Characterization of follicle stimulating hormone profiles in normal ovulating women

René Ecochard, M.D. Ph.D., a Agnes Guillerm, M.D., a René Leiva, M.D. Ph.D., c Thomas Bouchard, M.D., b Ana Direito, M.D., a and Hans Boehringer, Ph.D. d

a Service de Biostatistique, Hospices Civils de Lyon, Lyon; Université de Lyon, Lyon; Université Lyon 1, Villeurbanne; and Equipe Biostatistique-Santé, Laboratoire de Biométrie et Biologie Évolutive, UMR5558, CNRS, Villeurbanne, France; b Department of Family Medicine, University of Calgary, Calgary, Alberta, Canada; c CT Lamont Primary Health Care Research Centre; Bruyère Research Institute, and Department of Family Medicine, University of Ottawa, Ottawa, Ontario, Canada; and d DCN Diagnostics, Carlsbad, California

Objective: To describe FSH profile variants.

Design: Observational study.

Setting: Multicenter collaborative study.

Patient(s): A total of 107 women.

Intervention(s): Women collected daily first morning urine and underwent serial ovarian ultrasound.

Main Outcome Measure(s): FSH.

Result(s): The individual FSH cyclic profiles demonstrated a significant departure from the currently accepted model. A decline in FSH levels at the end of the follicular phase was observed in only 42% of cycles. The absence of this decline was significantly associated with a shorter luteal phase and higher pregnanediol-glucuronide, FSH, and LH levels at the time of ovulation. In 34% of the cycles, significant FSH variability was observed throughout the follicular phase; this variability was associated with higher body mass index and lower overall FSH and LH levels throughout the cycle. The FSH peak occurs on average 2 hours before ovulation. The FSH peak duration was shorter than the LH peak.

Conclusion(s): These results suggest that average FSH profiles may not reflect the more complex dynamics of daily hormonal variations in the menstrual cycle. It is possible that discrepancies between the average normal FSH profile and the individual day-to-day variants can be used to detect abnormalities. (Fertil Steril® 2014; 101:245–53. ©2014 by American Society for Reproductive Medicine.)

Key Words: Follicle-stimulating hormone, ovulation, menstrual cycle

Discuss: You can discuss this article with its authors and other ASRM members at http://fertstertforum.com/ecochard-follicle-stimulating-hormone-profiles-normal-ovulating-women/

Several recent publications have renewed interest in the assessment of individual hormonal profiles during the menstrual cycle (1–3). Although simplifications of the menstrual cycle are necessary for a basic understanding of physiology, there may be a place in clinical practice and research to take into account the departure of individual hormonal profiles from that of the average population, particularly for LH and FSH.

For example, it was recently shown that most individual LH profiles differed from the classic mean curves: Long or double LH surges are frequent and extremely variable in configuration, amplitude, and duration (3). Differences in hormonal profiles were associated with differences in the luteinization process (3). In another study, it was shown that a deficiency in corpus luteum function was associated with implantation failure, which may relate to individual hormonal profiles (4).

Individual FSH patterns also are of particular interest because this hormone is known to assist in the recruitment and growth of ovarian follicles as well as the selection of the dominant follicle. During the normal menstrual cycle, FSH rises in the late luteal or early follicular phase (5, 6). FSH levels are typically

Received October 26, 2013; revised March 14, 2014; accepted March 18, 2014.
R.E. has nothing to disclose. A.G. has nothing to disclose. R.L. has nothing to disclose. T.B. has nothing to disclose. A.D. has nothing to disclose. H.B. is employed by DCN Diagnostics, a company that specializes in the development of commercial lateral flow assays.
Reprint requests: René Ecochard, M.D. Ph.D., Service de Biostatistique, Hospices Civils de Lyon, 162, Avenue Lacassagne, F-69003 Lyon, France (E-mail: rené.ecochard@chu-lyon.fr).

Fertility and Sterility® Vol. 101, No. 3, 2014 0015-0282/$36.00
Copyright ©2014 American Society for Reproductive Medicine, Published by Elsevier Inc. http://dx.doi.org/10.1016/j.fertnstert.2014.03.034
assessed on days 2–4 of the cycle. Nevertheless, FSH has been shown to be rather unstable during this early follicular phase, with day-to-day variations (7, 8). During the late follicular phase, FSH falls to a relatively low level, a decline which is thought to interact with the follicular selection process (9). An FSH midcycle peak has been described as occurring the day of the LH peak, but many authors have questioned the temporal relationship between these two events (10–12). In the present study, individual FSH profiles are analyzed to describe variations in the overall trend from early to late follicular phase, the day-to-day variability in the follicular phase, the change in FSH during the transition between two successive cycles, and the temporal relationship between the FSH midcycle peak and ovulation.

**MATERIALS AND METHODS**

**Patients**

Patients were recruited from 1996 to 1997 from eight natural family planning clinics in France, Italy, Germany, Belgium, and Spain. The inclusion criteria consisted of women aged 19–45 years with previous menstrual cycle lengths of 24–34 days. Exclusion criteria included women with a consistent history of anovulatory cycles, infertility or active hormonal treatment of infertility in the past 3 months, use of hormonal contraception or hormonal replacement in the past 3 months, abnormal cycles (polycystic ovary syndrome or luteal defect), hysterectomy, tubal ligation(s), or pelvic inflammatory disease. In addition, runners and breastfeeding or postpartum mothers (<3 months) were excluded.

A total of 107 women were finally recruited, contributing an average of three cycles. The study examined 326 cycles which have been analyzed in other studies (3).

The study was approved by the local Ethics Committee (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale de Lyon). Each of the participants gave written informed consent, and the study procedures were carried out in accordance with the Ethical Standards for Human Experimentation established by the Declaration of Helsinki. Owing to legal-commercial disclosure agreements, the results regarding hormonal details were not published until now; this paper presents those results.

**Investigations**

Data collected from patients included information on age, age at menarche, parity, past oral contraceptives use, lifestyle habits, such as smoking, diet, and physical activity (h/wk), sleep duration (h/d), and stress levels (subjective assessment). Height and weight were measured and body mass index (BMI) calculated.

**Hormonal investigations.** The women collected first morning urine samples daily, which were stored frozen until assayed in the laboratory for quantitative hormone detection of estrone-3-glucuronide (E1G), pregnanediol-3α-glucuronide (PDG), FSH, and LH with the use of time-resolved fluorometric immunosorbent assays (Delfia). All samples from each woman were tested in duplicate in the same assay and the results were adjusted for creatinine (Cr). Interassay variations were negligible.

**Ultrasound investigations.** Serial transvaginal ovarian ultrasounds with follicle measurement were performed by a single physician per center. Ovarian scanning started on the first day women observed cervical mucus or when an LH surge was detected by LH home tests (Quidel Corp.), whichever came first. Scanning was performed every other day until a follicle reached 16 mm and then daily until evidence of ovulation. Details regarding ultrasound investigations were previously published (13).

**Other Characteristics of the Menstrual Cycle**

**Phases of the cycle.** The first day of the menstrual cycle was self-reported by the women. This was defined as the first day of the menstrual period where the woman observed bright red blood. Brown spotting was not considered to be a menstrual period.

For the purposes of this study, the menstrual cycle was divided into three phases: the latent phase, the fertile window, and the luteal phase. The latent phase is from the first day of the cycle to the day before the fertile window. The fertile window based on pregnancy probabilities has been shown to be a 6-day period ending on the day of ovulation (14). In the present study, the fertile window was defined as the first day of mucus observed at the vulva to the end of the ultrasound-determined day of ovulation (US-DO; the presence of mucus, felt or seen at the vulva by the woman, has been shown to be the main observable sign of fertility (15)). The luteal phase is from the day after US-DO until the day before the first day of next menses. Cycles with a luteal phase of >17 days were considered to be possible pregnancies. Proven pregnancies were defined by a positive urine β-hCG test.

**Hormonal levels.** To characterize hormonal levels during the three phases of the cycle, the average level of each hormone was calculated on days 2, 3, and 4 after the first day of menses (latent phase), on US-DO ± 1 day (fertile window), and on US-DO +5, +7, and +9 days (luteal phase).

To assess the evolution of FSH approaching ovulation quantitatively, we calculated the average FSH level on US-DO−12, −11, and −10 days (early follicular phase), and on US-DO−3, −2, −1 days (late follicular phase). The trend was estimated with the use of the difference between these two values (without logarithm transformation). The variance of logarithm-transformed FSH levels from day −11 to day −2 was estimated to reflect the stability or fluctuation of FSH.

The day of peak concentration for FSH and LH was identified within a 10-day window beginning 5 days before and ending 5 days after US-DO, which was designated as day 0. The days of maximum concentration of FSH, i.e., the midcycle peak, was identified, and the number of days from US-DO to the day of that peak was recorded.

**Statistical Analysis**

The geometric means of all 283 FSH and LH profiles were calculated and displayed graphically. US-DO was used as a reference day.
To classify the FSH hormonal profiles during the preovulatory phase, two criteria were used: 1) The overall trend from early follicular phase to the late follicular phase: increasing (+1 mIU/mg Cr or more), unchanged, or decreasing (−1 mIU/mg Cr or more); 2) The day-to-day variability (variance of logarithm-transformed FSH levels) during the same period (no variability, some variability, marked variability; terciles were used to divide the cycles into these three groups).

Because FSH rises in the late luteal or early follicular phase and typically reaches a peak in the early follicular phase (5, 6), the transition between two successive cycles was used to examine the latent phase FSH pattern. The cycles were then classified into three terciles: very early FSH peak (before the end of previous menstrual cycle or before day 2 of the current cycle); early FSH peak (on day 2 or day 3); and later FSH peak (day 4 or later).

The distribution of delays from US-DO to FSH midcycle peaks was described with the use of histograms.

The descriptive analysis of FSH hormonal profiles characteristics was performed with the use of the geometric mean ± SEM for quantitative variables.

Women and cycle characteristics associated with these different patterns of FSH hormonal profiles were compared with the use of a Fisher exact test for categoric variables and Student t test for quantitative variables. For the latter tests, variables whose distributions were not normal underwent a log transformation. To assess statistically significant differences in FSH hormonal profiles according to demographic characteristics (age, age at menarche, and BMI), a linear mixed model was used to take into account that most of the women provided more than one cycle for this study.

All statistical analyses were performed with the use of R software (version 3.0.0; R Foundation for Statistical Computing). A likelihood ratio test was used for all comparisons. A P value of < .05 was considered to be statistically significant.

RESULTS

Demographic and Cycle Characteristics

Participant and cycle characteristics have been described previously (3). Regarding parity, 66 out of 107 (62%) had at least one pregnancy in the past; 12 (11%) had at least one miscarriage. Forty out of 107 (34%) had ever used hormonal contraception. In 28 of the 326 monitored cycles, the first ultrasound was performed after ovulation and in 15 others it was not possible to confirm ovulation by ultrasound, leaving 283 ovulatory cycles for the analysis (Supplemental Fig. 1, available online at www.fertstert.org). That number is not uniform throughout the paper: 12 missing values were observed in case of short cycle, for which we had < 10 days to estimate the FSH trend.

Typical FSH Profile

Supplemental Figure 2 (available online at www.fertstert.org) shows the FSH geometric mean levels with a higher baseline in the early follicular phase (latent phase) and decreasing toward the end of the follicular phase (early fertile window). The surge occurs close to US-DO, followed by a second decline during the first part of the luteal phase. Finally, FSH rises during the days preceding menses. Note that duration of the average of FSH surge is ~2–3 days shorter than that of LH, which is shown for comparison. The majority of FSH surges take place on US-DO and the day after (Fig. 1).

Examples of Six FSH Profile Variants during the Entire Cycle

Figure 2 illustrates six representative profiles of variants in the FSH profile:

Cycle a is a typical profile for FSH: During the early follicular phase, FSH continues to increase; during the late follicular phase, FSH levels decrease; an FSH surge occurs the day before US-DO; during the early luteal phase, the FSH level is low; at the end of the luteal phase, the FSH increases.

Cycle b is marked by a low and flat level of FSH during the entire cycle, except during the periovulatory phase, marked by two distinct surges.

Cycle c is remarkable for an increase in FSH during the follicular phase with some day-to-day irregularity.

Cycle d is remarkable for the day-to-day irregularity during the follicular phase of the cycle.

Cycles e and f have in common delayed ovulation. But the mechanisms seem to differ: Cycle e is marked by a first double FSH surge, between days 10 and 15, followed 1 week later by a second FSH surge followed by ovulation; cycle f is marked by a delay in the onset of the surge (day 17) followed several days later by ovulation (day 21).

Examples of FSH Profiles during the Follicular Phase of the Cycle

Supplemental Table 1 (available online at www.fertstert.org) provides the frequency of different patterns of FSH during the preovulatory phase of the cycle. Figures 3 and 4 present...
categories of FSH profiles during the 11 days preceding ovulation. Three main trends were observed during the late follicular phase: increasing, unchanged, or decreasing in levels before ovulation.

Figure 3A, 3C, and 3E show the geometric mean hormonal profiles of the 50 (18%), 107 (39%) and 114 (42%) out of 271 cycles for which the FSH levels are increasing, unchanged, or decreasing, respectively. Figure 3B, 3D, and 3F show individual examples of each of these variants. The absence of a decline in the FSH level at the end of the follicular phase was significantly associated with slightly delayed ovulation ($P<.01$), a shorter luteal phase ($P<.01$), and higher PDG, FSH, and LH levels at ovulation ($P<.01$).

**Fluctuations of FSH levels.** Figure 4A, 4C, and 4E show the geometric mean hormonal profiles of the 94 (33%), 93 (33%) and 96 (34%) out of 283 cycles in which FSH levels exhibit respectively no day-to-day variability, some day-to-day variability, or marked variability during the late follicular phase. Figure 4B, 4D, and 4F are individual examples of each of these variants.

Supplemental Table 2 [available online at www.fertstert.org] provides the results of the analysis of the relationship between the degree of the day-to-day variability of FSH during the follicular phase of the cycle and other characteristics of the menstrual cycle. Low FSH variability throughout the follicular phase was significantly correlated with a higher number of sleep hours ($P<.05$). Greater FSH variability during the follicular phase was observed for women with a higher BMI ($P=.01$) and a higher level of physical activity ($P=.02$). Moreover, women with greater FSH variability also had lower overall levels of FSH throughout the cycle ($P=.01$) and lower LH levels on day 2–4 of the cycle ($P<.01$), at ovulation ($P<.01$) and during the luteal phase ($P=.06$).

**Very Early Follicular Phase FSH Peak**

The analysis of FSH profile variants during the transition between two successive cycles was limited to the 166 available transitions over 283 cycles, because two successive cycles were necessary to evaluate the transition.

The early follicular FSH peak occurred before day 2 in 41 cycles (25%), on day 2 or 3 in 46 cycles (28%), and on day 4 or later in 79 cycles (47%) (Supplemental Fig. 3, available online at www.fertstert.org). In 21 cycles (13%), the FSH peak occurred before the onset of the menses.

As expected, those cycles with the later FSH peak (in the early follicular phase) were associated with later ovulation occurrence ($P<.01$) and longer cycles ($P=.04$). No other studied covariate was associated with the precocity of the early follicular FSH peak.
FSH Midcycle Peak (Periovulatory)

The FSH midcycle peak duration is generally shorter than the LH midcycle peak (see Supplemental Fig. 2 for comparison). The histogram in Figure 1 demonstrates the temporal relationship of FSH and US-DO. The FSH peak occurs in 66% of cycles on the day before US-DO, US-DO, or the day after US-DO. Including all ovulatory cycles analyzed, the overall average delay between the FSH peak and ovulation was 2 hours (0.08 ± 2.04 days); 116 of 283 (41%) of FSH peaks occurred after US-DO.

DISCUSSION

This study replicates the well established basic physiologic pattern of FSH changes through the cycle when analyzed as a geometric mean of all cycles (Supplemental Fig. 2). However, this study also demonstrates that individual FSH profile variants may be dramatically different from the average. Although average hormonal profiles can be useful to make generalized statements about physiology, individual profiles need to be evaluated when exploring more subtle physiologic mechanisms.

One of the major strengths of this paper is the use of US-DO, which has been used in other studies (16) and is the criterion standard for identifying the ovulation event. Our study has a comparatively large number of cycles to be analyzed with ultrasound-confirmed ovulation. In many studies, surrogates are used to estimate ovulation, including the FSH surge itself or a day of luteal transition based on the changing concentrations of estrogen or P or the LH peak (11, 17). It should be noted that ultrasound-confirmed ovulation is operator dependent, and although it is the criterion standard it must still be externally validated (18). Hormone-based surrogates for ovulation are easier to obtain on many cycles, and not operator dependent, but they do not necessarily reflect the exact day of ovulation. For example, many studies use the LH peak as a reference day, assuming that ovulation occurs systematically ~1 day after this peak, but it has been confirmed recently that the delay between ovulation and the LH peak is highly variable (3). This delay is due to the maintenance of LH at a high level during the process of luteinization of the follicle: Even if the initial LH rise occurs before ovulation, the peak itself may be delayed, sometimes several days after ovulation. The latter phenomenon was not observed for FSH: The FSH peak took place close to US-DO in two-thirds of the cycles in our study. FSH levels are not maintained at high levels during the days after ovulation. The FSH peak may in fact be a better surrogate for the precise day of ovulation than the LH peak when the US-DO is not available. One study (12) concluded that urinary FSH is a useful biomarker for estimating the day of ovulation in population-based studies. In their sample, the urinary FSH peak was closer to
the day of follicular collapse (−0.85 day, compared with −0.08 day in our study) than was the peak day of serum E\textsubscript{2} and the day of luteal transition. In 65 cycles for which urinary hormone data and ultrasound evaluations were available in that sample, the urinary FSH peak occurred within 1 day of follicular collapse in 97% of cycles (66% in our sample).

The average FSH profiles presented in the present study could be used to support the physiologic assumptions made in the literature. However, although it is conventional to describe a decrease in FSH levels before ovulation, that decrease was observed in only 42% of the cycles. In other cycles, there was either no trend (39%) or even an increase (18%) in FSH levels before ovulation. From a physiologic point of view, the FSH decline before ovulation is thought to result from increasing E\textsubscript{2} levels which inhibit GnRH; GnRH inhibition leads to decreased FSH secretion, which in turn causes the smaller follicles in the current cohort to undergo atresia because they lack sufficient sensitivity to FSH to survive. If this physiologic process is valid, an increase in FSH rather than the usual decrease may be potentially deleterious for the ovulation process. In our dataset, the lack of decline in FSH at the end of the follicular phase was associated with slightly delayed ovulation, a shorter luteal phase, and higher PDG, FSH, and LH levels at ovulation, which may imply ovulatory dysfunction.

In one-third of the cycles, significant day-to-day variability was observed during the follicular phase. This marked variability may explain the existence of multiple waves of follicle development during the follicular phase that has been recognized (19); Figure 2E and F may be reflections of this phenomenon. The FSH variability also has implications for hormonal measurements in the clinical setting. Our data suggest that before women are counseled regarding their reproductive potential, FSH should be measured in at least two successive menstrual cycles (20). Moreover, it has been shown in IVF patients that higher variability in day 3 FSH levels was associated with a significant decline in ovarian reserve and a poor ovulation-induction response (21). In our dataset, based on ostensibly healthy menstruating women, marked variability in FSH during the follicular phase was observed for women whose BMI was higher or who declared to have greater physical activity, both of which are factors known to affect a woman’s fertility. Additionally, another sign that fertility may be affected is that the cycles with this marked variability were also associated with lower FSH and LH levels during all phases of the cycles.

Factors known to affect fertility, such as elevated BMI and greater physical activity, along with other factors that are not as well known (such as poor sleep and globally reduced FSH and LH levels), were affected by FSH variability. It is possible that increased FSH variability may be a physiologic correlate of these clinical factors. Moreover, the variability in FSH correlated with not only the clinical factors...
related to lower fertility but also the hormonal factors of lower fertility, like delayed ovulation and lower PDG levels.

The early follicular FSH peak was found before day 2 of the cycle and sometimes before the onset of menses in one-fourth of the women. As expected, a later FSH peak in the early follicular phase was associated with significantly later ovulation occurrence. A shorter delay from onset of the cycle to this peak has been shown in another study to be followed by an earlier ovulation (6). In our dataset, the precocity of this peak was correlated with US-DO but not associated with other characteristics of the woman or the cycle. Therefore, the precocity of an early follicular FSH peak may not have a significant impact on overall menstrual physiology.

With increasing age, FSH levels were previously shown to increase progressively (22). In the present study, this same finding was observed: Age is associated with a global increase of FSH, but without a clear modification of the profile itself.

CONCLUSION

The assessment of individual FSH profiles could provide more subtle analyses of menstrual cycle physiology. The results of the present analysis call for caution when using reference values from average profiles to study feedback and other interactions between the hormones of the menstrual cycle. The discrepancies between the average (Supplemental Fig. 2) or typical (Fig. 2A) FSH profile and individual variants may represent cycle abnormalities and particular cycle characteristics such as slightly delayed ovulation, a shorter luteal phase, and higher PDG, FSH, and LH levels at the time of ovulation. In addition, increased day-to-day variability in FSH was shown to be associated with lower FSH and LH levels during all phases of the cycles. These findings suggest that further study into individual FSH variants is warranted.

Acknowledgments: The initial data collection was partially supported by Quidel Corp. The authors thank Drs. Sophie Dubus, Anne Leduy, Isabelle Ecochard, Marie Grisard Capelle, Enriqueta Barraco, and Marion Gimmler. They also thank the natural family planning clinics as well as all of the women who took part in this study.

REFERENCES

SUPPLEMENTAL FIGURE 1

Flow diagram showing inclusion and exclusion characteristics of woman and cycles.

SUPPLEMENTAL FIGURE 2

Averages of FSH and LH profiles over 283 cycles. The dots and the dashed lines joining them represent the mean, and the vertical segments represent the SEM.

Transition between two successive cycles: average of FSH profiles according to the day of early follicular phase FSH peak profile. The cycles were classified into three terciles: (A) occurrence of the FSH peak very early, before day 2; (C) day 2 or day 3; and (E) day 4 or later. (B, D, F) Examples of each category.

## SUPPLEMENTAL TABLE 1

Frequency of different patterns of FSH during the preovulatory phase of the cycle.

<table>
<thead>
<tr>
<th>FSH trend during the follicular phase</th>
<th>Average of FSH profiles according to FSH stability during the follicular phase</th>
<th>No. of cycles (n = 271*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing level of FSH</td>
<td>Day to day stability of FSH</td>
<td>9 (3%)</td>
</tr>
<tr>
<td></td>
<td>Low day-to-day variability of FSH</td>
<td>19 (7%)</td>
</tr>
<tr>
<td></td>
<td>High day-to-day variability of FSH</td>
<td>22 (8%)</td>
</tr>
<tr>
<td>Stable level of FSH</td>
<td>Day to day stability of FSH</td>
<td>38 (14%)</td>
</tr>
<tr>
<td></td>
<td>Low day-to-day variability of FSH</td>
<td>38 (14%)</td>
</tr>
<tr>
<td></td>
<td>High day-to-day variability of FSH</td>
<td>31 (11%)</td>
</tr>
<tr>
<td>Decreasing level of FSH</td>
<td>Day to day stability of FSH</td>
<td>42 (15%)</td>
</tr>
<tr>
<td></td>
<td>Low day-to-day variability of FSH</td>
<td>35 (13%)</td>
</tr>
<tr>
<td></td>
<td>High day-to-day variability of FSH</td>
<td>37 (14%)</td>
</tr>
</tbody>
</table>

*The 12 missing values were observed in a case of short cycle, for which we had <10 days to estimate the FSH trend.

### Suppamental Table 2: Preovulatory FSH day-to-day variability from US-DO —11 to —2 and other characteristics of the menstrual cycle.

<table>
<thead>
<tr>
<th>Characteristic of women or menstrual cycles</th>
<th>Preovulatory FSH day-to-day variability from US-DO —11 to —2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low variability</td>
</tr>
<tr>
<td>No. of cycles</td>
<td>94 (33%)</td>
</tr>
<tr>
<td>Age (y)</td>
<td>32.64 (0.12)</td>
</tr>
<tr>
<td>Menarche (y)</td>
<td>13.10 (0.12)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.67 (0.11)</td>
</tr>
<tr>
<td>Phases of the cycle (d)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>27.62 (0.12)</td>
</tr>
<tr>
<td>Latency</td>
<td>8.23 (0.15)</td>
</tr>
<tr>
<td>Periovulatory phase</td>
<td>5.60 (0.17)</td>
</tr>
<tr>
<td>Postovulatory phase</td>
<td>13.12 (0.12)</td>
</tr>
<tr>
<td>US-DO</td>
<td>14.37 (0.13)</td>
</tr>
<tr>
<td>Hormone levels</td>
<td></td>
</tr>
<tr>
<td>Early follicular phase</td>
<td></td>
</tr>
<tr>
<td>E1G (ng/mg Cr)</td>
<td>9.55 (0.18)</td>
</tr>
<tr>
<td>PDG (µg/mg Cr)</td>
<td>2.02 (0.16)</td>
</tr>
<tr>
<td>LH (mIU/mg Cr)</td>
<td>3.25 (0.19)</td>
</tr>
<tr>
<td>FSH (mIU/mg Cr)</td>
<td>3.80 (0.23)</td>
</tr>
<tr>
<td>US-DO</td>
<td></td>
</tr>
<tr>
<td>E1G (ng/mg Cr)</td>
<td>46.28 (0.20)</td>
</tr>
<tr>
<td>PDG (µg/mg Cr)</td>
<td>2.53 (0.16)</td>
</tr>
<tr>
<td>LH (mIU/mg Cr)</td>
<td>13.25 (0.22)</td>
</tr>
<tr>
<td>FSH (mIU/mg Cr)</td>
<td>4.84 (0.25)</td>
</tr>
<tr>
<td>Luteal phase</td>
<td></td>
</tr>
<tr>
<td>E1G (ng/mg Cr)</td>
<td>25.79 (0.19)</td>
</tr>
<tr>
<td>PDG (µg/mg Cr)</td>
<td>10.85 (0.17)</td>
</tr>
<tr>
<td>LH (mIU/mg Cr)</td>
<td>4.80 (0.24)</td>
</tr>
<tr>
<td>FSH (mIU/mg Cr)</td>
<td>1.54 (0.26)</td>
</tr>
<tr>
<td>Follicle max. diameter (mm)</td>
<td>22.50 (0.12)</td>
</tr>
<tr>
<td>Sport activity (h/wk)</td>
<td>1.79 (0.41)</td>
</tr>
<tr>
<td>Sleep duration (h/d)</td>
<td>7.94 (0.11)</td>
</tr>
</tbody>
</table>

Note: BMI = body mass index; Cr = creatinine; E1G = estrone-3-glucuronide; PDG = pregnanediol-3α-glucuronide; US-DO = ultrasound-determined day of ovulation.