except AKL (C2:[DELTA]+GR VV IER; $[\text{DELTA}] = -3.1^\circ \pm 6.6^\circ$) was significantly different from the change in KIER from T1 to T2 in males who did not change their knee laxity ($[\text{DELTA}] = 0.7^\circ \pm 5.8^\circ$), females who increased AKL but not IER (C3:[DELTA]+AKL GR VV/-IER = $[\text{DELTA}]1.0^\circ \pm 4.5^\circ$) and females who increased both AKL and IER (C4:[DELTA]+ALL++IER = $[\text{DELTA}]5.0^\circ \pm 4.3^\circ$). Although these observed changes from T1 to T2 within each cluster were not significant, the relative difference in the magnitude and direction of these changes between clusters resulted in -4.1° , -8.1° , and -3.8° greater relative movement toward knee internal rotation from T1 to T2 in C2:[DELTA]+GR VV IER compared with C3:[DELTA]+AKL GR VV/-IER, C4:[DELTA]+ALL++IER, and males, respectively. Although a large effect size ($d = 1.1$) was noted in the change in KIER from T1 to T2 between C4:[DELTA]+ALL++IER ($5.0^\circ \pm 4.3^\circ$) and C1:[DELTA]-VV IER ($0.4^\circ \pm 4.3^\circ$) (those with the greatest vs least overall change in knee laxity), this difference did not reach statistical significance ($P = 0.06$). When examining the three-way interaction, trend analysis and graphic representation of the data (Fig. 2) indicate that C2:[DELTA]+GR VV IER continued to move toward greater knee internal rotation during the first half of the landing at T2 compared with T1. Comparatively, C3:[DELTA]+AKL GR VV/-IER remained in 1° – 2° greater external rotation throughout the landing at T2 compared with T1 (significant linear trend, $P = 0.034$), whereas males initially moved toward greater internal rotation (first 20% of landing) and then returned to and maintained more external rotation near 50% of the landing at T2 compared with T1 (significant linear and cubic trends, $P < 0.03$). There were no differences between clusters for KFE motion (P value range for cluster main effects and interactions = 0.152–0.736).

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Analysis of knee moments

Analysis of multivariate tests for sagittal, frontal, and transverse plane knee moments (as N·m per body weight per height $\times 102$) indicated a significant cluster main effect ($P = 0.020$) and cluster-by-%landing phase interaction ($P < 0.001$) but no significant cluster-by-time ($P = 0.551$) or cluster-by-time-by-%landing phase interaction ($P = 1.00$). Knee extensor moments were generally lower in males across the entire landing phase (1.7 ± 1.7) compared with both female clusters who decreased IER laxity from T1 to T2 (C1:[DELTA]-VV IER = 3.4 ± 1.3 ; C3:[DELTA]+AKL GR VV/-IER = 2.9 ± 2.4) ($P = 0.028$). Knee internal rotation moments were generally greater in C2:[DELTA]+GR VV IER (-2.8 ± 1.4) compared with C3:[DELTA]+AKL

GR VV/-IER (-2.0 ± 1.0) and males (-1.5 ± 1.8) ($P = 0.042$). These cluster differences in KIER moments were also dependent on %landing phase ($P = 0.042$). Graphic representation (Fig. 3) with trend analysis (linear and quadratic terms, $P < 0.05$) revealed that the rate and absolute magnitude of increase in knee internal rotation moments across the landing was greater for C2:[DELTA]+GR VV IER until about 53% of the landing phase, whereas the rate of increase was more gradual and began to slow earlier (~40% of the landing phase) for C3:[DELTA]+AKL GR VV/-IER and males. This resulted in significantly higher internal rotation moments for C2:[DELTA]+GR VV IER from 49% to 79% of the landing phase compared with C3:[DELTA]+AKL GR VV/-IER and from 16% to 100% of the landing phase compared with males. Follow-up univariate tests revealed no differences between clusters for KVV moment (P value range for cluster main effects and interactions = 0.132–0.727).

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Analysis of muscle activation

Table 2 lists prelanding and postlanding activation amplitudes (%MVIC), stratified by cluster, muscle, and time. Significant cluster-by-time ($P = 0.039$) and cluster-by-time-by-muscle ($P = 0.05$) interactions for prelanding activation revealed that from T1 to T2, C4:[DELTA]+ALL++IER had greater increases in quadriceps activation ([DELTA] = $6.1\% \pm 4.7\%$) compared with C1:[DELTA]-VV IER ([DELTA] = $-0.4\% \pm 5.3\%$), C3:[DELTA]+AKL GR VV/-IER ([DELTA] = $-0.1\% \pm 7.4\%$), and males ([DELTA] = $-1.2\% \pm 3.8\%$), whereas C2:[DELTA]+GR VV IER ([DELTA] = $7.3\% \pm 20.4\%$) and C3:[DELTA]+AKL GR VV/-IER ([DELTA] = $5.6\% \pm 14.2\%$) had greater increases in gastrocnemius activation compared with males ($-4.5\% \pm 17.7\%$). Significant cluster main effects for prelanding and postlanding activation amplitudes ($P \leq 0.001$) revealed that males generally had lower prelanding activation amplitudes (25.1 ± 7.0 %MVIC) than all female clusters who experienced cyclic increases in knee laxity (C2:[DELTA]+GR VV IER = 32.6 ± 8.7 %MVIC; C3:[DELTA]+AKL GR VV/-IER = 30.3 ± 9.6 %MVIC; C4:[DELTA]+ALL++IER = 34.8 ± 6.1 %MVIC) but not compared with the female cluster who did not experience cyclic increases in knee laxity (C1:[DELTA]-VV IER = 29.4 ± 5.8 %MVIC). Males also had lower postlanding activation amplitudes ($51.0\% \pm 23.9\%$) than all female clusters (C1:[DELTA]-VV IER = $68.3\% \pm 15.7\%$; C2:[DELTA]+GR VV IER = $71.5\% \pm 23.8\%$; C3:[DELTA]+AKL GR VV/-IER = $80.0\% \pm 27.0\%$, all $P < 0.05$), except C4:[DELTA]+ALL++IER, although the lack of difference between C4:[DELTA]+ALL++IER and males is likely due to its small sample size (69.5 ± 17.8 %MVIC; $P = 0.06$, effect size = 0.77).

DISCUSSION

To assist in the collective interpretation of these findings, Table 3 provides a summary of the relevant findings as they pertain to cluster and time effects. Our results confirmed our hypotheses that females with greater cyclic knee laxity changes across their menstrual cycle would demonstrate greater changes in knee joint motion patterns when landing from a jump and that the relative direction of these kinematic changes would in part depend on the proportional changes that occurred across different anatomical planes. Specifically, female clusters who increased both sagittal and frontal plane laxity from T1 to T2 (C3, C4) had greater relative net change toward knee valgus from T1 to T2 compared with clusters who did not increase sagittal and frontal plane laxity (C1); and females who increased transverse plane laxity without increasing AKL from T1 to T2 had a greater relative net change toward knee internal rotation than females who increased all laxity variables except IER (C3), females who increased both AKL and IER (C4), or males who did not change AKL and IER values from T1 to T2. These observed changes in knee joint kinematics from T1 to T2 occurred without appreciable concomitant changes in knee joint moments or muscle activation strategies between time points.

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Regarding frontal plane knee motion, female clusters who increased both sagittal and frontal plane laxity from T1 to T2 had a 3.7° to 5.2° greater net movement toward knee valgus during the landing from T1 to T2 compared with the female cluster who did not increase either sagittal or frontal plane laxity. This greater net change toward knee valgus was particularly apparent for females in C4:[DELTA]+ALL++IER who had the greatest absolute increase in cyclic knee laxity and had mean knee valgus angles at T2 that were two to six times greater than all other clusters. Conversely, from T1 to T2, females in C1:[DELTA]-VV IER decreased their knee valgus from T1 to T2. Although not significant, it is interesting to note that the other female cluster with no cyclic increase in AKL from T1 to T2 (C2:[DELTA]+GR VV IER) had a small net decrease in knee valgus, although they had modest increases in GR, VV, and IER. These findings suggest that the ACL (the primary restraint to AKL) provides some degree of passive restraint to knee valgus motion in weight bearing, particularly if the medial collateral ligament (the primary restraint to knee valgus loading) is lax; this is consistent with findings of somewhat greater increases in knee valgus rotation in cadaveric knees when sectioning both the ACL and MCL compared with sectioning only the MCL (25).

The magnitude of change in AKL relative to other anatomical planes also appeared to impact the net change in the magnitude and direction of KIER from T1 to T2 (Fig. 2). These changes are

most apparent in the female clusters who increased their IER from T1 to T2 (C2 and C4). At both time points, the knees of all clusters (and males) were initially positioned in some degree of external rotation at initial ground contact, which then internally rotated during the first 30%–40% of the landing. However, C2:[DELTA]+GR VV IER (who increased IER without increasing AKL) moved toward greater relative tibial internal rotation at T2 compared with T1 when compared with C4:[DELTA]+ALL++IER (who increased both IER and AKL) and went through less tibial internal rotation at T2 ([DELTA] = 5.0°); this resulted in a net relative difference between clusters in their change in transverse plane knee rotation of 8.1°. Close inspection of these data at T1 indicates that females in C4:[DELTA]+ALL++IER initially landed in a similar amount of knee external rotation (4.8°) as other clusters (range = 1.1°–4.7°), then moved into substantially more knee internal rotation during the landing (-10.6°) than all other clusters (range = -4.0° to 6.5°) (Fig. 1A). However, at T2 when both AKL and IER laxity were substantially increased, females in C4:[DELTA]+ALL++IER landed in 3.2° more external rotation (resulting in a mean initial landing angle of 8° external rotation) then moved toward less tibial internal rotation during the landing compared with T1. Conversely, females who had no change in AKL and only a modest increase in IER (C2:[DELTA]+GR VV IER) had little change in their initial tibial position at ground contact between T1 and T2 but then moved toward 4.2° greater internal rotation during the latter half of the landing at T2 compared with T1. Although the individual net changes from T1 to T2 within cluster for both C2:[DELTA]+GR VV IER and C4:[DELTA]+ALL++IER were not significant and ultimately resulted in a movement toward a more neutral knee rotation during the latter half of the landing at T2 versus T1, the 8.1° relative difference between clusters in the change in transverse plane knee motion from T1 to T2 early in the landing suggests that females in these clusters may experience very different knee joint kinematic patterns during times of the menstrual cycle when knee laxity values are at their minimum versus maximum.

Perhaps of greatest concern is the small subset of females in C4:[DELTA]+ALL++IER who experience disproportionately large increases in IER. These females were initially positioned at ground contact in 3.2° greater tibial external rotation (8.0° vs 4.8°; $d = 0.47$), 1.6° greater knee valgus (2.3° vs 0.7°; $d = 1.40$), and 4° greater knee extension (9.6° vs 13.6°; $d = 0.74$) at T2 compared with T1. Although differences in each plane are relatively small and within the measurement error, together they may have altered joint congruency upon ground contact, leading to significant differences in movement patterns during the ensuing landing when compared with C1 and C2 (i.e., 5.2° greater net movement toward knee valgus than C1 and 4.6°–8.1° less net movement toward knee internal rotation than C1 and C2 throughout the landing at T2 vs T1). Of particular concern is that, with the exception of 6% greater quadriceps prelanding activation at T2 versus T1 (and a nonsignificant 27% increase in quadriceps activation after landing; effect size = 0.66), which may have increased joint compression and led to the reduction

in internal tibial rotation, these individuals showed little change in muscle activation across time. In fact, none of the female clusters who increased knee joint laxity from T1 to T2 (C2:[DELTA]+GR VV IER, C3:[DELTA]+AKL GR VV/-IER, C4:[DELTA]+ALL++IER) demonstrated an appreciable change in hamstring activation, a muscle widely considered to be important in controlling tibial motion. Thus, when considering the initial position of the tibiofemoral joint upon landing as being in greater extension, valgus, and tibial external rotation (commonly described as the position of no return about injury risk [14]), with little change in dynamic muscle activation, females with these large multiplanar cyclic knee laxity changes may be particularly susceptible to high-risk joint positions, and the potential for dynamic valgus collapse upon ground contact. The potential risk associated with this initial joint positioning is supported by reviews of ACL injury mechanisms that indicate that ACL ruptures occur early in the landing phase (19) and that the ACL is more likely to be loaded when anterior directed loads are applied in combination with frontal and/or transverse-plane knee loadings, particularly with the knee near full extension (32). Although knee valgus produces greater ACL strain when coupled with internal rotation (16), external rotation also increases ACL strain in weight bearing (9) and the potential for ACL impingement against the intercondylar notch of the femur with anterior tibial translation (11). Moreover, a recent study of ACL injury mechanisms reported a mean tibial position of 5° external rotation at the time of ground contact (17).

Also of concern may be the female cluster who had moderate increases in all laxity variables except AKL (where the ACL is the primary passive restraint) (C2:[DELTA]+GR VV IER) because this was the only cluster to experience a relative increase in knee internal rotation from T1 to T2 when compared with other clusters (C3, C4, males). Females in this cluster had little change in their initial knee joint position at ground contact from T1 to T2 (Fig. 2), which supports the role of the ACL in guiding skeletal motion and maintaining tibiofemoral position on ground contact (3). However, as the knee transitioned to weight bearing, they experienced greater relative movement toward knee internal rotation from T1 to T2 early in the landing when compared with C3 and males. During this same time, there is a natural tendency of the tibia to translate forward relative to the femur (because of the anterior to posterior inferior inclination of the proximal tibia), which is restrained by the ACL (9). When these biomechanical factors are considered along with the higher knee internal rotation intersegmental moments observed in this cluster at both time points (compared with C3 and males), it is possible that cyclic increases in frontal and transverse plane knee laxity, without a proportional increase in AKL, may lead to greater loads on the ACL. This may be particularly true if the knee is also positioned in some degree of valgus (9,16), as was the case for females in this particular cluster.

In summary, intersubject variability in multiplanar cyclic knee laxity changes across the menstrual cycle (both in terms of the overall magnitude of change, as well as the proportional change occurring in different anatomical planes) can affect the magnitude and direction of knee kinematic patterns during the initial phase of a drop landing. Moreover, these changes occurred without appreciable changes in joint moments and muscle activation strategies. These findings suggest that greater transverse and frontal plane knee motions during landing, which are thought to place the ACL at greater risk for knee trauma, may in part result from reductions in passive restraint capabilities, which can affect both initial joint positioning at ground contact and the coupled knee motion patterns occurring early in the landing. The implication of these findings on ACL loads (particularly when AKL does not increase proportionally as other knee laxity values across the menstrual cycle) requires further study. Although a more lax knee may be able to be displaced further before the ligament is exposed to high magnitudes of load, further work is needed to understand how loading characteristics of the ACL may be differentially affected by the observed altered arthrokinematics, particularly at ground contact.

The following limitations deserve consideration in light of our findings. First, this study is limited to the assessment of in vivo dynamic knee function using skin-mounted motion sensors, which increases the potential for errors in assessing in vivo dynamic function (1,29). Although skin-mounted motion sensors have been used extensively to assess joint kinematics during high-impact activities (6,10,24,27) as alternate methods of assessing dynamic joint kinematics that pose significant invasive risk to the participants (1,29), identifying subtle differences in the participant's knee biomechanics across time due to cyclic changes in laxity is challenging. As such, individual time-related differences that do not exceed the reported measurement error should be interpreted with caution and should be confirmed in future studies. Second is the unequal sample sizes obtained from the cluster analyses, which was particularly problematic for C4:[DELTA]+ALL++IER (n = 5). Although this was unavoidable (females were not specifically recruited based on their multiplanar cyclic knee laxity) and these few subjects clearly represent an important subset of these women (as evidence by the relatively small deviations around their mean values), low statistical power associated with this small sample may have prevented us from identifying other important differences in this group compared with other clusters. As such, we reported effect sizes where we felt this would further aid the interpretation of the findings. The potential for low statistical power is particularly evident in the cyclic changes in knee moments observed from T1 to T2, which tended to be more variable (please refer to Supplemental Digital Content 1, <http://links.lww.com/MSS/A150>). It will be important to develop screening methods that allow us to oversample this subset of the population in future studies.

Finally, it is important to note that the cyclic knee laxity changes by which females were clustered were based on values obtained at two time points of the menstrual cycle: the estimated day of minimum (T1) and maximum (T2) AKL after following these females over two consecutive cycles. Although this allowed us to reasonably capture substantial changes in knee laxity between these time points, we only captured, on average, a little more than 50% of the true magnitude of their observed cyclic AKL and GR changes over the two tracking cycles (33). Moreover, because we only measured VV and IER at T1 and T2 (measurement procedures were too time intensive to measure these daily during the tracking months), we cannot be sure if we captured the true magnitude of these changes. Thus, it is likely that the true magnitude of neuromechanical changes that occur across the menstrual cycle may be greater than what we observed here, had we captured the full magnitude of cyclic knee laxity changes. Continued efforts are needed to accurately identify females prone to large, multiplanar cyclic knee laxity changes, and to understand the physiological mechanisms that promote their greater cyclic knee laxity changes, thus their potential for high-risk knee joint kinematics.

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