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Changes in Proprioceptive Control in the Menstrual Cycle: a Risk Factor for Injuries? A Proof-of-Concept Study

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SUMMARY

Introduction. Over the past three decades, there has been an increase in female sport participation attributable to the growing development and investment in professional women's sports. For an effective preventive strategy, it is necessary to analyze all risk factors that expose women to a higher probability of incurring injuries. The aim of our study is to evaluate the hormonal influence on proprioception and neuromuscular control, to identify whether a particular phase of the menstrual cycle may be related to a higher probability of injuries.

Materials and methods. A group of female participants was objectively evaluated through baropodometric platform test, postural assessment (Tecnobody, Bergamo, Italy), and functional tests at different phases of the menstrual cycle.

Results. Eleven participants (age = 29 ± 3.41) were enrolled in the study. The results showed slight fluctuation ($p > 0.05$) of postural and proprioceptive control related to hormonal variations of the ovarian cycle.

Discussion and conclusions. Despite no significant differences, it is conceivable that, during an athletic gesture with a high functional demand, the different performances shown in relation to the different hormonal concentrations could influence the risk of sustaining an injury. These assumptions assume significance in the context of the development of neuromuscular strategies to prevent lower limb injuries during sports activities.

KEY WORDS

Rehabilitation; menstrual cycle; proprioception; injuries; hormonal variations.

INTRODUCTION

Over the past three decades, there has been an increase in female participation in sport attributed to the growing development and investment in professional and recreational women's sport (1). In general, female sport participation has skyrocketed in the past 25 year, with approximately 53% of female students reported participating on one or more sports teams in school and/or non-school setting. Moreover, the number of female athletes participating in the Olympic Games has increased significantly from 34%

in Atlanta 1996 to 48% at the last Olympic Games in Tokyo 2020, with a high probability of achieving full gender parity for the Paris 2024 Olympic Games (2).

There is great interest in preventing ACL injuries to protect the athletes' health, reduce out of competition time, and save on health care costs. At this regard, it is estimated that the short-term cost associated with an ACL incident is $11,500 per injury, with approximately $2 billion per year being spent in the United States (3).

For an effective preventive strategy, it is necessary to analyze all risk factors that expose women to a higher probability of incurring this type of injury.

Several studies have shown that women are at particularly high risk for ACL injuries, with 3 to 6 times greater rates than men. This higher odd may be related to intrinsic factors related to knee joint (intercondylar notch, "loose jointendness", anatominc alignment, Q-angle, or hormones), and extrinsic factors (playing surface, muscle imbalance, hamstrings-to-quadriceps strength ratio, neuromuscular control) (4, 5). Recently, the effects of hormones on ligamentous tissues have gained more attention in ACL injuries. Wojtys *et al*. highlighted a higher probability of ligamentous lesions during ovulation within the menstrual cycle, due to increased laxity of these structures under the influence of estradiol (6). However, results in the literature are discordant, according to Slauterbeck *et al*. (7) the risk of ACL injury would increase at the beginning of the follicular phase (7), on the other hand, the results of Fridén *et al*. indicates a higher risk at the end of the luteal phase (8).

Moreover, the influence of endocrine system on postural control has gained attention. Estrogen and progesterone have direct and indirect influence on $GABA_A$ and several neurotransmitter receptors; in addition, direct link of the menstrual cycle on visual-vestibular function has been shown with menopausal women presenting a lower postural stability and, consequently, higher risk of fall, that improves with hormone replacement therapy (9). Another study, on female athletes taking oral contraceptives showed a higher stability than the group without the oral therapy (10). The physiology under the correlation between postural control has not been fully explored. However, it could be related to a change in proprioception, associated with a negative effect on sensory feedback from peripheric afferences (11). The cyclic hormone oscillation has a plausible influence the dynamic neuromuscular control of the knee joint suggesting a hormonal effect in altering the balance and/or proprioception of young women within a menstrual cycle (10).

In this context, the advancement in rehabilitative technologies has provided new tools for the functional evaluation of athletes. In particular, baropodometric and balance platforms include an assessment procedure of the patients' proprioception, monitoring through a force platform, the displacement of the patient's center of pressure (COP), with a high grade of accuracy (12).

Thus, the aim of our study is to evaluate the hormonal influence on proprioception and neuromuscular control in an objective and detailed way, trying to identify whether a particular phase of the menstrual cycle may be related to a higher probability of injuries.

MATERIALS AND METHODS

This study was conducted at the Department of Physical Medicine and Rehabilitation of the University of Padua. The study was conducted in accordance with the Declaration of Helsinki and all participants signed a written consent to participate in the study.

A group of female voluntary participants, resident in Physical and Rehabilitation Medicine at the University Hospital of Padua were enrolled. Inclusion criteria were: 1) age between 18 and 45 years old (fertile age), and 2) regular menses. Exclusion criteria were: 1) previous pregnancies, 2) vestibular problems, 3) previous lower limb injuries in the last 2 years, 4) central and/or peripheral neurological problems, 5) taking contraceptives, 6) endocrine pathologies, 7) muscle skeletal pathologies that could affect testing (*e.g.*, scoliosis > 20°), 8) muscle injuries in the last 6 months. The sample size was determined based on previous analogous studies (11).

During the entire trial period, the female participants performed their usual daily activities.

Each subject was assessed during the 3 phases of the menstrual cycle: follicular phase, ovulation, and luteal phase. The days on which the tests were carried out were chosen on the basis of the model adopted by Ellen Casey (13).

In women with a total cycle length of 27 to 29 days, measurements were taken in the different phases according to the following time intervals:

- Follicular phase: days 1-3.
- Ovulatory phase: days 12-14.
- Luteal phase: days 21-25.

In those with a total cycle length between 24 and 26 days as follows:

- Follicular phase: day 1-3.
- Ovulatory phase: days 10-12.
- Luteal phase: days 19-23.

In those with a total cycle length between 30 and 35 days as follows:

- Follicular phase: day 1-3.
- Ovulatory phase: days 14-16.
- Luteal phase: day 23-27.

Day 1 coincided with the onset of menstruation. The tests were performed in each phase of the menstrual cycle.

Procedure

The participants were evaluated in each phase of the menstrual cycle through a series of objective and detailed instrumental and functional tests. The participants were asked to keep a menstrual diary. Test day included a first phase of familiarization with the instruments utilized, in which the physiotherapist explained the procedure, and a light warm-up.

Bipodal balance with open eyes

This test was performed with the subject placed on a MF - STABILITY system (Tecnobody, Bergamo, Italy). The system evaluates postural control, the oscillation of the Pressure Center (COP) in anterior-posterior and right-left direction, as well as the area and perimeter of the latter. The patients were in orthostatic position, with tibial extrarotation of 30°, a distance of 2 cm between the tibial malleoli, the intermalleolar line placed on the fulcrum of the platform and the arms along the sides.

The subject was then asked to stand upright for 30" while looking at a visual stimulus on a screen.

The sway area was then measured, *i.e.*, 95% of the area of the COP excursions, the perimeter of the COP excursions, the antero-posterior and mid-lateral standard deviations from the COP, the mean COP and the trunk standard deviation, which is the vector sum of the antero-posterior and mid-lateral standard deviations of the trunk inclinations.

Bipodal balance with eyes closed

The procedure was the same as the previous test but was performed with eyes closed.

Dynamic bipodal balance with eyes open

This test was performed on the ProKin 252 (Tecnobody, Bergamo, Italy) for a proprioceptive-stabilometric assessment of the dynamic balance (14); an electro-pneumatic baropodometric platform able to provide a an starting assessment analysis, and a series of exercises biofeedback guided. Patient is positioned with the tibiae in neutral position, tibial malleolar distance of 2 cm and intermalleolar line placed 3 cm posterior to the fulcrum of the platform. The subject was asked to maintain balance and equilibrium with the aid of visual feedback. A tracing of the movements of the footplate expressed in degrees of inclination was then obtained, which made it possible to identify any imbalances of the subject, the motor strategies of response and counter-balance, and the dynamic balance midpoint.

Star excursion balance test

The Star Excursion Balance Test is a dynamic test requiring strength, mobility and proprioception, to assess dynamic postural-control deficits in lower extremity injury, used to identify individuals at increased risk of lower-limb injuries (15, 16).

The original test involves 8 directions of movement, but Plisky *et al.* (17) showed that even just 3 particular directions (anterior, posteromedial and posterolateral) can identify the risk of lower limb injury.

The test therefore involves holding the weight-bearing on one of the lower limbs and reaching with the contralateral limb to the furthest point along a line drawn on the floor (anterior, posteromedial and posterolateral) and then returning to the starting position.

Before collecting the data, six simulation tests were performed, as indicated by the results of the study by Hertel *et al.* (18) in order to standardize the results.

The distance achieved in each of the 3 directions was also normalized according to the following formula:

Distance standardized by limb length = (distance achived / lower limb length) × 100.

The Total Performance Value for the entire test was obtained according to the following formula:

Total Performance Value = (sum of distances achieved in the 3 directions / lower limb length × 3) × 100.

A Total Performance Value of less than 94% of the lower limb length correlates with a 6 times higher probability of a lower limb injury (17).

The lower limb length was measured as the distance between the antero-upper iliac spine and the tibial malleolus.

Single hop leg test

This test identifies global knee dynamic stability and is useful tools for a bilateral comparison of knee strength and function (19). Each participant was asked to perform a monopodalic jump trying to reach the maximum distance forward, keeping their hands on their hips. After falling back to the ground, the subject had to maintain single-podal balance for no less than three seconds.

The test was performed by alternating both limbs so that the limb symmetry index (LSI) could be calculated:

LSI = (worst performing limb / best performing limb) × 100.

An LSI value < 85% correlates with an increased risk of injury (20).

Postural analysis

Postural analysis was performed through an automatic Postural Bench (Tecnobody, Bergamo, Italy) to perform an accurate postural analysis without load on the limbs;

a two inclinable tops system with several electronic inclinometers that detects the inclinations of the multiple planes to analyze difference in the symmetry of 3 body segments, namely, scapular, lumbar and hip plane. The tool allows to evaluate the state of the muscular structure, kinetic chain, and posture.

Statistical analysis

The data were analyzed with SAS 9.4 (SAS Institute, Inc., Cary, NC, USA) for Windows. Descriptive statistics were expressed as means and standard deviations for each of the three phases considered (follicular, ovulatory, luteal). Shapiro-Wilk test was utilized to determine if the continuous variables were normally distributed. We performed generalized repeated measures model (ANOVA) to assess the variation between the three phases. We reported P-value for the variation and as an estimate of the difference between the phase averages, and the corresponding 95% confidence interval. The correlation between the results obtained for each phase was assessed with Spearman's correlation coefficient. Statistical significance was considered for $p \leq 0.05$.

RESULTS

Out of fifteen volunteers, 11 female participants with a mean age of 29 ± 3.41 years and a mean BMI of 21.24 ± 1.84 kg/m² were included. All results are shown in **table I**.

In the functional tests a worse performance was observed during menstruating period. In the Star Excursion Balance Test, a worse performance was recorded in the follicular phase, while in the Single Hop Leg Test a greater asymmetry (LSI) was recorded in the follicular and luteal phases (**figure 1**).

In addition, in the ProKin balance test, a greater fluctuation of COP was observed in the luteal phase, while in closed and open eyes stability tests (**figure 2**), a greater fluctuation of COP was recorded in the ovulatory and luteal phases, respectively (**figure 3**).

Moreover, even if there are not significant differences, the postural analysis showed a higher pelvis load during ovulatory phase, with a more asymmetric load distribution between scapular, lumbar e pelvis segment, compared with follicular and luteal phase (**table II** and **figure 4**).

DISCUSSION

The assessment of balance and neuromuscular control represent an indirect measure of the risk of injury. In literature, the link between hormonal fluctuations and changes in neuromuscular control has been extensively evaluated. In particular, several theories have been proposed to define the

Table I. Differences in proprioceptive tests during follicular, ovulatory and luteal phase comparing the same study population (n = 11).

	F phase	O phase	L phase	P-value	Difference F-O phase (95%CI)	Difference F-L phase (95%CI)	Difference F-L phase (95%CI)
Star excursion balance test dominant leg	0.83 (0.06)	0.84 (0.06)	0.84 (0.04)	0.741	-0.01 (-0.05-0.02)	-0.01 (-0.04-0.02)	0.00 (-0.03-0.03)
Star excursion balance test non-dominant leg	0.83 (0.07)	0.84 (0.07)	0.84 (0.06)	0.353	-0.01 (-0.05-0.03)	-0.02 (-0.05-0.01)	0.00 (-0.01-0.03)
Single hop leg test	0.92 (0.05)	0.93 (0.10)	0.92 (0.07)	0.978	-0.01 (-0.08-0.06)	0.00 (-0.08-0.08)	0.01 (-0.10-0.09)
Dynamic bipodal balance test	0.85 (0.59)	0.60 (0.31)	0.64 (0.24)	0.497	-0.24 (-0.17-0.66)	0.20 (-0.17-0.59)	0.04 (-0.11-0.18)
Closed-eye bipodal stability test (mm²)	233.76 (166.47)	226.26 (172.17)	291.39 (274.53)	0.688	7.49 (-67.66-82.86)	-57.62 (-286.26- 171.00)	-65.12 (-125.71-255.96)
Open-eye bipodal stability test (mm²)	85.62 (38.32)	146.05 (114.75)	111.20 (64.78)	0.687	-60.43 (-130.41-9.55)	-25.29 (-11.59- 26.02)	-34.84 (-39.45-109.13)

Means (SD) for continuous variables; balance test and single hop test are expressed as ratio; stability tests are expressed as mm2 of the area described by COP; Statistical analysis performed to assess the inter-group differences was ANOVA; CI: confidence Interval 95%.

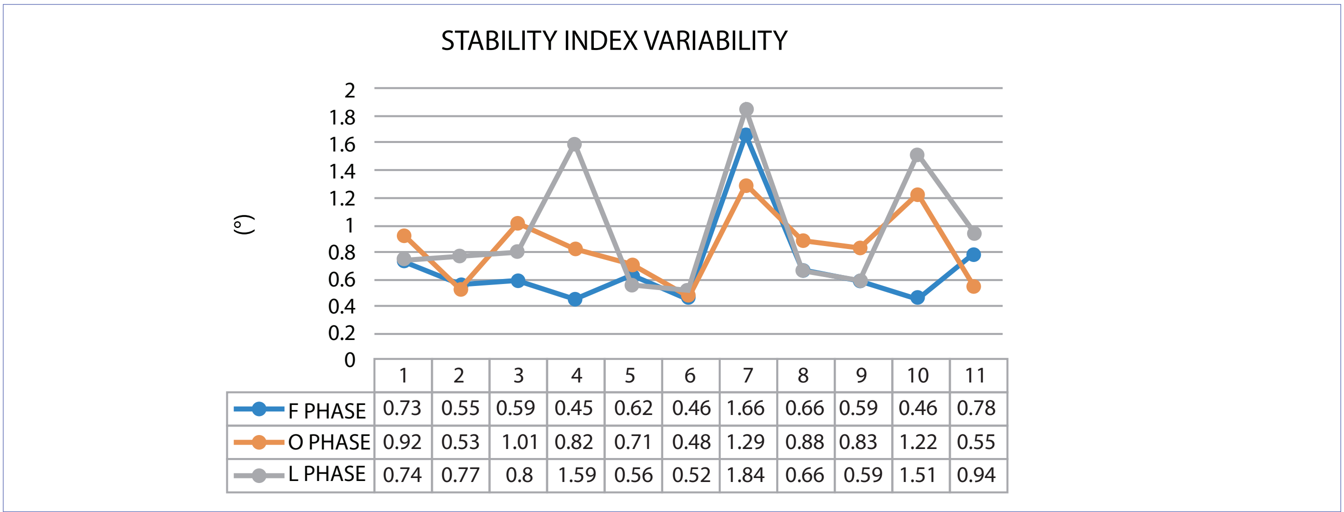

Figure 1. Stability Index Variability. SD of the trunk stability index at balance platform test (Prokin-Tecnobody, Bergamo, Italy).
F: follicular; O: ovulatory; L: luteal.

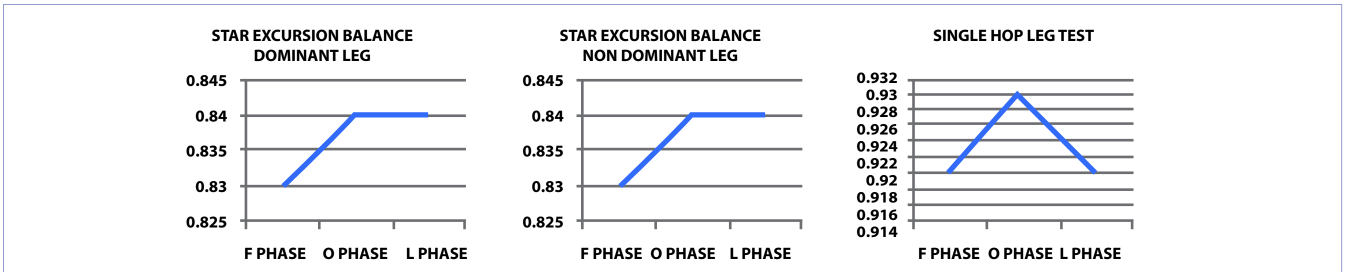

Figure 2. Star Excursion Balance Test (Total Performance Value) and Single Hop Leg Test (Limb Symmetry Index).
F: follicular; O: ovulatory; L: luteal.

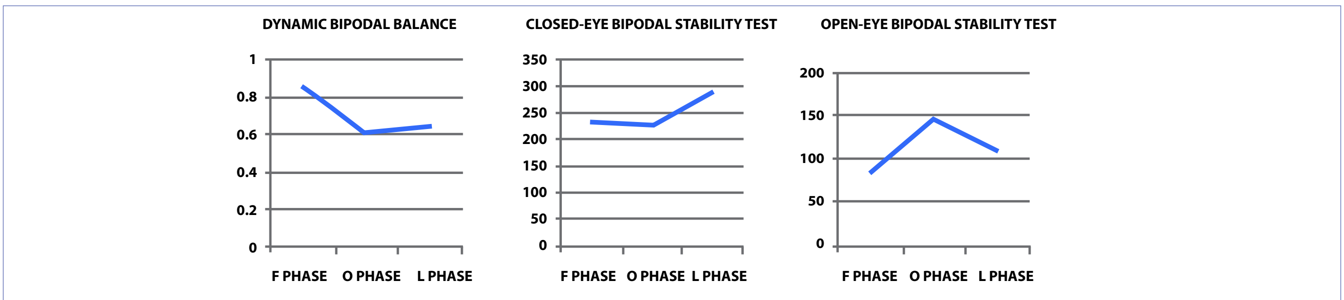

Figure 3. Centre of Pressure displacement (blue line) during dynamic bipodal balance with eyes open (ProKin baropodometric platform), closed and open-eye bipodal stability test.
F: follicular; O: ovulatory; L: luteal

Table II. Postural test. Percentage of segmental scapular, lumbar, and pelvis load during follicular, ovulatory, and luteal phase comparing the same study population (n = 11).

	F phase	O phase	L phase	P-value
Scapular	28.9 (3.88)	25.1 (6.97)	29.3 (5.32)	0.161
Lumbar	31.9 (6.22)	32.3 (12.2)	36.9 (10.54)	0.433
Pelvis	37.6 (4.45)	42.7 (15.23)	33 (9.84)	0.123

Means (SD) for continuous variables. Statistical analysis performed to assess the inter-group differences ANOVA; C.I. Confidence Interval 95%.

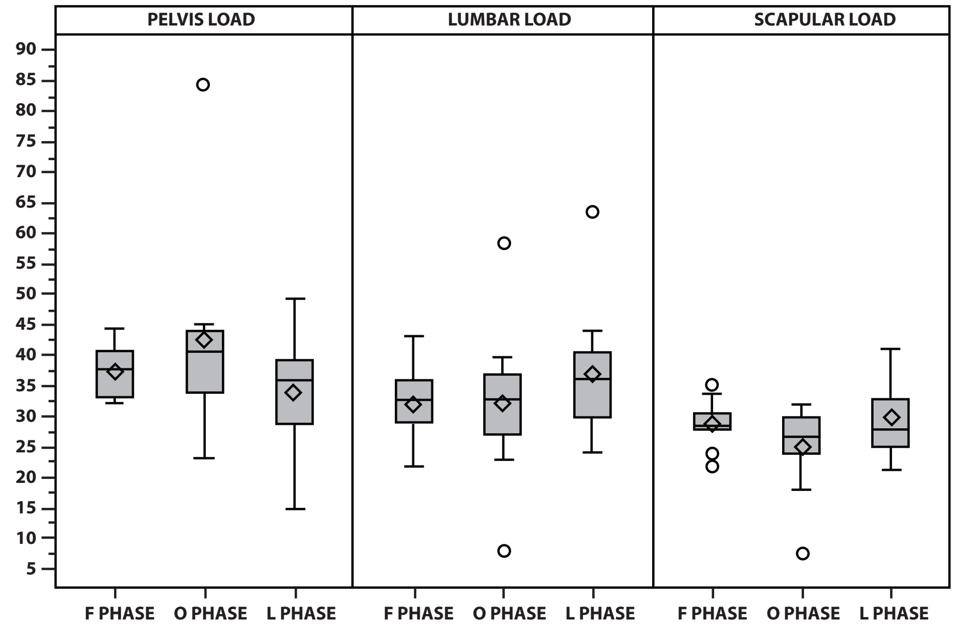

Figure 4. Box and Whisker Plot of the postural load distribution during follicular, ovulatory and luteal phase.

mechanisms that explain gender differences in injury rates. These theories include gender differences in both anatomical and motor patterns, hormonal differences and neuromuscular imbalances (4, 5).

In our study, we aimed to identify possible postural and balance alterations in a homogeneous sample of female participants, objectively evaluating the oscillation of the COP using baropodometric platforms; dynamic gestures, such as those required in daily life or during a sporting activity through functional tests, and finally, postural symmetry load of the participants using postural bench.

Taken together, these results reveal slight fluctuations in the trend of analyzed outcome, even if not statistically significant, that could be correlated with in estrogen blood concentration within the menstrual cycle.

Estrogen peaks during the ovulatory phase, with a gradual decline during the luteal phase, until reaching minimum levels during the follicular phase, which corresponds to the beginning of a new cycle. The role played by hormonal fluctuation during the menstrual cycle in increasing the probability of anterior cruciate ligament (ACL) rupture and lower limb injuries has long been debated (21). In particular, ACL injury has been hypothesized to be influenced by hormones with a direct effect on ligament laxity or stiffness throughout due to estrogen, progesterone, testosterone, and relaxin receptors on the ACL that modify collagen synthesis and tensile properties, or throughout neuromuscular modifications affecting knee alignment (21). However, the overall strength of evidence on this topic in literature is low, influenced by both the difficulties in measuring the exact hormone concentration of the participants during the experimental trials, and from the multiplicity of factors inherent in the injury mechanism. Moreover, the reason of no consensus could be attributable to the high heterogeneity of age, and sociodemographic data (21).

Wojtys *et al.* (6) were the first authors who addressed the correlation between hormone concentrations and the risk of ACL, suggesting that the risk of ligament injuries increases during the ovulation phase due to the increased laxity of these structures following the estrogen peak, which influences the collagen production of the fibroblasts and, consequently, the tensile strength of the ACL. On the other hand, the risk would be reduced in the follicular phase (6) or during the luteal phase (22).

These findings have been confirmed more recently by other authors, who reported increased plantar fascia elasticity, reduced balance, and increased tremor during the ovulatory phase with an increased potential risk of falling (23-25).

In contrast, other authors have shown that the risk of ACL injury increases and neuro-muscular control worsens at the beginning of the follicular phase (7, 26) or in the luteal phase in women with Premenstrual Symptoms (8, 27, 28). In fact, premenstrual syndrome may reduce concentration causing an alteration in the correct execution of a complex motor movement. Darlington *et al.* (9) confirmed these results by showing worst test performance under unstable conditions during the follicular and luteal phase. Several studies have also evaluated the effect of oral contraception on the risk of injury in women. In particular, Wojits *et al*. and Nielsen *et al*. (22, 27) have demonstrated the protective role of oral contraception in the risk of injury, probably due to the reduction of hormonal fluctuation during a menstrual cycle.

On the other hand, Naessen *et al*. (29) confirmed the protective effect of oral contraception demonstrating that postural balance function is better preserved in long-term estrogen users' menopausal women than in nonusers (29).

The proprioceptive system and neuromuscular control are fundamental in determining joint stability. Their disruption therefore leads to an increased joint injuries risk.

Analyzing the results of our study, it is plausible that an alteration of this system, although very slight, can be identified during the follicular and luteal phases, in which there is a lower estrogen blood concentration. The parameters investigated in this study should be, also, interpreted in consideration of the characteristics of the sample considered; indeed, the fluctuations of balance and proprioception are negligible during the activity of daily life in a young and healthy population.

In addition, we found an asymmetrical distribution between lumbar and pelvis load in ovulatory phase, corresponding to a higher lordosis angle. According to Kim *et al*. (30), there is a link between menstrual cycle and pelvis imbalance, due to body fluid and uterus contraction, more evident in women with menstrual pain. Our study confirms the results of Legerlotz *et al*. (11), namely, premenstrual symptoms are responsible of a postural sway, that can be improved with aerobic training. This is particularly relevant in the management of female athletes, that should include aerobic trainer to relieve fluid retention and menstrual symptoms. This could be particularly relevant in athletes, because an higher lordosis and a retraction of the posterior kinetic chain could be a predisposing factor for overuse injuries at lower limbs (31). To the best of our knowledge, this is the first study based on an objective, and comprehensive approach for the change in proprioceptive control across the menstrual cycle.

This proof-of-principle study had some limitations: the small sample size and the indirect method of hormone assay based on Casey's model (13) could affect the generalizability of the results.

CONCLUSIONS

The results of this study show no statistically significant relationships between proprioceptive control and hormonal variations due to the ovarian cycle. However, it is conceivable that, during an athletic gesture with a high functional demand, the different performances in relation to the different hormonal concentrations become decisive in predisposing to the genesis of an injury. Thus, we confirm the results of previous study, on the likely influence of the ovarian cycle on the neuromuscular control and the importance to consider the ovarian cycle of an athlete during the sport season to plan a tailored program of exercises based on the athlete's needs.

FUNDINGS

None.

DATA AVAILABILITY

Data are available under reasonable request to the corresponding author.

CONTRIBUTIONS

AF: conceptualization, writing – original draft. AF, DB: methodology. FP, SF: formal analysis, investigation, data curation. AF, FO, AD: writing – review & editing. DB, SP: visualization. CC: supervision. AF: project administration. All authors: final approval.

CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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