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The influence of the menstrual cycle on anterior cruciate ligament injury

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SUMMARY

Knee joint injury is one of the most common injuries in the human musculoskeletal system. The risk is higher in women, usually during training. It is currently believed that, apart from visible anatomical differences, menstrual cycle phases seem to play a role in this increased incidence of trauma. Studies on joint stability reveal that gender determines the activation of different knee joint stabilization strategies, particularly with respect to the quadriceps femoris and hamstrings. The anterior cruciate ligament contains estradiol and progesterone receptors, which means that it changes its parameters during the menstrual cycle. Hormonal fluctuations during the menstrual cycle affect the responsiveness of the nervous system and cause changes in neuromuscular control of the knee joint. Estrogen level fluctuations contribute to the risk of injury within the knee. The risk is lower in women who use hormonal contraception. The aim of this study was to present and analyze the available literature in order to evaluate the risk of knee joint injury during the menstrual cycle.

Key words: menstrual cycle; sex hormones; knee joint injuries; ACL injury; neuromuscular control

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INTRODUCTION

Knee joint injury is one of the most common traumas within the musculoskeletal system. Sports such as basketball, volleyball and handball are characterized by dynamic changes in movement directions as well as sudden acceleration and deceleration movements. It is estimated that 70% of knee joint injuries result from incorrect rotation, landing or deceleration movements[1]. The incidence is 4–6-fold higher in women[2], particularly with respect to the anterior cruciate ligament (ACL) [3]. Statistically, the mean age of women undergoing ACL reconstruction is 14–17 years and 18–21 years, while the average age of men is 18–34 years [4]. The ACL provides 85% of the static restraint to the anterior tibial translation, thus contributing to normal joint arthrokinetics, and has a proprioceptive function. It contains 4 types of mechanoreceptors and free nerve endings that initiate protective muscle contraction[5,6].Research shows that 80% of all knee joint injuries occur by non-contact mechanisms. The analysis of ACL trauma has shown that 95% of injuries in female handball players and 65% of injuries in female basketball players, sustained over a dozen or so seasons, are non-contact injuries. Thirty-one per cent of patients with ACL injury have a moderate difficulty in moving on one's own, 44% of patients experience difficulty in everyday activities, while 77% of athletes can never return to the level of sport performance from before injury [7]. ACL injury is one of the prime causes of early degenerative changes when compared to individuals without such an injury [8].

One of the main causes of ACL injury is different anatomical structure in men and women. Greater susceptibility to ACL injury in women may be associated with greater joint

laxity and lower stiffness [9] as well as differences in pelvic structure, position of the iliac joints (smaller angle of inclination) [10], Q angle [2] and posterior slopes of the tibial plateau[11]. It must be underlined that the results of studies in this area are not conclusive. Recent research has not shown any association between the different anatomic structure and ACL injury.

The second hypothesis, analyzed in recent years, states that a different neuromuscular control strategy is responsible for the greater susceptibility of women to ACL injury. Studies have shown that muscle structures in the knee are activated in a different way in women compared to men. During physical activity, the knee joint is stabilized mainly by adequate quadriceps femoriscontraction. Appropriate activation of this muscle is the basic strategy of knee joint stabilization in the sagittal plane in women. This is associated with weaker hamstrings and greater ligament laxity. As for men, sEMG examinations prove that the hamstrings are activated first and followed by the quadriceps femoris, which provides better anterior drawer control. Up to 45 degree flexion, the quadriceps femoris function is antagonistic towards the ACL, whichincreases stress on the anterior cruciate ligament [3]. In women, the knee joint stabilization strategy is primarily based on greater domination of the ligamentous complex, whereas men activate the muscle tissue, mainly the hamstrings and gastrocnemius muscle. Research also indicates that increased physical activity in women does not affect the knee joint stabilization strategy. Greater quadriceps femoris contractionrelative to the hamstrings is believed to be the primary risk factor of ACL injury [3,6].

The third hypothesis combines the susceptibility to ACL injuries with the impact of sex hormones on ligament laxity and neuromuscular control [12]. Hormonal fluctuations during the menstrual cycle significantly affect the musculoskeletal system; they cause changes in soft tissues, muscle strength and collagen fiber formation [22].

MENSTRUAL CYCLE

The menstrual cycle is a cyclic phenomenon that depends upon numerous factors, including function of the central nervous system and endocrine system as well as intercellular metabolic processes [7,14]. It can be divided into 2 phases: follicular and luteal. A more detailed division reflects hormonal fluctuations [15]. A strict association between hypothalamic, pituitary and steroid hormones that determine normal cyclical changes in the reproductive system as well as the function of the hypothalamus–pituitary–gonadal axis play themajor role in menstrual cycle regulation from puberty until menopause.

During menstruation (1–5 days), lower estrogen and progesterone levels as well as decreased follicle-stimulating hormone (FSH) and luteinizing hormone (LH) concentrations are observed [13]. In the follicular phase (6–13 days), estrogen secretion increases, whereas progesterone values remain low. Relaxin secretion increases as well. FSH values continue to be low, but its secretion is of pulsatile nature until the LH surge. FSH secretion increases markedlyduring ovulation. In the post-ovulation phase, the level of estrogen falls, while the level of progesterone rises. The luteal phase is the final phase of the menstrual cycle. It is characterized byhigh progesterone values and low estrogen secretion [13]. The last 3 days of the cycle are referred to as the pre-menstrual phase in which estrogen secretion decreases whereas the progesterone level remains high, but falls at the end of this phase. Moreover, FSH and LH concentrations decrease as well.

INFLUENCE OF HORMONES ON LIGAMENT LAXITY

Estrogens are sex steroids that include estradiol, estrone and estriol. Estradiol (17ß-estradiol) is the basic natural estrogen secreted by granulosa cells of the dominant ovarian follicle. It controls oocyte development and is responsible for maintaining appropriate structure of the female reproductive organs. Estrone is a steroid estrogen with action similar to that of estradiol but considerably weaker. Finally, estriol is a steroid estrogen that elicits a shorter physiological response compared to the remaining estrogens [16].

Studies on the influence of sex hormones on ligament laxity indicate that there is a relationship between changing hormone levels and physical properties of the ACL. Research in this area is focused mainly on the influence of estradiol and progesterone on physical properties of the ACL, while the influence of other hormones is not discussed. Apart from the mechanoreceptors mentioned above, the ACL also contains receptors for estradiol and progesterone [17]. The levels of these hormones change during the menstrual cycle, which contributes to collagen network changes [12][5]. Increased

estradiol concentration, mainly in the pre-ovulatory phase where the highest blood levels of this hormone are observed, limits fibroblast proliferation and reduces the quantity of collagenous connections in the ACL, while increased progesterone concentration coexists with increased fibroblast proliferation and collagen fiber formation[12]. Higher estradiol levels have a direct influence on lower amounts of IGF-I (a mediator of collagen production) and ICTP (a marker of type I collagen degradation)[5]. Physiologically, IGF-1 exhibits analogous action to insulin, stimulates cartilage growth, promotes collagen and proteoglycan synthesis and maintains calcium, magnesium and potassium homeostasis.

Romani et al. investigated several estrogens (estradiol, estrone and estriol) as well as sex hormone-binding globulin (SHBG). The study tested whether these hormones and SHBG are correlated with ACL stiffness during three phases of the menstrual cycle in healthy women with regular menstruation. The results showed a negative correlation between blood estradiol concentration and ACL stiffness in the pre-ovulatory phase and a positive correlation between blood estriol concentration and ACL stiffness also in the pre-ovulatory phase [12]. The influence of sex hormones on target tissues can be modulated by interactions between them. By monitoring the influence of other sex hormones and SHBG, researchers have found that estriol and progesterone are partially and positively correlated with ACL stiffness in the pre-ovulatory phase [5]. Eiling et al. demonstrated that an increased quantity of estradiol increases ACL laxity by 0.5 mm in the ovulation phase and by 0.2 mm in the follicular and luteal phases[18], thereby increasing the risk of ACL injury.

Clinical trials have confirmed these results, showing that women who skied recreationally sustained ACL injury twice as often in the pre-ovulatory phase when the level of estradiol is the highest compared with other menstrual cycle phases. Beynnon et al., however, did not obtain results that would indicate changes in ligament laxity depending on menstrual cycle phases[19].

NEUROMUSCULAR CONTROL IN RELATION TO SEX HORMONES

The literature does not provide many examples of the influence of estrogens on neuromuscular control. Most reports focus on the outcome of movement rather than on the process of performing a given activity. Neuromuscular control can be defined as a reciprocal relation between the nervous system and the musculoskeletal system in response to afferent stimuli from proprioceptive receptors. Proprioception is understood as individual sense of the limb position and spatial movement as well as proper muscle and ligament activation [20]. The central nervous system plays the superior role in neuromuscular control. It is responsible for receiving stimuli from the peripheral, vestibular and visual systems, and subsequently for their processing to the appropriate level of motor control [21].Available studies on the influence of sex hormones on proprioception are inconclusive. Aydog et al. [22] demonstrated that knee joint proprioception is weaker in the menstruation phase compared to the follicular and early luteal phases. This can be caused by a change of distal latency (time needed for eliciting muscle contraction) or mechanoreceptor responsiveness. This phase is characterized by low levels of estrogen and progesterone. The authors believe that estrogen and progesterone exert their action by synergy. Fouladi measured knee joint position sensing. The greatest error was noted in the menstruation phase, and the lowest in the luteal phase [21,29]. Nevertheless, Hertel et al.[22], based on their own studies, propagate a different theory. They believe that there is no statistical association between proprioception and the menstrual cycle. Investigations on the influence of sex hormones, estrogens in particular, on the CNS indicate that motor abilities in physically active females do decrease at given stages of the menstrual cycle [23].

TRAUMA INCIDENCE

The incidence of non-contact ACL injuries in female athletes is three times higher than in men in the case of basketball and four times higher in the case of soccer [25]. Numerous studies have shown that the incidence of non-contact ACL injury increases in the pre-ovulatory phase, which is characterized by a high blood estrogen level[28]. Slauterbeck[26], however, has a different opinion. He proves that the incidence of ACL injury is higher in the first 2 days of the cycle, which is associated with a change in the values of estrogen and progesterone enzymes that can mediate expression of genes encoding tissue-remodeling proteins and enzymes. This situation may cause greater tissue destruc-

tion or regeneration depending on the cycle phase. Load on the knee joint upon landing from a jump and coronal deflection towards valgus or varus deformity have been observed to be lower in women using hormonal therapies. Moreover, these women also presented increased activity of the hamstrings in relation to the quadriceps femoris. This group was characterized by superior stability and lower laxity of the knee joint compared to the group of women who did not use hormonal therapies[27].

CONCLUSION

Anatomical differences between women and men as well as differences in psychophysical aspects, attitudes to sport and involvement in physical activity have been investigated on numerous occasions. Most research reports confirm the hypothesis about an existing fundamental gender-specific difference. Injury is an inseparable phenomenon of both sport and everyday activity [1].The knee joint is one of the joints in the human anatomic system that have received the greatest attention in research. Injury to this joint, the anterior cruciate ligament in particular, is 4 to 6 times more common in women than in men [2]. Some studies point to anatomical differences as significant factors in the process of injury. A number of authors, however, share the belief that anatomical differences do not cause knee joint injury directly, but are merely an indirect or predisposing factor.

Sports such as soccer, basketball or volleyball require the joint to exert proper motor control for forces generated by given movements that predispose to non-contact ACL injury [20,21]. Investigations on the influence of muscle control during the menstrual cycle are inconclusive due to complex interactions of sex hormones in women. It seems that sex hormones have a significant impact on neuromuscular control. An increase in estrogen values in the follicular phase raises ligament laxity and decreases stiffness, which some authors associate with increased risk of ACL injury. The effect of greater joint laxity is potentiated by a different stabilization strategy of the anterior tibial translation, which puts more load on the ACL [21,22]. Low estrogen and progesterone levels during menstruation contribute to worse proprioception, which presumably delaysthe nervous system reaction, thereby increasing the risk of ACL injury. Studies in women using hormonal therapies compared with to those who use no contraception confirm lower risk of ACL injury in the former [27]. Hormonal fluctuations affect both neuromuscular control and the occurrence of injury. However, since study results are not uniform, it is not possible to specify the phase that would predispose to greater occurrence of injuries. Since not all studies confirm the impact of estrogen fluctuations on muscular control,further studies are necessary. Sex hormone interactions, neuromuscular control and anatomy are interrelated and contribute to higher risk of anterior cruciate ligament injuries.

1. **J.O.F. Orthopedics**. Review article mechanisms of anterior cruciate ligament injuries in female athletes: a narrative review M. ABATE, D. VANNI, A PANTALONE Department of Medicine and Science of Aging, University G. d' Annunzio, Chieti-Pescara, Italy Received Ju 2013;5,1:27–34.
2. **Belanger L, Burt D, Callaghan J et al.** Anterior cruciate ligament laxity related to the menstrual cycle: an updated systematic review of the literature. *J. Can. Chiropr. Assoc.* 2013;57,1:76–86.
3. **Park S.K, Stefanyshyn D.J, B. Ramage B et al.** Relationship between knee joint laxity and knee joint mechanics during the menstrual cycle. *Br. J. Sports Med.* 2009;43, 3: 174–179.
4. **Csintalan R.P, Inacio M.C.S, Funahashi T.T.** Incidence rate of anterior cruciate ligament reconstructions *Perm. J* 2008;12, 3:17–21.
5. **Shultz S.J, Wideman L, Montgomery M.M et al.** Changes in serum collagen markers, IGF-I, and Knee joint laxity across the menstrual cycle *J. Orthop. Res.* 2012; 30:1405–1412.
6. **Hewett T.E**. Neuromuscular and hormonal factors associated with knee injuries in female athletes. Strategies for intervention. *Sports Med.* 2000;29,5:313–327.
7. **Noyes F.R, Mooar P.A, Matthews D.S, Butler D.L.** The symptomatic anterior cruciate-deficient knee. Part I: the long-term functional disability in athletically active individuals *J. Bone Joint Surg. Am.* 1983;65,2:154–162.
8. **Lohmander L.S, Ostenberg A, Englund M, Roos H**. High prevalence of knee osteoarthritis, pain, and functional limitations in female soccer players twelve years after anterior cruciate ligament injury *Arthritis Rheum* 2004;50, 10: 3145–3152.
9. **Park H.S, Wilson N.A, Zhang L.Q.** Gender differences in passive knee biomechanical properties in tibial rotation *J. Orthop. Res* 2008;26,7:937–944.
10. **Glinkowski W, Ciszek B**. Antomy of the Proximal Femur - geometry and architecture. Morphologic investigation and literature review. *Ortop. Traumatol. Rehabil.* 2002;4, 2:200–208.
11. **Simon R.A, Everhart J.S, Nagaraja H.N, Chaudhari A.M.** A case-control study of anterior cruciate ligament volume, tibial plateau slopes and intercondylar notch dimensions in ACL-injured knees," *J. Biomech.* 2010;43, 9:1702–1707.
12. **Romani W, Patrie J, Curl L.A, Flaws J.A.** The correlations between estradiol, estrone, estriol, progesterone, and sex hormone-binding globulin and anterior cruciate ligament stiffness in healthy, active females *J. Womens. Health (Larchmt).* 2003;12,3:287–298.
13. **Jonathan S. Berek**. Berek and Novak's Gynecology. *Edition: Fifteenth, North American Edition* 2011;December 12.

14. **Traczyk W**. Fizjologia człowieka w zarysie *PZWL Warszawa* 2013; wyd.8.
15. **Park S.K, Stefanyshyn D.J, Ramage B et al.** Alterations in knee joint laxity during the menstrual cycle in healthy women leads to increases in joint loads during selected athletic movements *Am J Sports Med.* 2009;37,6:1169–1177.
16. **Hall J.E**. Guyton and Hall Textbook of Medical Physiology *Physiology* 2010:1091.
17. **Sciore P, Frank C, Hart D.** Indentification of sex hormone receptors in human and rabbit ligaments of the knee by reverse transcription-polymerase chain reaction: Evidence that receptors are present in tissue from both male and female subjects *J Orthop Res* 1998;16:604.
18. **Eiling E, Bryant L. Petersen W et al.** Effects of menstrual-cycle hormone fluctuations on musculotendinous stiffness and knee joint laxity *Knee Surgery, Sport. Traumatol. Arthrosc.* 2007;15, 2:126–132.
19. **Beynnon B.D, Bernstein I.M, Belisle** A **et al.** The effect of estradiol and progesterone on knee and ankle joint laxity *Am. J. Sports Med.* 2005;33,9:1298–1304.
20. **Lehtonen J, Kokko H.** Sex *Curr. Biol.*2014;24,8:305–6.
21. **Lephart S.M, Giraldo J.L, Borsa P.A et al.** Knee joint proprioception: a comparison between female intercollegiate gymnasts and controls. *Knee Surg. Sports Traumatol. Arthrosc.* 1996;4,2:121–124.
22. **Aydog S.T, Hasçelik Z, Demirel Z.H.** The effects of menstrual cycle on the knee joint position sense: preliminary study. *Knee Surg. Sports Traumatol. Arthrosc.* 2005;13,8:649–653.
23. **Hertel N.I, Williams L.C, Olmsted-Kramer H.J et al.** Neuromuscular performance and knee laxity do not change across the menstrual cycle in female athletes *Knee Surgery, Sport. Traumatol. Arthrosc.* 2006; 14,9: 817–822.
24. **Lebrun C.M, Rumball J.S.** Relationship between athletic performance and menstrual cycle. *Curr. Womens. Health Rep.* 2001;1,3:232–240.
25. **Hootman J.M, Dick R, Agel J.** Epidemiology of collegiate injuries for 15 sports: Summary and recommendations for injury prevention initiatives. *Journal of Athletic Training* 2007;42,2:311–319.
26. **Slauterbeck J.R, Fuzie S.F, Smith M.P et al.** The Menstrual Cycle, Sex Hormones, and Anterior Cruciate Ligament Injury *J. Athl. Train.* 2002;37,3:275–278.
27. **Montagnani C.F, Arena B, Maffulli N.** Estradiol and progesterone during exercise in healthy untrained women *Med. Sci. Sports Exerc.* 1992;24,7:764–768.
28. **Karageanes S.J, Blackburn K, Vangelos Z.** The association of the menstrual cycle with the laxity of the anterior cruciate ligament in adolescent female athletes *Clin J Sport Med.* 2000;10,3:162–168.
29. **Clark R, Bartold S, Bryant A.L.** Tibial acceleration variability during consecutive gait cycles is influenced by the menstrual cycle *Clin. Biomech.* 2010;25, 6:557–562.