Yoga Practice and Physiotherapy

Robert-McComb JJ, et al. Yoga Practice Phys Ther: YPPT-133.

Research Article

DOI: 10.29011/YPTR-133. 000033

The Effect of Phases of the Menstrual Cycle on Frontal Plane Knee Kinematics During Landing

Jacalyn J Robert-McComb[1], C Roger James[2], Jennifer Merkle Ford[1], Reid Norman[2], Greg Dedrick[2]

[1]Texas Tech University, Lubbock, Texas, USA

[2]Texas Tech University Health Science Center, Lubbock, Texas, USA

***Corresponding author:** Jacalyn J Robert-McComb, Department of Health, Exercise, and Sport Sciences, Texas Tech University, Lubbock, TX 79409-3011, USA. Tel: +18068346306; +18067981073; +18067421688; Email: jacalyn.Mccomb@ttu.edu

Citation: Robert-McComb JJ, James CR, Ford JM, Norman R, Dedrick G (2017) The Effect of Phases of the Menstrual Cycle on Frontal Plane Knee Kinematics During Landing. Yoga Practice Phys Ther: YPPT-133. DOI: 10.29011/YPTR-133. 000033

Received Date: 19 August, 2017; **Accepted Date:** 7 September, 2017; **Published Date:** 14 September, 2017

Abstract

Knee valgus, a known Anterior Cruciate Ligament (ACL) injury risk factor, is subject to hormonal changes during the menstrual cycle. Therefore, the purpose of this study was to analyze 2D frontal plane knee kinematics during drop-jump landing across phases of the human menstrual cycle (days 1-3;11-13;21-23). Twenty-seven (18-25 years) females with normal menstrual cycles initially met inclusion criteria for study participation. Twenty two-females were used for data analysis. The protocol consisted of drop-jumps from a 50cm platform while the participant's frontal plane movement was recorded using a single digital video camera (60 Hz). The initial time period for data collection was counterbalanced across days of the menstrual cycle and randomized. The procedures were identical for all repeated testing. Two separate one-way repeated measures ANOVAs were used to analyze landing patterns. Alpha was set at .05. There was a significant difference for valgus knee angle among days 1-3, 11-13, and 21-24 of the menstrual cycle, $F(2, 42) = 3.92$, $p = .037$. Post-hoc tests revealed a significant difference for valgus knee angle between days 1-3 and days 11-14, $t(21) = 2.733$, $p = .012$. No other significant differences were found. The largest magnitude of valgus knee angle occurred during the late follicular phase (days 11-14) of the menstrual cycle, when there was a large spike in estradiol.

Keywords: ACL Injury; Human Menstrual Cycle; Landing Pattern; Valgus Knee Angle

Introduction

The number of female athletes participating in competitive athletics has increased dramatically since the origination of Title IX in 1972. In tandem, there has been in increase in the rate of injury in female athletes, particularly knee injuries. Female athletes are anywhere from two to eight times more likely to sustain a debilitating Anterior Cruciate Ligament (ACL) injury than their male counterparts while engaging in similar activities [1-3]. This is a serious concern because the ACL is vital to the stability of the knee, as it prevents anterior tibial translation and secondarily assists in valgus control of the knee. Not only do female athletes present a much greater incidence of ACL injury, they are also more vulnerable to re-injury and have increased knee laxity after ACL reconstruction than their male counterparts [4]. Though the incidence of knee injury in females is so much greater than that of males, no single causative factor has been identified for this discrepancy. The increased injury rate of the ACL in females has been attributed to many variables including but not limited to: anatomical and biomechanical sex differences; neuromuscular imbalances in females that may affect motor patterns; increased valgus at the knee (an abnormal outward turning of the knee); as well as hormonal fluctuations during the menstrual cycle [5-8]. Females demonstrate greater valgus knee motion during stop-jump and landing tasks than do male athletes [5,6]. This motion can translate to a greater number of ACL injuries, because excessive valgus motion is a mechanism for ACL rupture [6].

While there is most probably a combination of risk factors that contribute to this discrepancy in injury rate between sexes, fluctuations of the ovarian hormones throughout the menstrual cycle may influence both ligament strength [9,10] and ligament loading via alterations in neuromuscular control [11]. During the menstrual cycle, females are exposed to cyclic hormonal alterations in secretions of the steroid hormones, estrogen and progesterone. These ovarian steroid hormones may affect the formation, metabolism and functioning of collagenous tissues in both animal models and human structures [12-14]. Furthermore, receptors for these hormones have been identified in the human ACL [12] and tissues related to neuromuscular functioning [15]. If motor patterns and neuromuscular functioning of the tissues around the ACL are affected by changes in the levels of the sex hormones, then it is possible that dynamic motion of the knee joint might be altered during hormonal fluctuations within the menstrual cycle.

Hormonal fluctuations have been suggested to contribute to both laxity of the knee joint [16] and altered neuromuscular control of the joint [4,10,11,13,15,17]. Therefore, the purpose of our study was to test the hypothesis that there would be a difference in frontal plane knee motion and peak valgus knee angle on days of the menstrual cycle when estrogen is elevated (day 11-13), when progesterone is elevated (days 21-24) and when both steroids are low (days 1-3). Figure 1 graphically displays the cyclic nature of the ovarian sex hormones. Frontal plane knee motion in this study was defined as the minimum distance between the bilateral knee markers (knee collapse) throughout the stance phase of the landing. Peak valgus knee angle was quantified as the minimum negative value observed during the landing between initial foot contact and take-off.

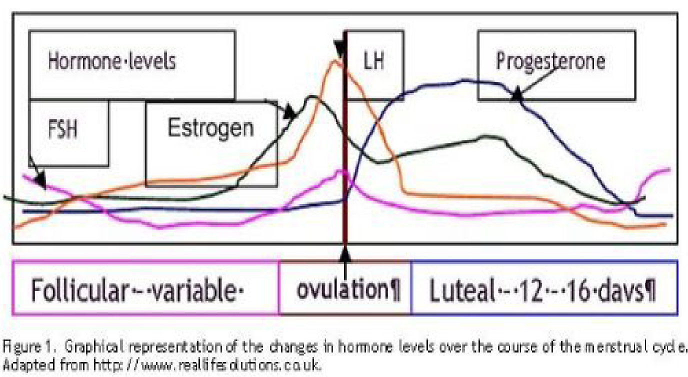

Figure 1: Changes in Hormonal Levels during a Normal Menstrual Cycle.

Methods

Subject Selection Criteria

We recruited female subjects from the local area through the use of advertising literature, posters and flyers. Subjects signed an informed consent as approved by the Institutional Review Board (IRB) prior to any data collection. A Women's Health History Questionnaire [18] was used to initially screen subjects for eligibility. Potentially eligible subjects were scheduled for an appointment in the Applied Physiology Laboratory to determine their hematocrit levels and assess anatomical abnormalities of the lower extremities that would prevent their full participation in the study. Full participation in the study required that subjects:

- were between 18 and 25 years of age
- menstrual cycle length fell between 26-32 days for at least 1 year prior to participation in the study;
- cycles were classified as eumenorrheic, as defined by Loucks and Horvath [19]
- had not used medicinal contraceptives six months prior to participation in the study;
- did not list medical conditions that would have abnormally affected hormonal fluctuations
- hematocrit level was at least 38% (per IRB regulations for blood collection)
- they were non-smokers
- were physically active (exercise at least 30 min a day, 3 times a week)
- did not have any current lower extremity injuries, or a history of lower extremity surgeries
- had never received training in proper jumping and landing techniques
- anthropometric measurements including: leg length discrepancy, femoral anteversion and retroversion, Q-angle, femoral length, and tibial length fell within an established range for each measurement.

A total of 27 eumenorrheic females (age 20.5 ± 1.9; height 164.9 ± 5.6 cm; weight 62.1 ± 13.7 kg; Wojty's [20] activity scale 5.4 ± 1.4) met the inclusion criteria for full study participation.

Procedures

Subjects who met all of the study eligibility requirements were given a menstrual history log and were asked to record the days of their cycles using this log for three months. The first two months were used to determine the average length of each subject's menstrual cycle and the last month was used to determine menstrual cycle phase. The participants reported to the Clinical Biomechanics Laboratory for data collection between days 1-3 (early follicular phase), between days 11-13 (late follicular phase), and between days 21-24 (mid luteal phase).

Randomization of the Testing Cycle

The initial time period for data collection was counterbalanced across days of the menstrual cycle and randomized. Subjects had their blood drawn and participated in the drop-jump protocol at three times during their menstrual cycle following a cyclic order after their first visit (days 1-3,11-13, 21-23 or days 11-13, 21-

23,1-3 or days 21-23,1-3, 11-13). The procedures were identical for all repeated testing.

Drop-Jump Protocol and Blood Collection

We collected participant's blood from the cubital fossa using a 21-gauge needle upon arrival at the laboratory. Vacutainers were utilized to draw 5-10 cc's of blood. All blood vials were labeled by subject number and day of the cycle, serum was collected and stored at -80ºC for later analysis.

The drop-jump protocol consisted of drop-jumps from a 50cm platform. We placed 6 retroreflective markers bilaterally on the skin using double-sided medical tape. The markers were placed bilaterally on the:

- greater trochanter of the femur,
- lateral femoral condyles, and
- lateral malleoli (see Figure 2).

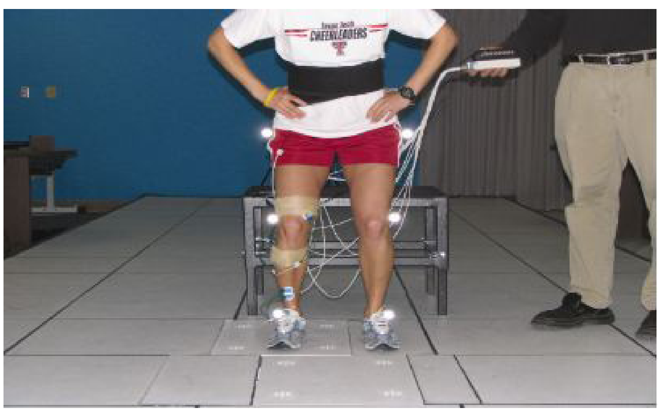

Figure 2: Retroreflective Markers on Participants.

We instructed participants verbally and by demonstration how to perform the drop-jump task. Once they verbally stated that they understood the protocol, they were allowed to practice the task until it was performed satisfactorily. The protocol consisted of the participant standing with their weight equally distributed over both feet on a 50 cm platform, with their hands at a comfortable position on their hips. When the participant was ready, she stepped off (without jumping) of the raised platform and landed bilaterally with the right foot on a force platform that was embedded in the floor (Plate Type 4060-10, Bertec Corporation, Columbus, OH) and the left foot on the adjacent ground. Immediately after landing, participants executed a maximum vertical jump with their hands remaining on their hips. Participants were asked to perform the drop-jump task until 3 successful trials had been recorded. The video data were sampled at 30 frames/second using a digital video camera (DCR-HC40; Sony Electronics, Inc., Oradell, New Jersey) and analyzed at 60 fields/second.

Hormonal Assays

Serum levels of estradiol (E_2 or 17β-estradiol, [100 □l]), progesterone (100 □l), and testosterone (50 □l), were measured in duplicate by solid-phase radioimmunoassay (Diagnostic Products Corporation, Los Angeles, CA) from blood samples taken prior to the biomechanical data collection. Estradiol (E2) represents the major estrogen in humans and is the most potent naturally-occurring estrogen. Testosterone levels were examined to screen for polycystic ovary syndrome which would skew the results. Estradiol levels are expressed in picograms/ml of blood, progesterone and testosterone levels in nanograms/ml of blood.

Biomechanical Analysis

Video images of the participant's drop-jumps were digitized (Peak Motus Systems, Englewood, CO) to determine the x, y coordinates of the reflective markers in space. Initial contact and take off were visually determined and recorded during the stance phase of the landing by viewing the frontal plane video. Raw x, y coordinates were smoothed (6 Hz; two-pass, fourth-order, no phase shift Butterworth digital filter in Motus), and the data files were exported to MATLAB for further analysis.

Knee valgus/varus angle was calculated from the coordinate data as the relative angle of the tibia to the femur in the frontal plane of the right leg, as projected on the frontal plane using a custom program (MATLAB, Version 7). For the analysis a convention was used in which varus and valgus angles were reported as positive and negative values, respectively. Peak valgus knee angle was quantified as the minimum negative value observed during the landing between initial foot contact and take-off. Frontal plane knee motion was measured as a function of the minimum distance between the bilateral knee markers (knee collapse) throughout the stance phase of the landing. Data were reduced and copied into an Excel spreadsheet and prepared for analysis in SPSS (version 13.0).

Data Analysis

At the completion of the study, we examined estradiol and progesterone values for the subjects who completed all phases of the protocol (N=26 [days 1-3, 11-13, and 21-24]). If the observed levels were not consistent with the specified day of the menstrual cycle, the participants were excluded from any further data analysis. Therefore, a total of five subjects were dropped from the data analysis because of invalid or incomplete data resulting in a sample size of 22 subjects. Descriptive statistics were run for the 22 subjects.

We used two (1x3) repeated measures ANOVA to observe the effects of menstrual cycle phase on knee motion (the minimum distance between the bilateral knee markers throughout the stance phase of the landing) and peak valgus knee angle (SPSS for Windows, Version 13.0). Alpha level was set at 0.05. We used paired t-tests to determine the presence of pair wise differences in knee valgus angle among the three menstrual cycle conditions. Alpha level was set at 0.05.

Results

Descriptive statistics for the 22 subjects can be found in Table 1. Levels of estradiol (E2), progesterone, and testosterone during days 1-3, 11-13, and 21-24 can be found in Table 2. The measures of estradiol, progesterone and testosterone were each within the normal range of published values for these

Variable	M ± SD	Range
Age	20.18 ± 1.82	18-24
Height (cm)	165.97 ± 5.42	158.8-180.3
Weight (kg)	64.22 ± 14.79	49.9-120
Activity level scale	5.23 ± 1.27	04-Aug
Age Began Menses	13.27 ± 1.08	Nov-15
Number of days of cycle	5.23 ± 1.27	03-Aug
Number of days between cycles	28.27 ± 1.45	26-31
Leg Length (cm)	85.41 ± 3.27	82-94
Tibial Length (cm)	38.60 ± 1.94	34.5-43
Craig's test (degrees)	10.19 ± 0.89	9.25-13.50
Quadriceps angle (degrees)	16.14 ± 1.13	15-20
Hematocrit (%)	41.59 ± 2.52	39-50

Table 1: Descriptive Characteristics of Subjects (N=22).

	Early Follicular	Late Follicular	Mid-Luteal
Estradiol (pg/ml)	61 ± 22.15	159 ± 27.95	132 ± 19.30
	(16.07-95.6)	(39.21-563.49)	(50.01-530.52)
Progesterone (ng/ml)	0.65 ± 0.09	1.20 ± 0.41	11.10 ± 1.54
	(0.16-1.93)	(0.19-4.06)	(1.07-24.51)
Testosterone (ng/ml)	0.26 ± 0.02	0.34 ± 0.03	0.36 ± 0.04
	(0.15-0.58)	(0.18-0.84)	(0.17-0.91)
Note: Values are M ± SD with the range in parentheses			

Table 2: Hormone Levels by Cycle Phase (N=22).

No significant differences were found for knee motion as defined in the study (knee distance) between days 1-3, days 11-13, and days 21-24 of the menstrual cycle, F (2,42) = 1.33, p = .286, f = .22, power = .254. We did find a significant difference for peak valgus knee angle as defined in the study among days 1-3, days 11-13, and days 21-24 of the menstrual cycle, F (2,42) = 3.92, p = .037, f = .32, power = 0.64. The Mean (M) and Standard Deviation (SD) values for knee distance and valgus knee angle are listed in Table 3.

	Early Follicular	Late Follicular	Mid-Luteal
Knee Distance (cm)	32.92 ± 4.55	32.32 ± 4.37	33.03 ± 4.61
	(26.43-45.85)	(24.77-45.60)	(27.21-45.86)
Knee Angle (degrees)	−7.83 ± 5.74	−9.70 ± 7.26	−7.53 ± 6.44
	(−.47- −25.92)	(−3.22- −31.91)	(1.23- −31.07)
Note: Values are M ± SD with the range in parentheses			

Table 3: Knee Distance and Knee Angle by Cycle Phase (N=22).

A significant difference was found for peak valgus knee angle between the early follicular (days 1-3) and late follicular phases (days 11-13) of the menstrual cycle, t (21) = 2.733, p = .012. No other significant differences were found. The M and SD for knee distance and valgus knee angle are graphically displayed in Figures 3 and 4.

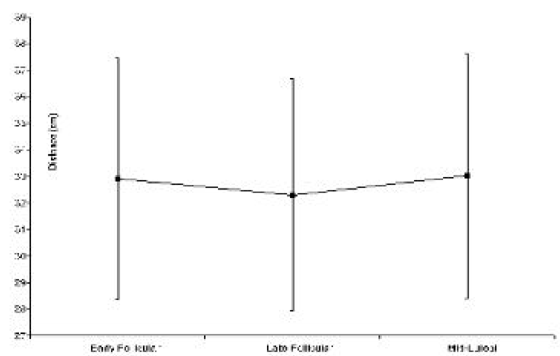

Figure 3: Mean Knee Distance.

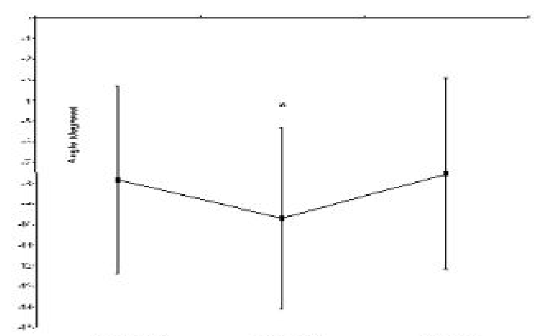

Figure 4: Mean Valgus Knee Angle.

Discussion

The goal of our study was to identify changes in knee kinematics as they relate to the cyclic changes in ovarian hormone levels. We think it is important to examine knee kinematics in females during cyclic hormonal alterations because of the higher incidences of ACL injury and complications following ACL reconstruction in females compared to males. Females have increased knee laxity after ACL reconstruction; increased reconstruction of ACL grafts; and less successful outcomes with ACL reconstruction than males [4,21] . Furthermore, the expression of estrogen and progesterone receptors in both the human ACL [12,14] and the brain [15] provides the theoretical basis for examining the landing patterns of females at peak exposure to estrogen and progesterone as well as during times when both of these hormones are low in the human menstrual cycle.

The hypothesis that frontal plane knee kinematics would vary with hormonal fluctuations during the menstrual cycle is supported in the current investigation. A significant difference was observed for peak valgus knee angle between days 1-3 and days 11-13 The greatest valgus knee angle was observed during the late follicular phase (days 11-13) following a peak in estrogen secretion. The late follicular phase is when circulating estradiol levels are highest, but it is also when tissues have had the longest exposure to estrogen without a concomitant exposure to progesterone.

Work by Yamauro, Hama, Takeda, Shikata, and Sanada [22] has shown a significant decrease in collagen in rats given only estrogen, or estrogen in combination with progesterone. When rats were given progesterone alone, the collagen content increased significantly. Progesterone has also been shown to down regulate the estrogen receptor in certain rodent and primate connective tissue models. Through the action of progesterone, the effects of estrogen are inhibited [23]. Since days 11-13 represent the time when exposure to progesterone has been minimal, it could be argued that the effects of estrogen on connective tissue are the most potent at this time in the cycle.

In an ACL tissue model, a physiological concentration of estrogen (similar to the amount circulating throughout the menstrual cycle) resulted in a decrease in fibroblast metabolism and collagen synthesis [24]. Similarly, Yu and colleagues [14,23] found that with increased estradiol, there was a decrease in fibroblast proliferation in Type I collagen synthesis. Estrogen has also been shown to acutely decrease total collagen content in rat tendon and other connective tissues [25].

The effect of estrogen on collagen is critical to the integrity of the ACL because Type I collagen is the primary component of ligament strength. An alteration in the collagen matrix may have an effect on the remodeling capabilities of the ACL and could alter its mechanical properties [4]. In ovariectomized rabbits, estradiol replacement resulted in a significant reduction in force required to cause ligament failure [13].

Several human studies have also demonstrated a relationship between spikes in estrogen levels and laxity changes in ACL tissue quality [4,16,24]. Tissue laxity and diminished stress tolerance occur due to decreased fibroblast activity and increased metallomatrix protease activity associated with exposure to estrogen [17]. Estrogen, in particular, has been shown to affect soft tissue strength, muscle strength and central nervous system function [26]. The amount of peak valgus knee angle observed during days 11-13 in our present study may also be attributed to a hormonal alteration in neuromuscular control as hypothesized by Dedrick et al. [11] .

Concluding Remarks

Knee joint laxity and the feed forward central drive associated with motor movements may affect the kinematics of the knee in females during sport activities such as jumping and landing, and especially during specific days of the menstrual cycle. Abnormal biomechanics during sports activities such as jumping and landing can cause high joint reaction forces and increased dynamic valgus motion and valgus angle at the knee, both of which can be a contributor to non-contact ACL injury.

Park and colleagues [27,28] suggest that there is an increase in knee joint laxity and decreased stiffness at ovulation (late follicular phase corresponding to days 11-13). The researchers further state that an increase in knee laxity may result in an increase in adduction impulse in a cutting maneuver, an increase in knee adduction moment, and an increase in external rotation loads during jumping and stopping tasks. Myer et al. [21] further postulated that this increase in laxity caused an increase in anterior-posterior displacement which may increase the incidence of ACL injury.

There were no significant differences found for knee motion as measured by knee distance among days 1-3, days 11-13, and days 21-24 of the female menstrual cycle. This is somewhat surprising in light of the fact that there was a significant difference found for knee angle. Knee angle and knee distance are both measures of frontal plane knee kinematics measured using a common reference marker. However, both variables peaked during the late follicular phase (Figures 3 and 4), suggesting that they followed a similar trend. The relationship between these two variables was explored using correlation: Only a small positive correlation ($r = .30$) was found in this sample. Knee distance is a 2 dimensional measurement resulting from 3 dimensional movements of the hip, knee, ankle and foot. This composite lower extremity movement pattern includes knee valgus, femoral internal rotation, foot pronation and ankle flexion. Perhaps the measured increase in valgus knee angle was offset by lesser changes in femoral internal rotation or foot pronation. Additionally, the knee distance variable could have been influenced by changes in stance width, which was not quantified in the current study.

A limitation of this study is that the results of this study are only applicable to the population utilized for the study. The participants here were young, healthy, eumenorrheic females who were recreationally active. Many athletes at risk for ACL injury who are participating in organized high energy output sports are oligomenorrheic. Also, not controlling for stance width may also have influenced the knee valgus measurement using a 2-dimenstonal method of analysis. A two dimensional analysis of a complex three dimensional process (knee valgus) cannot determine where the increased valgus originates (hip, knee, ankle or foot).

A strength of this study was the prospective nature of the data collection, exacting and well controlled entry criteria for study eligibility, serum analysis of sex hormones (which allowed us to eliminate women who were not in the menstrual cycle phase that corresponded to our stated days for analysis), and the observation of 3 months of normal menstrual activity during the study period.

Summary and Conclusion

We found a significant difference in peak valgus knee angle during days 11-13 when serum estradiol was highest. This time frame in the menstrual cycle could have important implications since progesterone inhibits the effects of estrogen [23]. With minimal inhibition from progesterone, the effects of estradiol could be magnified. Estrogen has been previously shown to affect soft tissue strength, muscle strength, and central nervous system function [26] and the quality of ACL tissue following peak exposure to estrogen. These coupled with altered neuromuscular control resulting in an increased valgus knee angle could suggest a possible dual mechanism for the effects of hormonal fluctuations on ACL injury in female athletes. Even though our study did not examine ACL injury in females, researchers who have examined ACL injury in female athletes have found increased injury during the phase of the menstrual cycle correlated with days 11-13 [29].

Acknowledgement

We would like to acknowledge Brittany McCullough, MS, Texas Tech University for her editing contributions to the manuscript. We would also like to acknowledge Ms. Xuping Qian for the hormone assays and her continual dedication to scientific research. Lastly, we would like to thank the National Athletic Training Association for their funding to conduct this research.

References

1. Arendt E, R Dick (1995) Knee Injury Patterns Among Men and Women in Collegiate Basketball And Soccer - Ncaa Data And Review Of Literature. American Journal of Sports Medicine 23: 694-701.
2. Gray J, Taunton JE, McKenzie DC, Clement DB, McConkey JP, et al., (1985) A Survey of Injuries to the Anterior Cruciate Ligament of The Knee in Female Basketball Players. International Journal of Sports Medicine 6: 314-316.
3. Toth AP, FA Cordasco (2001) Anterior cruciate ligament injuries in the female athlete. J Gend Specif Med 4: 25-34.
4. Slauterbeck JR, Fuzie SF, Smith MP, Clark RJ, Xu TK, et al. (2002) The Menstrual Cycle, Sex Hormones, and Anterior Cruciate Ligament Injury. J Athl Train 37: 275-278.
5. Chappell JD, Yu B, Kirkendall DT, Garrett WE (2002) A comparison of knee kinetics between male and female recreational athletes in stop-jump tasks. American Journal of Sports Medicine 30: 261-267.
6. Ford KR, GD Myer, TE Hewett (2003) Valgus knee motion during landing in high school female and male basketball players. Med Sci Sports Exerc 35: 1745-1750.
7. Shultz SJ, RJ Schmitz, AD Nguyen (2008) Research Retreat IV: ACL injuries--the gender bias: April 3-5, 2008 Greensboro, NC. Journal of athletic training 43: 530-531.
8. Shultz, S.J, Schmitz RJ, Nguyen AD, Chaudhari AM, Padua DA, et al. (2010) ACL Research Retreat V: an update on ACL injury risk and prevention, March 25-27, 2010, Greensboro, NC. J Athl Train 45: 499-508.
9. Dragoo JL, Padrez K, Workman R, Lindsey DP (2009) The effect of relaxin on the female anterior cruciate ligament: Analysis of mechanical properties in an animal model. Knee 16: 69-72.
10. Zazulak BT, Paterno M, Myer GD, Romani WA, Hewett TE (2006) The effects of the menstrual cycle on anterior knee laxity - A systematic review. Sports Medicine 36: 847-862.
11. Dedrick GS, Sizer PS, Merkle JN, Hounshell TR, Robert-McComb JJ, et al. (2008) Effect of sex hormones on neuromuscular control patterns during landing. J Electromyogr Kinesiol 18: 68-78.
12. Liu SH, al-Shaikh R, Panossian V, Yang RS, Nelson SD, et al. (1996) Primary immunolocalization of estrogen and progesterone target cells in the human anterior cruciate ligament. Journal of Orthopaedic Research 14: 526-533.
13. Slauterbeck J, Clevenger C, Lundberg W, Burchfield DM (1999) Estrogen level alters the failure load of the rabbit anterior cruciate ligament. Journal of Orthopaedic Research 17: 405-408.
14. Yu WD, Liu SH, Hatch JD, Panossian V, Finerman GA (1999) Effect of estrogen on cellular metabolism of the human anterior cruciate ligament. Clinical Orthopaedics and Related Research 366: 229-238.
15. McEwen B, Akama K, Alves S, Brake WG, Lee S, et al. (2001) Tracking the estrogen receptor in neurons: Implications for estrogen-induced synapse formation. Proceedings of the National Academy of Sciences of the United States of America 98: 7093-7100.
16. Shultz SJ, KIRK SE, Johnson ML, Sander TC, Perrin DH (2004) Relationship between sex hormones and anterior knee laxity across the menstrual cycle. Medicine and Science in Sports and Exercise. 36: 1165-1174.
17. Slauterbeck JR, DM Hardy (2001) Sex hormones and knee ligament injuries in female athletes. American Journal of the Medical Sciences 322: 196-199.
18. McComb JJR, Qian X, Veldhuis JD, McGlone JJ, Norman RL (2006) Neuroendocrine responses to psychological stress in eumenorrheic and oligomenorrheic women. Stress-the International Journal on the Biology of Stress 9: 41-51.
19. Loucks AB, SM Horvath (1985) Athletic Amenorrhea - A Review. Medicine and Science in Sports and Exercise 17: 56-72.
20. Wojtys EM, BB Wylie, LJ Huston (1996) The effects of muscle fatigue on neuromuscular function and anterior tibial translation in healthy knees. American Journal of Sports Medicine 24: 615-621.
21. Myer GD, Ford KR, Paterno MV, Nick TG, Hewett TE (2008) The effects of generalized joint laxity on risk of anterior cruciate ligament injury in young female athletes. American Journal of Sports Medicine. 36: 1073-1080.

22. Yamamuro T, Hama H, Takeda T, Shikata J, Sanada H (1977) Biomechanical and Hormonal Factors in Etiology of Congenital Dislocation of Hip-Joint. International Orthopaedics 1: 231-236.

23. Yu WD, Vahé P, Joshua H, Stephen L, Gerald F (2001) Combined effects of estrogen and progesterone on the anterior cruciate ligament. Clinical Orthopaedics and Related Research 383: 268-281.

24. Liu SH, Al-Shaikh RA, Panossian V, Finerman GA, Lane JM (1997) Estrogen affects the cellular metabolism of the anterior cruciate ligament: a potential explanation for female athletic injury. The American journal of sports medicine 25: 704-709.

25. Fischer GM (1973) Comparison of Collagen Dynamics in Different Tissues Under Influence Of Estradiol. Endocrinology 93: 1216-1218.

26. Wojtys EM, Huston LJ, Lindenfeld TN, Hewett TE, Greenfield ML (1998) Association between the menstrual cycle and anterior cruciate ligament injuries in female athletes. American Journal of Sports Medicine 26: 614-619.

27. Park SK, Stefanyshyn DJ, Loitz-Ramage B, Hart DA, Ronsky JL (2009) Changing Hormone Levels During the Menstrual Cycle Affect Knee Laxity and Stiffness in Healthy Female Subjects. American Journal of Sports Medicine 37: 588-598.

28. Park SK, Stefanyshyn DJ, Ramage B, Hart DA, Ronsky JL (2009) Alterations in Knee Joint Laxity During the Menstrual Cycle in Healthy Women Leads to Increases in Joint Loads During Selected Athletic Movements. American Journal of Sports Medicine 37: 1169-1177.

29. Beynnon BD, Johnson RJ, Braun S, Sargent M, Bernstein IM, et al. (2006) The relationship between menstrual cycle phase and anterior cruciate ligament injury - A case-control study of recreational alpine skiers. American Journal of Sports Medicine 34: 757-764.