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Original article

Relationship between knee joint laxity and knee joint mechanics during the menstrual cycle

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ABSTRACT

Background: An increase in knee laxity during the menstrual cycle may increase the risk of anterior cruciate ligament injury.

Objective: To investigate whether changing knee laxity during the menstrual cycle correlates with changing knee joint loads in a cutting manoeuvre.

Design: Cross-sectional study.

Setting: Laboratory testing.

Participants: 25 healthy women, with a normal menstrual cycle, no history of oral contraceptive use, and no previous knee injury

Interventions: Serum hormone concentrations were assessed and knee joint laxity at a load of 89 N was measured during the follicular, ovulation and luteal phases. Participants performed 10 trials of a cutting manoeuvre to quantify knee joint mechanics at each test session.

Main outcome measurements: Knee joint laxity (mm), peak knee angle (°) and knee joint moment (Nm) and knee joint impulse (Nms).

Results: Increased knee laxity was observed during ovulation compared with the luteal phase, but no significant changes in knee mechanics corresponding to menstrual phases were found. A positive correlation was found between changes in knee laxity and changes in knee joint loads (Δmoment or Δimpulse) from the follicular phase to ovulation, and from ovulation to the luteal phase ($p < 0.05$). Women in whom knee laxity increased showed increased knee loads, and those in whom knee laxity decreased showed decreased knee loads during the menstrual cycle.

Conclusions: Knee laxity correlates positively with knee joint loads, and increased knee laxity during the menstrual cycle may be a potential risk factor for anterior cruciate ligament injuries in certain women during sports activity.

Higher rates of anterior cruciate ligament (ACL) injury in female than male athletes has attracted attention into researching and understanding the injury mechanism.[1] Many studies have investigated ACL injury mechanisms in women by considering physical differences between men and women. Anatomical differences, such as the structure of the knee[2] or the alignment of the lower extremity,[3,4] have been suggested as risk factors for ACL injuries in females. Several studies have found different movement patterns and joint loading in females. A few studies found that women tend to flex their knee less[5,6] and bend their knees more inward[6,7] during cutting and landing, but it should be noted that some studies did not find any sex differences in movement pattern.[8,9] In addition, it has been observed that women show greater joint loading[5,7] and anterior

shear force[10] at the knee than men. Different muscle recruitment patterns such as high quadriceps relative to hamstrings contractions in women may increase stress on the ACL.[11,12] It has been speculated that these different risk factors in women lead to increased risk to the ACL during sports activity. As a result, ACL injury prevention programmes have been developed to decrease these potential risk factors, some of which have been successful at reducing the ACL injury rate.[13–16] However, it is likely that sex differences alone are not sufficient to explain subject variability in ACL injuries among women. As not all women are prone to greater sex-related risk factors, and thus ACL injury, it seems that more complex injury mechanisms are in play.

Girls tend to have greater joint laxity than boys,[17] and greater joint laxity may decrease the functionality of the knee. Studies have shown that greater joint laxity in females may delay the onset of muscle activation[18] and decrease the joint position sense.[19,20] As a result, females may have less time and less ability to control muscle function for external force during movement, exposing them to more injurious situations during sports. In general, more joint injuries occur in people with more-lax joints than in those with normal laxity, irrespective of their sex.[21,22]

More ACL injuries occur at a specific time of the menstrual cycle, suggesting that female hormones influence ACL injuries during sport.[23–25] A change in hormone concentrations, such as increased oestrogen, may increase passive knee laxity,[26–29] and it is speculated that this increase in knee laxity during the menstrual cycle may have an effect on the ACL injury mechanism in women. However, the actual ACL injury mechanism involved in increasing knee joint laxity during the menstrual cycle has not received adequate study.

Most recent studies have focused on the effects of hormones on joint laxity, or the influence of joint laxity on injury frequency in women, whereas there has been limited investigation into the effect of joint laxity, or hormones, on the actual joint mechanics that ultimately lead to injury.[8,30,31] No studies have researched the relationship between knee joint laxity and movement or joint loading during the menstrual cycle. Therefore, the aim of this study was to investigate whether knee joint laxity affects knee movement and joint loading during the menstrual cycle, to provide a better understanding of the injury mechanism behind the high ACL injury rate in a subset of female athletes. It was hypothesised that knee joint laxity correlates positively with resultant knee joint loads in sports-related movements during the menstrual cycle.

Figure 1 Cutting manoeuvre performed during motion analysis test.

METHODS

Participants

Twenty-five healthy women were recruited for this study (mean (SD) age 22.7 (3.5) years, height 170.2 (7.0) cm, mass 64.7 (9.6) kg, body mass index 22.3 (2.4), menstrual cycle 28.9 (2.8) days, activity levels 8.7 (4.6) h/week). The subjects regularly participated in sports activity at a recreational level. They were required to have a normal menstrual cycle, no history of oral contraceptive use, and no knee injury within the preceding 6 months. Subject criteria were prescreened by self-reported questionnaire before testing. The participants read and signed a written consent form approved by the institutional ethics review committee.

Follicular, ovulation and luteal phase

Each participant visited the laboratory to perform a series of tests at three different times during the menstrual cycle (a blood draw, knee laxity measurement and motion analysis test). The first test (follicular phase) occurred between days 5 and 8 of the menstrual cycle. After the first test, participants were asked to use an ovulation kit (Clearblue; Unipath, Bedford, UK) to detect the ovulation phase at home and schedule the second test. The second test coincided with ovulation and was performed 24–48 h after detection of the oestrogen surge with an ovulation predictor kit.

The ovulation predictor kit was recommended by a professional pharmacist in the regional fertility programme. Participants were instructed when to use the predictor kit on the basis of their menstrual history. A positive result was indicated by the appearance of a blue band on the test stick when it was held in the urine stream for 5 s or when the urine was collected in a paper cup and the test stick dipped into the cup for 20 s. As soon as a positive result was indicated, the participant contacted the tester to schedule the second data collection within the subsequent 24–48 h. The third test (luteal phase) occurred ~7 days after the second test and was based on an average 28-day menstrual cycle. Three blood samples were collected for each participant at the time of data collection to confirm the menstrual cycle phases.

Passive knee joint laxity

The participant's knee joint laxity was measured using a KT-2000 arthrometer (MEDmetric Corp, San Diego, California, USA) at each test session. To eliminate inter-rater differences in the laxity measure, only one examiner conducted the knee laxity measurements. With a passive drawer test at 89 N, an average displacement for three cycles was calculated. The intratester repeatability of the KT-2000 test was determined by an intraclass correlation coefficient (ICC). The repeatability test with seven women showed a mean (SEM) of 6.23 (1.52) mm for the first day and 6.27 (2.36) mm for the second day. Thus, highly repeatable results between two consecutive days were obtained ($ICC_{(3,2)} = 0.98$, $F_{(6,6.0)} = 75.42$, SEM = 0.37 mm, p<0.001).

Knee joint kinematics and kinetics

After the blood sample draw and knee laxity measurement, motion analysis testing was performed for cutting movements at each visit. Three-dimensional kinematics of the dominant right leg were quantified. The right leg (upper leg, lower leg and foot) was prepared using nine reflective markers (three per segment), which were attached to the following anatomical positions: proximal upper leg, mid-lateral upper leg, distal upper leg, proximal lower leg, mid-lateral tibial crest, distal lower leg, upper shoe heel, lower shoe heel and the lateral side of the shoe below the lateral malleolus (fig 1). The ideal marker placement to obtain reliable data was determined on the basis of previous studies.[32][33] The three-dimensional spatial positions of the markers on the leg were collected using a system of eight high-speed video cameras (Motion Analysis Corp, Santa Rosa, California, USA) at a sampling rate of 240 Hz. The predetermined criterion for tolerable error in space calibration of the camera system was set at 0.06% (ie, 0.6 mm maximum error for a 1 m³ capture volume). Ground reaction force data during movements were collected at 2400 Hz using a force platform (Kistler AG, Winterthur, Switzerland).

A neutral position was captured in a standing trial using the video system (1 s sample). In this case, the participant was asked to stand still in a position with feet pointing anteriorly and approximately hip width apart. The hip joint centre was identified by three reflective markers placed on the right and left

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Figure 2 Illustrations showing how internal knee adduction and abduction moment (Nm) is created about the knee in the frontal plane during a cutting manoeuvre. NB: positive represents adduction and negative represents abduction.
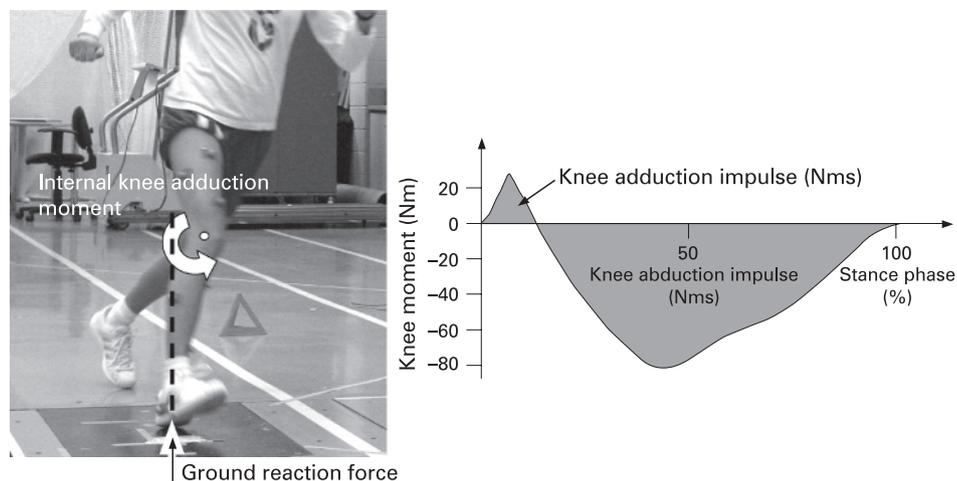
anterior superior iliac spine (ASIS) and right greater trochanter. The distance between the markers placed on each ASIS was used as a reference length. The hip joint centre was located at 14% of the inter-ASIS distance medial to the right ASIS, and 30% of the inter-ASIS distance downward to the right ASIS.[34] The knee joint centre was identified by the midpoint of two reflective markers, one from the lateral femoral epicondyle and a second at the medial femoral epicondyle. Similarly, the ankle joint centre was identified by the midpoint of two markers on the lateral and medial malleolus. Once joint centres had been defined, they were assumed to be fixed with respect to the segment coordinate system during data collection. The least squares method, using singular value decomposition,[32] was used to calculate the transformation of information from the marker-based coordinate system to an anatomical segmental coordinate system for each segment.

Data were collected from 10 trials of a cutting manoeuvre: V-Cut, performed by running straight forward, then planting the right foot on the force platform and cutting 45° to the left. The V-Cut was performed with a target approach speed of 3.5 m/s (fig 1). The running speed of the participants was monitored with photocells (Banner Engineering Corp, Minneapolis, Minnesota, USA) placed just before and after the force plate at a distance of 1.92 m. Trials were rejected if they were not within 5% of the target running speed. Participants performed 10 successful trials wearing neutral basketball shoes (female size US 7–12).

The kinematic and kinetic data were filtered using a fourth-order low-pass Butterworth filter with a cut-off frequency of 12 Hz and 50 Hz, respectively. Kintrak software (Motion Analysis Corp) was used to calculate kinematic and kinetic output variables. Three-dimensional knee joint kinematics

Table 1 Variables across the menstrual cycle

| | Follicular phase | Ovulation phase | Luteal phase | Overall phase effect | | Bonferroni-adjusted p value | | |
				F(df)	p Value	F vs O	O vs L	F vs L
Serum sample and knee joint laxity								
Days of test	6.12 (1.42)	16.16 (3.02)	22.84 (3.29)	320.564(2,48)	0.000*	0.000*	0.000*	0.000*
Oestradiol (pg/ml)	45.25 (23.93)	81.54 (41.17)	139.73 (86.81)	18.361(2,48)	0.000*	0.000*	0.015*	0.000*
Progesterone (ng/ml)	0.99 (0.46)	3.34 (2.37)	11.66 (7.06)	45.119(2,48)	0.000*	0.000*	0.000*	0.000*
Laxity at 89 N (mm)	4.78 (1.69)	5.20 (1.70)	4.62 (1.53)	3.526(2,48)	0.037*	0.243	0.015*	1.000
Peak knee angle (°)								
Knee abduction	5.25 (4.59)	5.61 (4.87)	5.56 (5.18)	0.128(2,44)	0.880	1.000	1.000	1.000
Knee flexion	62.77 (6.12)	63.49 (6.77)	63.77 (8.55)	0.497(2,44)	0.612	1.000	1.000	1.000
Peak knee moment (Nm)								
External rotation	26.13 (14.44)	26.43 (15.65)	26.65 (15.20)	0.007(2,48)	0.993	1.000	1.000	1.000
Internal rotation	6.84 (5.96)	5.71 (3.10)	5.63 (3.14)	0.980(2,48)	0.383	1.000	1.000	0.708
Adduction	20.16 (18.37)	19.24 (20.00)	18.95 (20.35)	0.073(2,48)	0.930	1.000	1.000	1.000
Abduction	88.74 (43.34)	88.28 (46.75)	88.27 (39.96)	0.191(2,48)	0.827	1.000	1.000	1.000
Extension	231.99 (49.90)	235.38 (64.85)	232.42 (60.02)	0.112(2,48)	0.885	1.000	1.000	1.000
Knee impulse (Nms)								
External rotation	2.69 (1.81)	2.84 (1.87)	2.84 (1.81)	0.365(2,48)	0.696	1.000	1.000	1.000
Internal rotation	0.08 (0.06)	0.08 (0.06)	0.06 (0.04)	1.103(2,48)	0.340	1.000	0.852	0.462
Adduction	0.28 (0.30)	0.25 (0.24)	0.22 (0.23)	0.958(2,48)	0.391	0.975	1.000	0.621
Abduction	9.96 (6.70)	10.20 (6.64)	9.87 (5.66)	0.335(2,48)	0.717	1.000	1.000	1.000

Knee angle data from the first two subjects were not included because of technical problems during data collection. One-way repeated-measures analysis of variance was performed at α = 0.05. Post-hoc test included two-tail paired t test with a Bonferroni adjustment for multiple comparisons (p value was multiplied by the number of comparisons (n = 3)). *p<0.05.
F, follicular phase; O, ovulation; L, luteal phase.

Table 2 Correlation (R value) between laxity changes (ΔLAX1_2, ΔLAX2_3) and variable changes from the follicular phase to ovulation, and ovulation to the luteal phase

Knee laxity (mm)	Peak knee angle (°)		Peak knee moment (Nm)					Knee impulse (Nms)			
ΔLAX1_2	ΔAB1_2	ΔFL1_2	ΔEX1_2	ΔINT1_2	ΔADD1_2	ΔABD1_2	ΔEXT1_2	ΔEX1_2	ΔINT1_2	ΔADD1_2	ΔABD1_2
	−0.123	0.159	0.228	−0.003	0.176	−0.127	0.073	0.237	−0.116	0.523*	−0.063
ΔLAX2_3	ΔAB2_3	ΔFL2_3	ΔEX2_3	ΔINT2_3	ΔADD2_3	ΔABD2_3	ΔEXT2_3	ΔEX2_3	ΔINT2_3	ΔADD2_3	ΔABD2_3
	−0.127	−0.068	0.066	0.526*	0.379	−0.200	0.057	0.044	0.450*	0.408*	−0.217

ΔLAX1_2, changes (mm) in knee joint laxity at 89 N from the follicular phase to ovulation; ΔLAX2_3, changes in knee joint laxity at 89 N from ovulation to the luteal phase; Δ1_2, changes from the follicular phase to ovulation; Δ2_3, changes from ovulation to the luteal phase; AB, knee abduction angle; FL, knee flexion angle; EX, knee external rotation; INT, knee internal rotation; ADD, knee adduction; ABD, knee abduction; EXT, knee extension.
*p<0.05.

(knee abduction and flexion angles) were determined using a joint coordinate system.[35] Knee joint kinetics (internal knee moment (Nm) and impulse (Nms)) were calculated for the stance phase during the cutting motion using a standard inverse dynamics approach. Peak internal knee moment was calculated and represents the three-dimensional torque or twisting load on the knee. Internal knee impulse was quantified by integrating the moment–time curve and thus represents the cumulative twisting load on the knee during the entire stance phase (fig 2).[33]

Statistical analysis
One-way repeated-measures analysis of variance was conducted to assess whether knee joint kinematics and kinetics were altered across the menstrual cycle (follicular phase, ovulation and luteal phase). Post-hoc analysis included two-tail paired t tests (with Bonferroni correction) to compare the differences in variables from the follicular phase to ovulation, and ovulation to the luteal phase. Pearson's correlation coefficients were calculated to investigate the relationship between changes in knee laxity and changes in knee joint variables from the follicular phase to ovulation, and from ovulation to the luteal phase. Statistical analyses were performed using SPSS for Windows V14.0 at $\alpha = 0.05$.

Sample size was based on the ability to show differences in knee joint laxity between menstrual stages (eg, follicular phase and ovulation). On the basis of a previous study,[26] a 0.6 mm difference in knee joint laxity at 89 N (the follicular phase, 4.7 (0.8) mm; ovulation, 5.3 (0.7) mm) was expected. Thus, the sample size calculation showed that 22 subjects were required for a power of 0.8 in the knee joint laxity. No previous data were available for a sample size calculation to detect differences in knee joint kinematics and kinetics due to changing knee laxity during the menstrual cycle.

RESULTS
Knee laxity, knee joint kinematics and kinetics were compared across phases of the menstrual cycle (table 1). An increase in knee joint laxity at ovulation compared with the luteal phase was observed during the menstrual cycle (table1, p = 0.015). However, no significant differences in peak knee angle, peak knee moment and knee impulse were found across the menstrual cycle. Correlation coefficients were calculated between changes in knee laxity and changes in kinematic and kinetic variables during the cutting movement (table 2). Significant positive correlation between changes in knee laxity and changes in knee moment and impulse were found (table 2, p<0.05). The correlation (R value) between changes in laxity and changes in peak knee adduction impulse from the follicular phase to ovulation was 0.523 (fig 3A, p = 0.007). The correlation

between changes in laxity and changes in peak knee internal moment from ovulation to the luteal phase was 0.526 (fig 3B, p = 0.007). Correlations between changes in laxity and changes in knee internal rotation impulse, and changes in laxity and changes in knee adduction impulse from ovulation to the luteal phase were 0.450 (fig 3C, p = 0.024) and 0.408 (fig 3D, p = 0.043), respectively. The current correlations (R = 0.408, 0.450, 0.523 and 0.526) range from a fair (0.25–0.50) to a moderate to good (0.50 to 0.75) relationship with respect to characteristics in biological science.[36] Thus, changes in knee laxity were found to be related to changes in both knee joint moment and impulse during the menstrual cycle.

DISCUSSION
The purpose of this study was to investigate whether changing knee joint laxity during the menstrual cycle affects biomechanical risk factors at the knee. We found an increase in knee joint laxity at 89 N during ovulation compared with the luteal phase, confirming previous results showing increases in knee joint laxity during the menstrual cycle.[26–29] However, we did not detect any differences in knee joint angles and loading at ovulation compared with other phases (table 1). It appears that menstrual phase is not a good predictor of knee joint loading; rather joint loading is related to knee joint laxity.

On the other hand, changes in knee laxity between different menstrual phases (follicular versus ovulation, ovulation versus luteal) correlated with changes in knee joint loads. For example, we found that 15 women in whom knee laxity increased from the follicular phase to ovulation showed a tendency to increase knee loads (adduction impulse), whereas the other 10, in whom knee laxity decreased, showed a tendency to decrease knee loads. Conversely, 20 women in whom knee laxity decreased from ovulation to the luteal phase showed a tendency to decrease knee loads (internal rotation moment and impulse and adduction impulse), whereas the other five, in whom knee laxity increased, showed a tendency to increase knee loads. Thus, a positive correlation for changes in knee laxity was seen, coupled with changes in knee joint moment and impulse from the follicular phase to ovulation, and ovulation to the luteal phase (table 2). Greater knee laxity was related to increased knee joint loading in some women at specific times of the cycle.

Proposed ACL injury mechanisms
Valgus (adduction) and rotational moment at the knee has been proposed as an ACL injury mechanism that may cause sufficient stress to rupture the ACL during high-risk movement.[37] Piziali et al[38] found that 125–210 Nm of valgus or 35–80 Nm of internal rotation torque led to rupture of the ACL in a cadaveric study.

Figure 3 (A) Correlation between changes in knee laxity (mm) and changes in knee adduction impulse (Nms) from the follicular phase to ovulation. (B) Correlation between changes in knee laxity (mm) and changes in knee internal rotation moment (Nm) from ovulation to the luteal phase. (C) Correlation between changes in knee laxity (mm) and changes in knee internal rotation impulse from ovulation to the luteal phase (Nms). (D) Correlation between changes in knee laxity (mm) and changes in knee adduction impulse (Nms) from ovulation to the luteal phase.
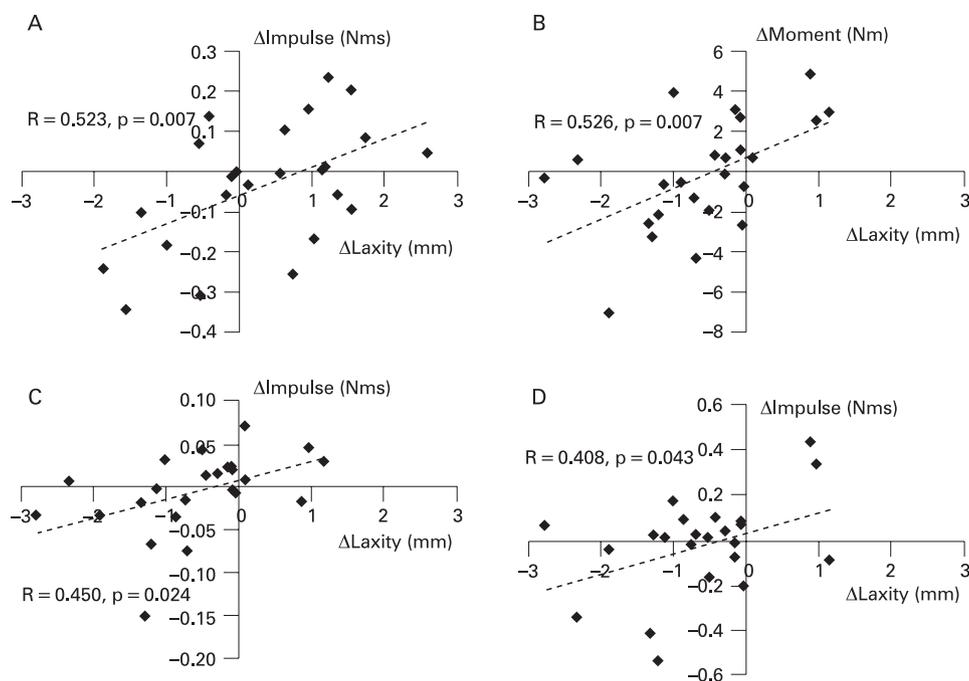
Whereas Piziali *et al* separated valgus and rotational loads, Kanamori *et al*[39] applied a combined 10 Nm valgus and 10 Nm internal tibial torque to 12 human cadaveric knees. They found that strain on the ACL is significantly increased when the valgus torque and the internal tibial torque were combined at the knee. Thus, the combination of these two loads may generate greater loading on the ACL than isolated loading in cadaveric tests.[37 39] In human studies, differences in knee mechanics between men and women suggest that a greater joint moment may be the key contributor to the ACL injury situation.[5 14 16] Hewett *et al*[40] prescreened biomechanical variables in 205 female athletes and prospectively observed ACL injury incidences during their sports session. They found a 2.5 times greater valgus loading in nine women who injured their ACL than in the uninjured group. They concluded that a valgus load is the primary predictor of high ACL injury risk in female athletes.

We have found that knee joint laxity correlates positively with knee joint loads during the menstrual cycle. Internal knee joint loads provide appropriate dynamic stability of the knee during the stance phase. Our results indicate increased knee internal rotation and adduction (valgus) loads with an increase in knee joint laxity at the initial contact of the cutting movement. At the initial touchdown of the cutting movement, the knee tends to be abducted (valgus) with tibial external rotation, and the foot is abducted and inverted (fig 2).[7] As most non-contact ACL injuries are observed at the first 10–20% of the stance phase of cutting or side stepping movements,[23] these internal knee adduction and internal rotation moments at an initial contact may be related to loading on the ACL.

Clinical relevance

Our dataset show a positive correlation between changes in knee laxity and changes in knee adduction as well as internal rotation loads during the menstrual cycle. An approximate change of 1–3 mm in knee laxity during the menstrual cycle caused a difference of ~3–4 Nm in internal rotation moments (fig 3B) and ~40–50 Nm in adduction moments. On the basis of

findings of previous cadaveric studies,[38 41–43] increased joint loads due to an increase in knee laxity during the menstrual cycle in the present study seem to be insufficient to rupture the ligaments. However, even with the controlled testing protocol used in this study (ie, a preplanned 45° cutting manoeuvre at 3.5 m/s to accommodate different skill levels of participants), increased knee joint laxity did increase the joint loading by ~50%. For example, an increase of 1 mm in knee laxity is associated with an increase of 50% in knee joint loads, indicated by the slope of a simple linear regression. In an actual game situation, more aggressive movements such as decelerating and accelerating the body quickly or changing direction in an unexpected situation may have a more significant effect on increasing knee joint loading. Thus, an increase in knee loads due to increases in knee laxity during the menstrual cycle may escalate the risk of ACL injury. It is also expected that the effect of knee rotational and adduction loads on the ACL is greater when these knee joint loads are combined, as seen in cadaveric studies.[37 39]

CONCLUSIONS

We believe that sex is an important contributor to ACL injury risk. However, most previous findings have not successfully explained subject variability in the risk of ACL injury among women. Our results indicate that knee joint laxity correlates positively with knee joint loads during the menstrual cycle. Even though the relationship between knee joint loads and the menstrual phase cannot be generalised because of subject variability in knee laxity across the menstrual cycle, changes in knee laxity correlated positively with changes in knee joint loads.

These are the first findings of a positive relationship between knee joint laxity and knee joint loads during the menstrual cycle, and as such may help to explain subject variability in ACL injuries during female sports activity. Categorising subject variability in knee joint laxity may be important in predicting knee joint loading and ACL injury risk.

What is already known on this topic

▶ Tearing of the anterior cruciate ligament (ACL) occurs more often in females than males.
▶ Sex differences in anatomy, movement patterns and hormones have been investigated to try to understand the mechanism of ACL injury in females.
▶ Subject variability of ACL injuries among females is not well understood.

What this study adds

▶ Knee joint laxity correlates positively with knee joint loads regardless of the menstrual phase.
▶ Increased knee laxity may be a potential risk factor for ACL injuries among females during sports activity.

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