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ORIGINAL ARTICLE

Distribution of the follicular and luteal phase lengths and their age-dependent changes in Japanese women: A large population study

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Abstract

Purpose: The current definition of menstrual cycle length in a Japanese woman is different from those of WHO definition, and the original data are outdated. We aimed to calculate the distribution of follicular and luteal phases length in modern Japanese women with various menstrual cycles.

Methods: This study determined the lengths of the follicular and luteal phases of Japanese women using basal body temperature data collected via a smartphone application from 2015 to 2019, and the data were analyzed using the Sensiplan method. Over 9 million temperature readings from more than 80000 participants were analyzed.

Results: The mean duration of the low-temperature (follicular) phase averaged 17.1 days and was shorter among participants aged 40–49 years. The mean duration of the high-temperature (luteal) phase was 11.8 days. The variance and maximum-minimum difference of the length of the low temperature period were significant in women under 35 years old than women aged more than 35 years.

Conclusions: The shortening of the follicular phase in women aged 40–49 years implied a relationship with the rapid decline of ovarian reserve in these women, and the age 35 years old was turning point of ovulatory function.

KEYWORDS
aging, basal body temperature, female fertility, menstrual cycle, Sensiplan

1 | BACKGROUND

The length of a normal menstrual cycle ranges 24–38 days, including less than or equal 8.0 days of menstruation, and ±7–9 days of cycle-to-cycle variation depending upon age is considered regular.[1] This definition is statistically derived from relatively small population studies conducted over 30 years ago.[2] Nearly 60 years have passed since menstrual disorders and regularity were reported in Japanese women in the 1960s,[3] and the lifestyles of these women have changed significantly. Environmental factors, diet, and lifestyle have been reported to influence body temperature measurements, which have been used to collect menstrual cycle data.[4] However, differences in body temperature have not been studied in women of different ages. Normal body temperature values related to

menstruation may change with age, as a previous study reported that aged women have a shorter follicular phase and menstrual cycle.[5] The change of menstruation with age is also reflected by the fact that menstrual blood flow increases as women age.[6]

Basal body temperature (BBT), which is deep body temperature, is controlled by the thermoregulatory centre in the anterior thalamus and increases after ovulation due to the ovaries' secretion of progesterone.[7,8] BBT can be measured easily and is useful as an indicator of ovulation,[9] although its accuracy has been questioned.[10] Recently, BBT has been used as an indicator of healthy aging and longevity.[11] It is stable and relatively unaffected by environmental factors such as outside temperature, hours of sunlight, and precipitation.[12,13] Recently, women have started using smartphone applications to record their BBT. There are currently over 100 fertility awareness-based smartphone applications that aim to help women of reproductive control conception.[14,15] These data are easily accessible for scientists after obtaining informed consent from the application users. As the World Health Organization and International Federation of Gynecology and Obstetrics are emphasizing the highest possible standards of physical, mental, reproductive, and sexual health and wellbeing throughout women's lives, it is important for women to understand their body's condition and ovulation dates. Therefore, an updated definition of normal menstruation based on the number of days of low (follicular phase) and high (luteal phase) BBT is necessary. Additionally, it is difficult to determine whether the follicular or luteal phase is involved in specific irregular menstrual cycles.[8] In the present study, a smartphone application (LunaLuna, MTI Ltd.) was used to collect data as this application is free and is one of the most popular healthcare applications for women in Japan. It is currently downloaded by over 18 million as March 2022. A previous study that used this application indicated that the length of the menstrual period and BBT are not different based on time of the year or participant location.[12] Therefore, this study aimed to calculate the distribution of menstrual cycle length in modern Japanese women into follicular and luteal phases using the Sensiplan method from BBT values collected from a large population with various menstrual cycles, although we should be careful to apply the term "normal menstrual cycle" because we tend to assume that normal women are exempt from diseases including infertility. We also aimed to examine whether these is an age-dependent changes of length of follicular and luteal phases.

2 | METHODS

2.1 | Study design

This study was approved by the Ethics Committee of the Graduate School of Medicine, University of Tokyo (ethics approval number, 2019241NI). All current users of the "LunaLuna" application were notified within the application regarding the research protocol, use of individual BBT data, and the procedures required to withdraw from the study. For past users that met our inclusion criteria, MTI Ltd. published a press release regarding the study and directions for withdrawal from the study. Participant characteristics were obtained by mandatory questions during the application's sign-up process. Daily BBT data were measured sublingually by the participants. Physiological data that may affect the results of BBT, such as body mass index, were not obtained because the study population closely resembled that of a previous report on Japanese women.[12] Moreover, the study reported that participant location and height were not correlated to cycle length distribution by age.[12] It was assumed that the collected data might not accurately represented the untreated female Japanese population, and the participants might possess health consciousness bias.

2.2 | Cycle selection

BBT data of women aged 18–59 years with at least 10 cycles of BBT data input between 1 January 2015 and 31 December 2019 were included in this study. Data from biphasic menstrual cycles were extracted. Data in which the high temperature period lasted for >20 days without a menstrual period were excluded due to the possibility of pregnancy. Additionally, data in which each temperature period lasted <4 days or >80 days,[12] and participants who did not enter data for two or more consecutive cycles were excluded from the study due to a high possibility of data entry errors.

The Sensiplan method[16] was used to define the shift of BBT from low to high temperature or from high to low temperature. A total of 9 314 081 BBT values obtained from 81 972 participants were included (Figure S1). Up to 4 consecutive days of missing data were permitted according to the Sensiplan method, which uses the maximum and minimum values of the previous 6 days' data. BBT data that differed by more than ±0.2°C from the previous or subsequent day were considered abnormal and were excluded as missing values and replaced by the average of the previous and subsequent days' data.

2.3 | Statistical analysis

The number of days in the menstrual cycle was calculated using the BBT data. Each cycle was divided into low- and high-temperature periods[8] based on the Sensiplan method.[16] Histograms were created using JMP Pro15 software (SAS Institute Inc.). The central 95% and 50% of the data were calculated and referred to as the "95% range" and "50% range," respectively. Furthermore, age-dependent changes in the length of the menstrual cycle and BBT were examined. The mean BBT and number of days in each period were stratified by age, and to take into account the correlation of measurements within each participant the population mean for each age group was estimated using the random-effect model in which study participants were specified as a random-effect. Difference of the population mean of BBT between the follicular and the luteal phase and between age groups were tested through the above random-effect model. The graphs were created using Microsoft Excel (Microsoft

Corporation). Data from the cycles that showed biphasic behavior in each age group and each temperate period were extracted. The correlation between the variability of menstrual cycle days and age was examined by calculating the variance and the maximum-minimum difference of the number of days of each period for each age group.

The participants were further divided into groups based on age: groups A (≤35 years of age) and B (>35 years of age) and groups C (≤40 years of age) and D (>40 years of age). The variance and maximum-minimum difference were calculated, and the random-effect model was used to compare the variability between groups A and B and groups C and D using the JMP Pro15 software. Statistical significance was set at $p < 0.05$.

3 | RESULTS

3.1 | Distribution of extracted data

A total of 9314,08 BBT values were collected from 81 972 participants. These data were used to examine the distribution of BBT and menstrual cycles of follicular phase and luteal phase in whole population.

The data were analyzed among users ranging in age from 18.0 to 59.0 years, we confirmed that 95% of participants were in the 20–45 years old reproductive age group, with the largest number of participants in the 30–34 years old age group.

The median BBT in the follicular phase was 36.4°C (95% range: 36.0–36.7°C, 50% range: 36.3–36.5°C) (Figure 1A) and that in the luteal phase was 36.7°C (95% range: 36.4–37.0°C, 50% range: 36.6–36.8°C) (Figure 1B). The median length in the follicular phase was 16.5 days (95% range: 10.3–27.5 days, 50% range: 14.3–19.0 days) (Figure 1C) and that in the luteal phase was 11.8 days (95% range: 7.5–16.0 days, 50% range: 10.5–13.0 days) (Figure 1D).

3.2 | Age-related changes in cycle length and BBT

Of these data, age data were extracted and used to examine age-dependent changes in BBT and menstrual cycles because age dependent change of BBT data can be an important hallmark that reflects ovarian function. Extraction of data with age data resulted in 368 031 follicular phase and 274 492 luteal phase BBT values being included in this study as demonstrated in Table 1. First, we confirmed the temperature in all age groups. The mean BBT during the follicular phase was 36.4°C (Figure 2A) and that during the luteal phase was 36.7°C (Figure 2B), both highest in the 30s. Next, we aimed to examine the duration of the follicular phase and luteal phase. It was shown that the follicular phase was significantly longer

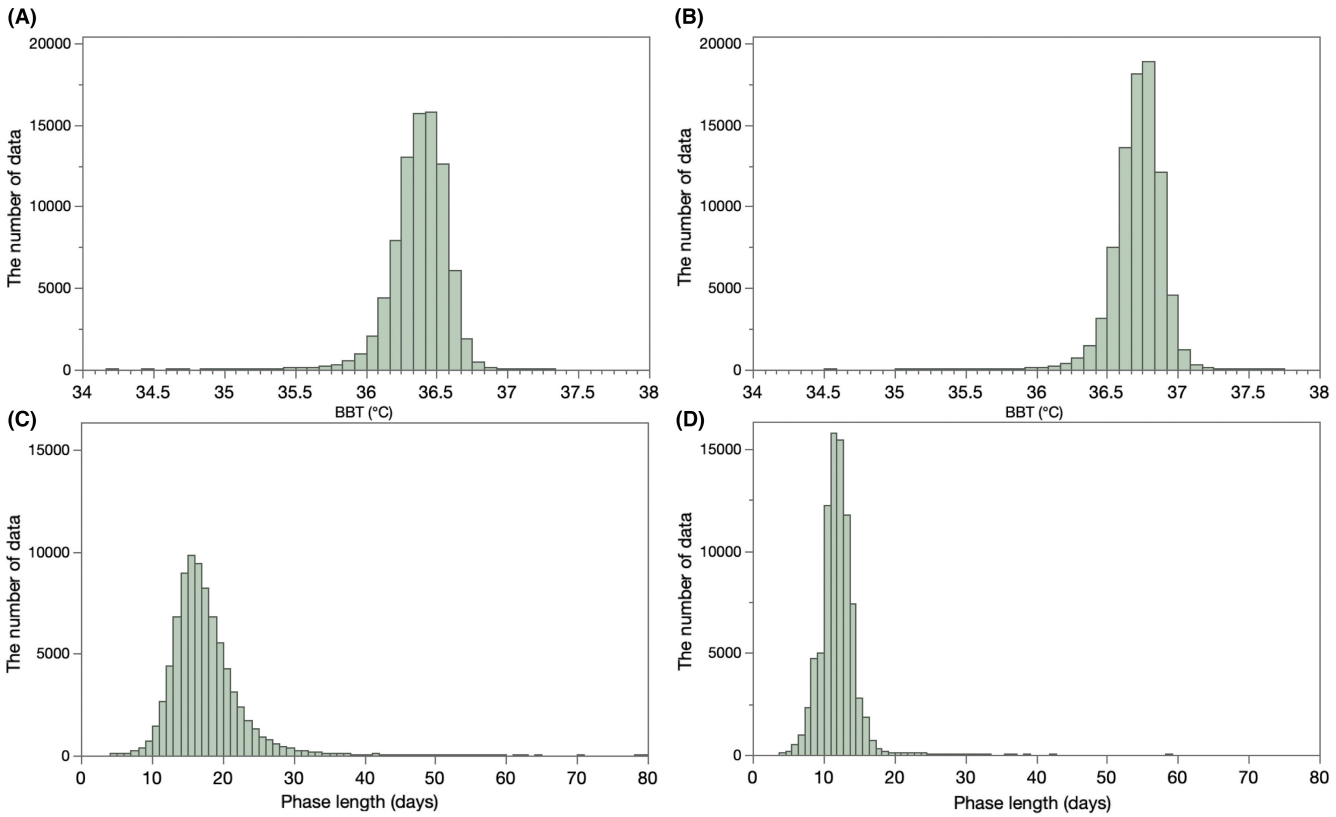

FIGURE 1 Distribution of mean basal body temperature and menstrual cycle phase length. (A) The median basal body temperature (BBT) in the follicular phase was 36.4°C (95% range: 36.0–36.7°C, 50% range: 36.3–36.5°C). (B) The median BBT in the luteal phase was 36.7°C (95% range: 36.4–37.0°C, 50% range: 36.6–36.8°C). (C) The median length in the follicular phase was 16.5 days (95% range: 10.3–27.5 days, 50% range: 14.3–19.0 days). (D) The median length in the luteal phase was 11.8 days (95% range: 7.5–16.0 days, 50% range: 10.5–13.0 days).

for participants aged 20–29 years (18.0 days) than for those aged 40–49 years (15.4 days) ($p < 0.0001^{***}$; Figure 2C). In contrast to the follicular phase, the length of the luteal phase was not significantly different between the age groups (Figure 2D).

Although BBT data in the follicular and the luteal phase did not differ significantly, we hypothesized that there might be a variance and maximum-minimum difference of menstrual cycles. We further extracted data with >2 consecutive years of records and divided them into two groups, namely groups A (≤35 years of age), B (>35 years of age), groups C (≤40 years of age) and D (>40 years of age). In the comparison between Group A and Group B, the variance ($p = 0.0162^{*}$) and maximum-minimum difference ($p = 0.0359^{*}$) of the length of the low temperature period were significantly greater in Group A compared to Group B (Figure 3A,B), but the variance ($p = 0.289$) and maximum-minimum difference ($p = 0.405$) of the duration of the high temperature period were not significantly different between Groups A and B (Figure 3C,D). These data suggested that there was a large variation in the low-temperature period among relatively younger people. In consistent to this finding, the variance ($p = 0.604$) and the maximum-minimum difference ($p = 0.869$) of the length of the low temperature period did not differ significantly in Groups C (≤40 years of age) and D (>40 years of age). The variance ($p = 0.835$) and maximum-minimum difference ($p = 0.969$) of the duration of the high temperature period were also not significantly (data not shown).

TABLE 1 Age distribution of BBT values.

	Number (%) of bbt values	
Age (years)	Follicular phase	Luteal phase
18–19	663 (0.180)	568 (0.207)
20–24	11 328 (3.08)	8060 (2.94)
25–29	70 192 (19.1)	53 879 (19.6)
30–34	114 067 (31.0)	87 239 (31.8)
35–39	99 292 (27.0)	74 287 (27.1)
40–44	56 316 (15.3)	39 537 (14.4)
45–49	14 850 (4.03)	10 172 (3.76)
50–54	1314 (0.357)	739 (0.269)
≥ 55	9 (0.002)	11 (0.004)
total	368 031	274 492

Abbreviations: BBT, basal body temperature.

4 | DISCUSSION

This study calculates the distribution of menstrual cycle length in modern Japanese women into follicular and luteal phases from BBT values collected from a large population and found that the follicular phase becomes significantly shorter as women age. In addition, Sensiplan was used to analyze low-temperature and high-temperature phases separately using person-specific data.

In this study, we used large-scale population data collected from a smartphone app to calculate the distribution of each

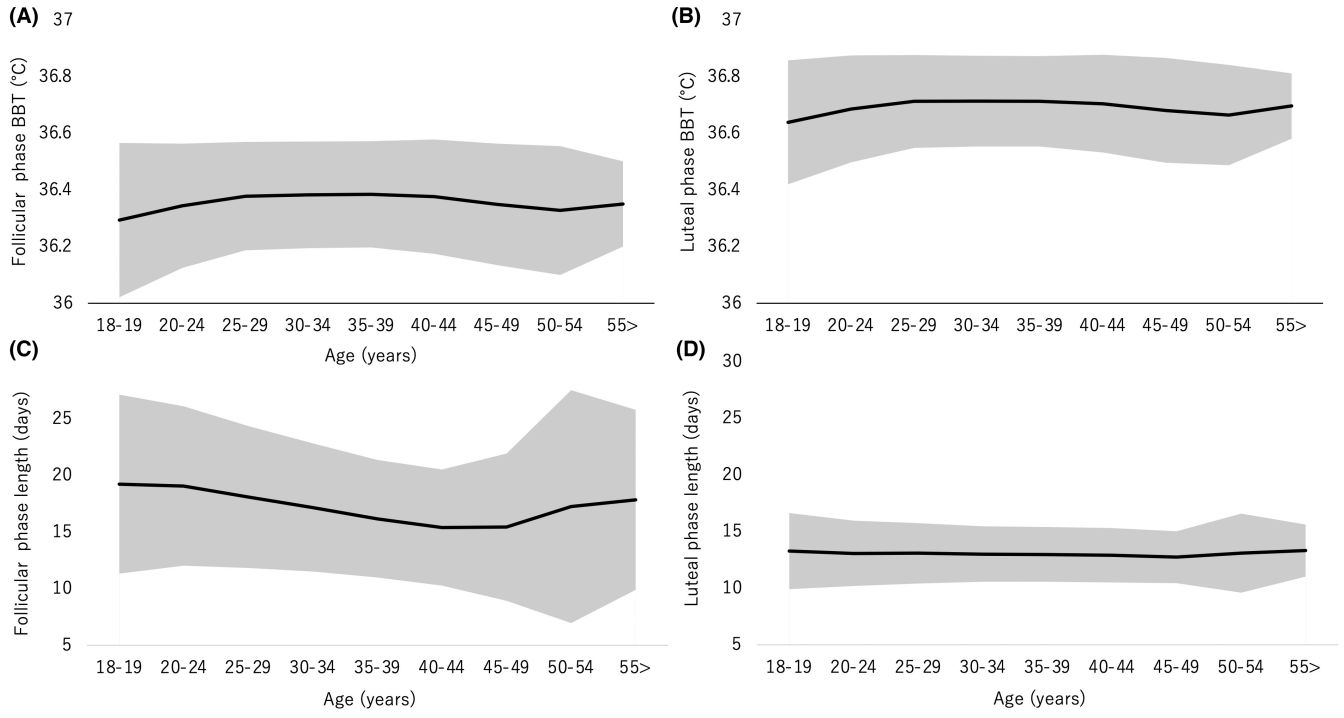

FIGURE 2 Age-dependent changes in basal body temperature and menstrual cycle phase length. The mean BBT during the follicular phase was 36.4°C (A) and that during the luteal phase was 36.7°C (B). The duration of the follicular phase was significantly longer for participants aged 20–29 years (18.0 days) than for those aged 40–49 years (15.4 days) ($p < 0.0001^{***}$; C). The length of the luteal phase was not significantly different between the age groups (D).

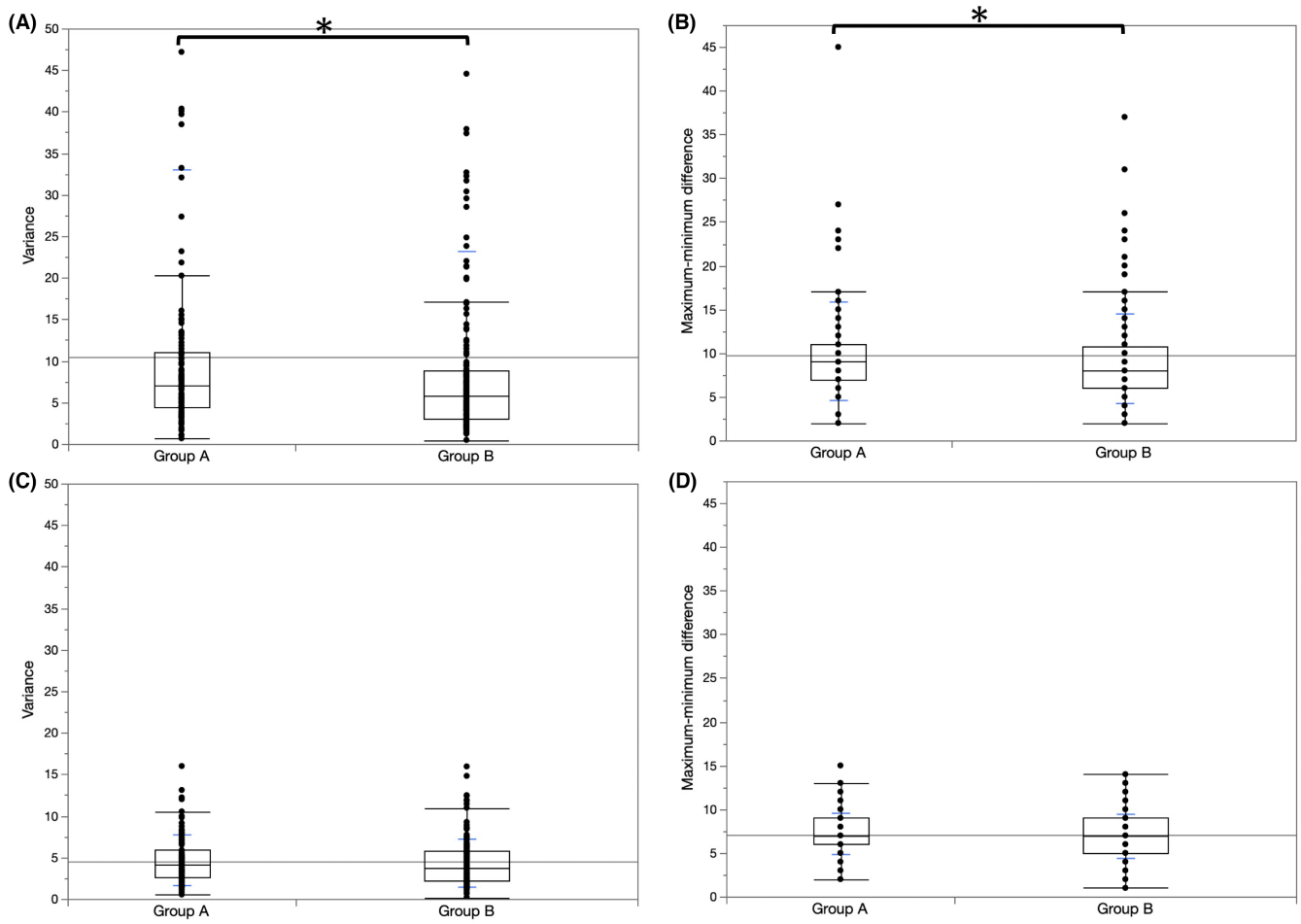

FIGURE 3 Variation and maximum-minimum differences in menstrual cycle length between Group A and B (*$p < 0.5$). (A) The variance ($p = 0.0162$*) of the length of the low temperature period were significantly greater in Group A (≦35 years old) than in Group B (>35 years old). (B) The maximum-minimum difference ($p = 0.0359$*) of the length of the low temperature period were significantly greater in Group A than in Group B. (C) The variance ($p = 0.289$) of the length of the high temperature period were not significantly different Group A and B. (D) The maximum-minimum difference ($p = 0.405$) of the length of the high temperature period were not significantly different Group A and B. Values that do not fit within the range of the vertical axis of the graph are included in the calculation but are not shown in the graph. No significant differences were found in any of the comparisons.

temperature phase for modern Japanese women. The median length in the follicular phase was 16.5 days and that in the luteal phase was 11.8 days. Since no study has so far investigated the menstrual cycle by dividing it into each temperature period, this study is considered to be an important precedent study for analyzing each temperature period in future research on the menstrual cycle. Regarding the luteal phase in particular, it was found that there was a deviation from the current standard for luteal dysfunction (luteal phase less than 10 days). Future studies should re-examine the diagnostic criteria for luteal dysfunction. The number of days in each phase of the menstrual cycle determined in this study, as well as height[17] and body surface temperature,[18] can be approximated to a normal distribution. It is believed that the normal distribution of height is subject to the influence of various genetic and social factors.[17] Moreover, the number of days of the menstrual cycle is affected by several factors and can be approximated to a normal distribution.

This is the first study to use the Sensiplan method to analyze BBT data from a large population, resulting in the ability to divide individual menstrual cycles into high- and low-temperature phases. The American Society for Reproductive Medicine has reported that BBT is an inconvenient method for determining luteal phase insufficiency.[19] However, BBT can be easily measured by patients.[20] If missing BBT values can be compensated for, as in this study, and the Sensiplan method is used to divide a patient's menstrual cycle into high- and low-temperature phases, the accuracy of women's fertility control will be improved. A smartphone application that can determine the high- and low-temperature phases for a user will allow patients to understand the characteristics of their menstrual cycle without relying on a standardized cycle and accurately estimate the date of ovulation using BBT values. It has already been shown that educational interventions using smartphone applications can contribute to improving literacy regarding infertility treatment and combining such educational interventions

with individualized normal values will lead to more effective fertility management.[21] To accurately determine the presence or absence of ovulation, a commercially available ovulation test kit is currently required.

Although this study was conducted using data from Japanese women, the Sensiplan method is applicable to other regions and ethnic groups. This method may be useful to help solve infertility problems in developed countries, including Japan. The first step in infertility treatment is to predict the date of ovulation and provide guidance on the timing of sexual intercourse.[22] The accuracy of the prediction of ovulation is critical using any prediction method, including BBT.[23] If the Sensiplan method can be used to easily and accurately predict ovulation, the success rate of fertility treatment may improve. In addition, improper use of contraception and inadequate knowledge of reproductive health are important issues in developing countries, especially when paired with inaccurate estimations of the fertile period.[24] Smartphone applications that can estimate fertility more accurately may help overcome these challenges.

In this study, although aging changes were observed in the BBT itself, both the low and high temperature phases changed by less than 0.2°C, which is not considered to be of much clinical significance. On the other hand, with respect to the duration in each phase calculated from the BBT, the length of the low temperature (follicular) phase was found to be shorter in women in their 40s, which may be due to aging of the ovaries,[25] and it was also indicated as a feature of ovarian aging that the variance and maximum-minimum difference in the length of the low-temperature period declined as women age (Figure 3). During the transition to menopause, the menstrual cycle gradually loses its regularity due to the insufficient number of follicular stimulating hormone-positive follicles in the ovaries. The first persistent shortening of the cycle is due to the selection of dominant follicles, which begins earlier in the luteal phase of the previous cycle and shortens the duration of the follicular phase.[26] The shortened follicular phase has been reported in previous studies[5,27]; however, only the shortening of the menstrual cycle has been previously confirmed in Japanese studies.[12] The results of this study indicate that the length of the follicular phase is shortened as women age, which may be an effect of ovarian aging. Furthermore, a shortened follicular phase may be related to rapid decline in fertility that occurs in women in their 40s.[28] Because the length of the menstrual cycle and BBT are known to differ among ethnic groups,[29] the results of this study should be verified in other ethnic groups. However, age-related changes in BBT have been reported to be independent of ethnic differences,[11] suggesting that a shortened follicular phase may be a useful indicator of ovarian aging. The use of a smartphone application to record self-reported BBT data and calculate the duration of follicular phase using the Sensiplan method can help detect a shortened follicular phase, encouraging patients to seek medical care at an earlier stage.

As the duration of the high temperature (luteal) phase remains constant with age, the presence or absence of ovulation can be determined based on the presence or absence of the high temperature period, not on changes in its length. By recording self-reported BBT data using a smartphone application and determining the presence or absence of the luteal phase using the Sensiplan method, women themselves can detect anovulation and encourage early medical consultation. As shown in this study, the Sensiplan method is a useful tool to accurately divide the menstrual cycle into high- and low-temperature phases based on BBT data.

This study has some limitations. First, there may be a selection bias associated with the active use of the smartphone application, as women using the application may be more anxious than the general population regarding their menstrual cycles. Similar to previous studies,[27,30,31] this study included data from cycles that showed normal biphasic phases. However, additional biases may exist. Second, some participants in this study may have used oral contraceptives (OCPs), which would affect the regularity of the menstrual cycle. However, only 1.0% of Japanese females use OCPs for contraceptive purposes[32] and OCP generally elevates BBT; therefore, the impact of the data obtained from OCP users is negligible. Similarly, we were not able to completely exclude infertility treatment cases and chemical pregnancy cases. Lower limit of the luteal phase might be influenced by contamination of cycles without ovulation and higher limit of the luteal phase might be influenced by contamination of cycles with pregnancy. The latter can be excluded by treating cycles with a high-temperature period of 20 days or more as pregnancies, but our calculation method is not based on hormonal dynamics or imaging studies, thus it is theoretically impossible for us to exclude all iatrogenic effects. Third, the device used to measure BBT likely differed among the participants. In future studies, the use of the same device will improve the accuracy of the data but will limit the number of participants. Fourth, these results of this study are specific to Japanese women and should not be generalized. A previous study[12] found no regional differences in BBT among Japanese women, and studies conducted in the Netherlands[5] and Sweden[27] showed that the length of the follicular phase decreased with age. However, these results require verification in other ethnic groups. Fifth, although the menstrual cycle length may differ based on body mass index (BMI),[27] no participants were excluded from this study based on BMI, according to a previous report of no association between height or weight and cycle length among Japanese women.[12] More research regarding the length of the menstrual cycle in women with extremely large or small BMIs is necessary. Sixth, the follicular phase and the luteal phase were considered separately based on Sensiplan, and normal values were estimated for each in this study. We used only BBT values, which can be easily measured at home and did not consider whether hormone dynamics are normal. A future research topic is to estimate the normal menstrual cycle by combining BBT and hormone dynamics. Finally, the analysis methods used in this study did not allow for the detection of longitudinal changes in a single participant throughout the study period. A large-scale prospective cohort study is needed to study the longitudinal changes of the menstrual cycle more accurately.

The distribution of menstrual cycle length in modern Japanese women from a large population was calculates in this study and the duration of the follicular phase was found to be shorter in older

women. We should be careful to translate the results of this study because the collected data might not accurately represent the general female Japanese population because infertile women using ovarian stimulation drugs are included in this study, and the participants using smartphone app might possess health consciousness bias, thus these participants might be far from normal population. The Sensiplan method was determined to be useful in defining the biphasic nature of the menstrual cycle. The results of this study may help women of reproductive age understand the status of their menstrual cycles.

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FUNDING INFORMATION

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CONFLICT OF INTEREST STATEMENT

The authors declare no possible conflicts of interest to disclose. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval for this study was obtained from The University of Tokyo Hospital Institutional Review Board (approval number: 2019241NI). All current users of the "LunaLuna" application were notified within the application regarding the research protocol, use of individual BBT data, and the procedures required to withdraw from the study. For past users that met our inclusion criteria, MTI Ltd. (Shinjyuku-ku, Tokyo) published a press release regarding the study and directions for withdrawal from the study.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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