Changes in the Width of the Tibiofibular Syndesmosis Related to Lower Extremity Joint Dynamics and Neuromuscular Coordination on Drop Landing During the Menstrual Cycle

Michie Okazaki,*† RPT, PhD, Masaaki Kaneko,† RPT, PhD, Yukisato Ishida,‡ PhD, Norio Murase,§ MD, PhD, and Toshihito Katsumura,§ MD, PhD

Investigation performed at the Department of Physical Therapy, Bunkyo Gakuin University, Tokyo, Japan

Background: Many injuries of the lower extremities, especially the knee and ankle, occur during sports activity, and the incidence rate is higher in women than in men.

Hypothesis: The hypothesis was that phases of the menstrual cycle affect the width of the tibiofibular syndesmosis during drop landing in healthy young women and that such changes at the tibiofibular joint also affect the dynamics and neuromuscular coordination of the lower extremities.

Study Design: Descriptive laboratory study.

Methods: Participants included 28 healthy young women (mean age, 21.0 ± 0.8 years). Blood samples were collected to determine plasma levels of estradiol and progesterone immediately before the performance of the task: drop landing on a single leg from a 30-cm platform. Using ultrasonography, the distance between the tibia and the distal end of the fibula, regarded as the width of the tibiofibular syndesmosis, was measured in an upright position without flexion of the ankle. The peak ground-reaction force (GRF) on landing was measured using a force platform. The time to peak GRF (Tp-GRF) was measured as the time from initial ground contact to the peak GRF. Hip, knee, and ankle joint angles during the single-leg landing were calculated using a 3-dimensional motion analysis system. Muscle activities of the lower extremities were measured using surface electromyography.

Results: The width of the tibiofibular syndesmosis was significantly greater in the luteal phase when compared with the menstrual, follicular, and ovulation phases (by 5%-8% of control). Also, during the luteal phase, the Tp-GRF was significantly shorter than in the follicular phase (by 6%); hip internal rotation and knee valgus were significantly greater than in the menstrual phase (by 43% and 34%, respectively); knee flexion was significantly less than in the menstrual and follicular phases (by 7%-9%); ankle dorsiflexion was significantly less than in the follicular phase (by 11%); ankle adduction and eversion were significantly greater than in the menstrual and follicular phases (by 26%-46%, and 27%-33%, respectively); and activation of the gluteus maximus before landing was significantly lower than in the menstrual and follicular phases (by 20%-22%).

Conclusion: The luteal phase appears to be associated with decreased strength and laxity of the ankle as well as lower extremity muscle activity in women. The changes presumably represent a greater risk for sports injuries.

Clinical Relevance: The results of this study suggest that the luteal phase may be related to the greater incidence of lower extremity injuries in women.

Keywords: menstrual cycle; tibiofibular syndesmosis; drop landing; lower extremity injury

Many injuries to the lower extremities, particularly the knee and ankle, occur during sports activity, and the incidence rate for women is higher than for men. In particular, female athletes have a greater risk for anterior cruciate ligament (ACL) ruptures and noncontact ACL injuries than their male counterparts when performing at similar levels of exercise intensity. ACL injuries in female athletes frequently occur during jumping and cutting activities in sports such as soccer, basketball, volleyball, and handball.
Because women modify the ankle planter flexor muscle across landing conditions, the ankle joint is a major area for lower extremity injuries in women. Ankle injuries induce functional ankle instability, resulting in the reduction of kinematic performance. Terada et al. reported that chronic ankle instability decreased knee flexion during double-leg vertical jump landing, although they did not measure the width of the tibiofibular syndesmosis.

As a mechanism for effective absorption of the landing impact, both hip and knee flexion increase on landing, although the hip has a greater role in impact reduction. Patients with a history of multiple ankle sprains have slower activation of the gluteus maximus (GM) and possess less vibratory perception at the ankle joint. Thus, these athletes often alter their biomechanics from the ankle to the hip after an ankle sprain.

The distal tibia, fibula, and talus are stabilized by the bone structure with the support of the interosseous membrane, the anterior inferior tibiofibular ligament, the posterior inferior tibiofibular ligament, the interosseous ligament, and the transverse ligament, which hold the bones in close contact. The syndesmosis is capable of moving a few millimeters during loading. Previously, dysfunction in the tibiofibular syndesmosis was reported to contribute to ankle ligament injuries caused by rotation or dilation of the fibula and tibia. Thus, in this study, we focused on the role of the tibiofibular syndesmosis in ankle stability.

Although controversial, some factors related to anatomic structure, neuromuscular coordination, and hormonal control have been thought to contribute to the increased incidence of injuries in female patients. In addition, some authors have suggested that hormone levels might influence ACL injuries because injuries have been associated with phases of the menstrual cycle. Changes in estradiol and progesterone levels have been found to alter knee laxity (anterior tibial displacement) during the menstrual cycle, and ACL injuries have been reported to occur mostly between the menstrual phase and ovulation phase. However, several studies have not found differences in the incidence rate during the menstrual cycle.

The purposes of this research were to evaluate the association between changes in serum estradiol and progesterone levels and the lower extremity joint-muscle dynamics of drop landing during the menstrual cycle in healthy young women and to determine whether a role exists for the width of the tibiofibular syndesmosis in stability of the lower extremity.

METHODS

Participants

Participants were originally 30 healthy young women with regular menstrual cycles. None of the women had a history of knee orthopaedic injuries or joint hypermobility as checked by the Beighton Hypermobility Score. As 2 participants were excluded because of their irregular menstrual cycles and health conditions, we analyzed 28 women (mean age, 21.0 ± 0.8 years; mean height, 158.1 ± 6.0 cm; mean weight, 52.8 ± 6.5 kg; mean body mass index, 21.1 ± 1.7 kg/m²) and the single-leg landing of 56 legs (both legs) in this study. All participants granted informed consent, and the study was approved by the ethics committee of our institution.

Menstrual Cycle

Because measurements for lower extremity joint dynamics and neuromuscular coordination at drop landing were performed in the menstrual phase (1st-5th day), follicular phase (7th-10th day), ovulation phase (12th-15th day), and luteal phase (7th-9th day from ovulation phase), we checked the menstrual cycle by asking about the previous 3-cycle periods and confirming the cycle term on the day of commencing the task by an assay of serum hormonal levels. The test examiner was blinded to the menstrual cycle of the participants.

Serum Hormonal Level. Venous blood samples were collected to assay estradiol and progesterone before each drop-landing test session. The samples were collected from the antecubital area by an experienced nurse under the supervision of a physician, according to Japanese medical law, using a holder-attached 21-gauge needle (11B18; NIPRO Medical Corp) and an 8.5-mL vacutainer tube (EXP201207; NIPRO Medical Corp). The serum was left at room temperature for 1 hour, centrifuged at 3000 rpm for 15 minutes, and then kept at 4°C to 5°C. Serum analysis was conducted at the blood laboratory of Mitsubishi Chemical Medience Corp within 24 hours after collecting the blood samples.

Identification of Ovulation Phase. We identified the ovulation phase using the One Step Ovulation Urine Test (Guangzhou Wondfo Biotech Co Ltd). A check was performed daily until luteinizing hormone surged in the urine for the expected term of the 12th to 15th day from the initiation of the menstrual cycle. In addition, we asked the participants about amounts of vaginal smear and ovulation pain to assist in identifying the time of ovulation.
Measurement Procedure

The participants rested in a chair for 10 minutes. Subsequently, they performed static stretching of the rectus femoris and hamstring as a warm-up. Each participant was instructed to change her posture from upright to bent forward by bending the trunk forward and flexing the knee with the hand grasping the ankle. This static stretching for 30 seconds was performed 3 times. Then, we measured the width of the tibiofibular syndesmosis. After all the above procedures, the single-leg drop landing task was performed. We analyzed lower extremity joint dynamics and neuromuscular coordination on drop landing. Considering the circadian rhythm, the task was conducted at the same time of day, but the time was determined by the participant.

Width of Tibiofibular Syndesmosis

The anterior inferior tibiofibular ligament functions to resist and control external rotation. Therefore, we chose this ligament for measurement as a potential site of ankle injuries. The distance between the tibia and the distal end of the fibula was regarded as representative of the width of the tibiofibular syndesmosis. Then, the width of the right and left anterior inferior tibiofibular ligaments in an upright standing posture at 0° in dorsiflexion and plantar flexion of the ankle was measured using ultrasonography (MyLab 25; Hitachi Medical Corp). The ultrasonography probe was placed on the anterior inferior tibiofibular ligament to obtain a long-axis view, and the objective distance was measured using image analysis software (Image; NIH, originally developed by Wayne Rasband) with a precision of 0.001 mm. Before drop landing, the distance measurement was performed 3 times, and the obtained mean value was regarded as a representative value.

For reliability of these measurements, we measured the tibiofibular syndesmosis width before and after landing using 6 healthy women (21-22 years old; 12 legs total) in additional experiments separate from the main experiments. The mean values were 2.72 ± 0.22 mm (range, 2.38-2.99 mm) and 2.71 ± 0.21 mm (range, 2.42-2.99 mm) before and after landing, respectively, and the correlation coefficient was 0.990, suggesting the reliability of measurements and no significant effects of drop landing on the width of tibiofibular syndesmosis.

Drop Landing

The participants stood on a wooden platform 30 cm high with their feet shoulder-width apart, then dropped off and landed with a single foot on the force plate. The participant was instructed to cross her arms over her chest to minimize the effects of upper extremity movement, to land as mildly as possible, and to be stable for a while after landing. Participants were also instructed to avoid intentional jumping upward or forward. After the participants practiced several times, we obtained 3 successful landings with either the right or left leg (total of 6 drop landings for analysis). If a participant lost her balance during the task, it was considered a false attempt, and the task was repeated.

The peak value of the vertical ground-reaction force (peak GRF) after landing was measured using a force platform (OR6-7; AMTI) at 1000 Hz. The peak GRF was normalized by body mass. The time to peak GRF (Tp-GRF) was measured as the time from initial ground contact to the peak GRF.

The angles of the hip, knee, and ankle joints during landing were measured using a 3-dimensional motion analysis system (VICON MX; Vicon Motion Systems) at a sampling rate of 100 Hz with 8 infrared cameras. Infrared reflective markers were placed at 16 sites on the body according to marker placement indicated by the Plug-in-Gait lower body model (Vicon Motion Systems). The anterior and posterior superior iliac spines, the external center of the thigh, the lateral joint line of the knee, the center of the shank, the lateral malleolus of the ankle, the center of the heel, and the head of the second metatarsal of the foot, on both the right and left side. We conducted the drop landing task after we confirmed that the measurement error was less than 0.7 mm to avoid errors in joint motion, as suggested by Kadaba et al. An experienced investigator affixed all markers and checked their positions during performance of the task. Marker trajectories were monitored with a Woltring low-pass filter with a 20-Hz cutoff frequency. The GRF was measured with a fourth-order Butterworth low-pass filter with zero lag and a 6-Hz cutoff frequency. The hip, knee, and ankle joint angles in the sagittal, frontal, and transverse planes were calculated using the Plug-in-Gait biomechanical model (Vicon Motion Systems).

Muscle activity of the lower extremity before landing was measured using a surface electromyography (EMG) system (TeleMyo 2400; Noraxon) at a 1500-Hz sampling rate. EMG data were processed with a 50-millisecond root mean square moving window, as previously reported. The EMG data for each muscle were obtained from 150 milliseconds before ground contact, which was regarded as preactivity of the muscle. This muscle activation has been reported to be crucial, affecting the manner of landing so as to maintain knee joint stability after ground impact. EMG data were collected from 4 muscles: the GM, semitendinosus, biceps femoris, and rectus femoris. The maximum voluntary contraction (MVC) was measured according to manual muscle testing. The preactivity of EMG in each muscle was normalized using the stable EMG obtained for 1 second in a 5-second MVC and was expressed as %MVC. The mean of 3 trials was used for analysis.

Statistical Analysis

Values of the serum hormonal level, width of the tibiofibular syndesmosis, and changes in lower extremity joint dynamics and neuromuscular coordination during drop landing were calculated as mean ± SD. The difference in each phase of the menstrual cycle was analyzed using repeated-measures analysis of variance and then the Tukey test for a multiple comparison (P < .05). All analyses were performed using SPSS 11.0 for Windows (SPSS Inc).
RESULTS

Serum Hormonal Level

The measured serum hormonal levels are presented in Table 1. During the menstrual cycle, estradiol levels in the ovulation and luteal phases were significantly higher (2.7- to 3.8-fold) than those in the menstrual and follicular phases (P < .05). Progesterone levels in the luteal phase were significantly higher (5.4- to 15.0-fold) than those in the menstrual, follicular, and ovulation phases (P < .05), and there was no difference in the mean progesterone levels in the ovulation, menstrual, and follicular phases. Although not significant, the mean progesterone level in the ovulation phase was greater (~3-fold) than those in the menstrual and follicular phases. The standard deviation for the estradiol level in the ovulation phase was relatively larger than those in the other phases, presumably because of the intrinsic greater variation in values as described.

Width of Tibiofibular Syndesmosis

The width of the tibiofibular syndesmosis in each menstrual cycle phase are presented in Table 2. The width in the luteal phase (2.86 ± 0.26 mm) was significantly greater than those in the menstrual (2.72 ± 0.28 mm), follicular (2.65 ± 0.25 mm), or ovulation phases (2.72 ± 0.27 mm) (P < .05).

Drop Landing

The results of peak GRF and Tp-GRF are presented in Table 3. Throughout the menstrual cycle, peak GRF values appeared constant between 32 and 33 N/kg. On the other hand, Tp-GRF in the luteal phase (61.3 ± 13.8 ms) was smaller than that in the follicular phase (64.9 ± 16.1 ms) (P < .05).

The results of lower extremity joint dynamics during drop landing are listed in Table 4. At peak GRF, hip internal rotation in the ovulation (15.80° ± 7.10°) and luteal phases (16.2° ± 11.41°) were significantly greater than that in the menstrual phase (11.3° ± 10.50°) (P < .05). With respect to the knee joint, knee flexion in the luteal phase (25.7° ± 6.00°) was significantly smaller than those in the menstrual (27.6° ± 5.67°) and follicular phases (28.1° ± 6.27°) (P < .05). Knee valgus in the ovulation (10.60° ± 5.67°) and luteal phases (10.60° ± 5.41°) were significantly greater than that in the menstrual phase (7.93° ± 6.50°) (P < .05). For the ankle joint, dorsiflexion in the luteal phase (9.4° ± 3.96°) was significantly smaller than that in the follicular phase (10.5° ± 4.01°) (P < .05). Ankle adduction and eversion in the luteal phase (4.07° ± 1.81° and 20.9° ± 8.42°, respectively) were significantly greater than those in the menstrual (2.79° ± 2.25° and 15.7° ± 11.10°, respectively) and follicular phases (3.24° ± 1.83° and 16.5° ± 8.62°, respectively) (P < .05). During the menstrual cycle, there were no significant changes in hip flexion, hip abduction, or knee internal rotation.

The muscle activation data in each menstrual cycle phase at 150 milliseconds before landing is presented in Table 5. Activation of the GM in the luteal phase (7.75% ± 1.81%) was significantly greater than that in the menstrual (6.50% ± 1.83%) and follicular phases (7.93% ± 15.7%). The muscle activation data in each menstrual cycle phase at 150 milliseconds before landing is presented in Table 5. Activation of the GM in the luteal phase (7.75% ± 1.81%) was significantly greater than that in the menstrual (6.50% ± 1.83%) and follicular phases (7.93% ± 15.7%).

DISCUSSION

Because Shimokoshi et al suggested that women may modify their ankle plantar flexor muscle across landing conditions more than men, we highlighted the relation of ankle function to serum hormonal levels. We found that ankle joint dynamics during drop landing were significantly altered as a decrease in ankle dorsiflexion or an increase in ankle adduction and eversion in the luteal phase, when both estradiol and progesterone levels were high. Concomitantly, we found that the width of the
The tibiofibular syndesmosis was greater during the luteal phase. Similarly, Harris and Fallat\textsuperscript{26} reported that increased widening of the ankle mortise by as little as 1 mm reduced the contact area of the tibiotalar joint by 42%, resulting in significant ankle instability, a finding that was confirmed by Hunt.\textsuperscript{29} Presumably, the increased width of the tibiofibular syndesmosis in the luteal phase causes an increase in ankle laxity, as measured on ankle width of the tibiofibular syndesmosis in the luteal phase that was confirmed by Hunt.\textsuperscript{29} Presumably, the increased widening of the ankle mortise by as little as 1 mm reduced the contact area of the tibiotalar joint by

### TABLE 3
Peak GRF and Tp-GRF During Drop Landing\textsuperscript{a}

|                        | Menstrual Phase | Follicular Phase | Ovulation Phase | Luteal Phase |
|------------------------|----------------|-----------------|----------------|-------------|
| Peak GRF, N/kg         | 32.4 ± 6.82    | 31.6 ± 5.78     | 33.0 ± 6.72    | 32.2 ± 6.29 |
| Tp-GRF, ms             | 63.9 ± 13.2    | 64.9 ± 16.1     | 62.6 ± 13.2    | 61.3 ± 13.8 |

\textsuperscript{a}Values are expressed as mean ± SD. GRF, ground-reaction force; Tp-GRF, time to peak GRF.

### TABLE 4
Lower Extremity Joint Dynamics During Drop Landing at Peak Ground-Reaction Force\textsuperscript{a}

|                        | Menstrual Phase | Follicular Phase | Ovulation Phase | Luteal Phase |
|------------------------|----------------|-----------------|----------------|-------------|
| Hip flexion, deg       | 28.0 ± 6.74    | 28.1 ± 5.35     | 27.9 ± 5.21    | 27.3 ± 7.14 |
| Hip abduction, deg     | 5.39 ± 3.91    | 5.41 ± 5.05     | 5.58 ± 4.70    | 5.67 ± 4.00 |
| Hip internal rotation, deg | 11.3 ± 10.50 | 12.7 ± 8.39     | 15.8 ± 7.10\textsuperscript{b} | 16.2 ± 11.41\textsuperscript{b} |
| Knee flexion, deg      | 27.6 ± 5.67    | 28.1 ± 6.27     | 26.7 ± 5.29    | 25.7 ± 6.00\textsuperscript{d} |
| Knee valgus, deg       | 7.93 ± 6.50    | 9.08 ± 6.97     | 10.60 ± 5.67\textsuperscript{b} | 10.60 ± 5.41\textsuperscript{b} |
| Knee internal rotation, deg | 0.80 ± 6.78 | 0.40 ± 6.79     | 0.37 ± 7.40    | 1.06 ± 6.73 |
| Ankle dorsiflexion, deg | 10.1 ± 3.31   | 10.5 ± 4.01     | 10.1 ± 3.48    | 9.4 ± 3.96\textsuperscript{d} |
| Ankle adduction, deg   | 2.79 ± 2.25    | 3.24 ± 1.83     | 3.90 ± 1.78    | 4.07 ± 1.81\textsuperscript{c} |
| Ankle eversion, deg    | 15.7 ± 11.10   | 16.5 ± 8.62     | 19.5 ± 8.53    | 20.9 ± 8.42\textsuperscript{c} |

\textsuperscript{a}Values are expressed as mean ± SD.

### TABLE 5
Muscle Activation Before Landing\textsuperscript{a}

|                        | Menstrual Phase | Follicular Phase | Ovulation Phase | Luteal Phase |
|------------------------|----------------|-----------------|----------------|-------------|
| Gluteus maximus, \% µV·s | 9.98 ± 5.22    | 9.73 ± 5.84     | 8.75 ± 5.19    | 7.75 ± 3.70\textsuperscript{b} |
| Biceps femoris, \% µV·s | 33.8 ± 33.1    | 32.2 ± 24.4     | 31.9 ± 30.5    | 40.0 ± 35.1 |
| Semitendinosus, \% µV·s | 15.4 ± 11.0    | 15.3 ± 11.9     | 15.2 ± 11.3    | 16.9 ± 14.3 |
| Rectus femoris, \% µV·s | 23.8 ± 17.7    | 23.1 ± 15.6     | 27.3 ± 22.1    | 21.7 ± 24.4 |

\textsuperscript{a}Values are expressed as mean ± SD.

### TABLE 6
Muscle Activation During Drop Landing\textsuperscript{a}

|                        | Menstrual Phase | Follicular Phase | Ovulation Phase | Luteal Phase |
|------------------------|----------------|-----------------|----------------|-------------|
| GM activation before landing |                |                 |                |             |
| GM activation during landing |                |                 |                |             |

\textsuperscript{a}Values are expressed as mean ± SD.
flexion of the hip joint\textsuperscript{30} and in resisting the knee valgus moment,\textsuperscript{34} thereby leading to increases in loads to soft tissues such as ligaments,\textsuperscript{35} which may be a causal factor for an ACL strain.\textsuperscript{13,32} Further, Dedrick et al\textsuperscript{14} reported that fluctuations in the estradiol level make a difference in neuromuscular control, which may be coincidental to our results. Because the GM appeared to play a pivotal role in response to sex hormone alteration, the decrease in GM activation during the luteal phase may be a risk factor for lower extremity injuries.

As another factor found in the present study, the Tp-GRF was significantly shorter in the luteal phase than in the other phases, suggesting that the ability of shock absorbance at landing may be least in the luteal phase, presumably because of the decrease in ankle and knee flexion discussed earlier. Values of the Tp-GRF were around 60 to 65 milliseconds, being nearly consistent to the reported values of 40 to 100 milliseconds after ground contact that cause ACL strains.\textsuperscript{13,32} Thus, it is conceivable that the risk of ankle injury as well as other lower extremity injuries is also increased in the luteal phase compared with the other menstrual cycle phases.

Many investigators have reported on the effects of sex hormones on muscle and ligament structure and metabolism.\textsuperscript{3,53} Briefly, estrogen and progesterone receptors are present in muscle cells\textsuperscript{19} and ACL fibroblasts.\textsuperscript{48} Sex hormones reduce collagen synthesis\textsuperscript{55,55,56} and collagen levels in ligaments.\textsuperscript{48} Secreting both estradiol and progesterone together enhances knee laxity.\textsuperscript{1,17,46} Those biochemical and functional results also suggest that surges in estradiol and progesterone levels are factors that lead to injuries in the lower extremity, including the ankle and ACL, in women.

There are some limitations to this study. The kinematics of the lower extremity joints during drop landing was analyzed using the Plug-in-Gait model. Kadaba et al\textsuperscript{31} indicated the disparity between the placement of infrared reflective markers in the Plug-in-Gait model and actual knee joint positions in the frontal and transverse planes. Future studies should use the point cluster technique, which allows for analysis of knee joint motion in detail.\textsuperscript{2} The participants in this study were healthy young women, thus limiting the generalizability of our results to the changes in lower extremity function during the menstrual cycle in younger females. Additionally, although all of the differences found in this study were statistically significant, they were small and not necessarily clinically significant. This needs to be evaluated in a follow-up study.

**CONCLUSION**

In this study, we investigated serum hormonal levels, the width of the tibiofibular syndesmosis, and changes in lower extremity joint dynamics and neuromuscular coordination during drop landing in the menstrual, follicular, ovulation, and luteal phases of the menstrual cycle. In the luteal phase, the width of the tibiofibular syndesmosis was significantly greater, the Tp-GRF was significantly shorter, hip internal rotation was significantly greater, knee flexion and ankle dorsiflexion were significantly less, and knee valgus and ankle adduction and eversion were significantly greater compared with some of the other phases. The increased width of the tibiofibular syndesmosis during drop landing in healthy young women also affected lower extremity joint-muscle dynamics and neuromuscular coordination. Such a finding suggests that changes in serum estradiol and progesterone levels in the luteal phase may decrease stability of the ankle during landing and also impair muscle balance and coordination.

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