



Measurement of endometrial thickness in premenopausal women in office gynecology

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Abstract

Purpose: To define the median endometrial thickness (ET) in office gynecology is thought to be important for clinical practice. However, there are few reports about ET

that have included the general female population on a large scale. The median ET was determined prospectively in premenopausal women who attended office gynecology for cervical cancer screening.

Methods: In total, 849 women were enrolled. The median ET was determined by using transvaginal ultrasound and the relationships between the ET and various clinical factors were analyzed.

Results: The participants' median age was 38.5 years. The median ET was 8.6 mm (90% and 95% quantiles: 13.8 and 15.8 mm). The ET was not related to their age, symptoms, obstetric history, geographical location, or risk factors for endometrial cancer. In the women with a menstrual cycle length of 28–30 days, the ET was 7 mm on days 1–6, but it increased from 5.4 mm immediately after menstruation (day 7 or 8) to 9.2 mm on days 13–14. Subsequently, the ET increased further to 11.1 mm on day 18.

Conclusion: In all the women, the upper limit of the ET was 13.8 mm and 15.8 mm in the 90% and 95% quantile, respectively, in office gynecology.

KEYWORDS

endometrial thickness, menstruation cycle, office gynecology, premenopausal women, transvaginal sonography

1 | INTRODUCTION

Endometrial sampling is the standard diagnostic method for detecting endometrial cancer, which is the most common gynecologic malignancy. However, this method can cause a great deal of anxiety for patients. Often, transvaginal sonography (TVS) is performed clinically as a screening method for endometrial cancer and there have been many reports about its use for cancer detection.^{1,2} However, most of the reported studies of TVS have enrolled postmenopausal women, rather than premenopausal women. This study's final goal was to determine the cut-off value of endometrial thickness (ET) to exclude endometrial disease in premenopausal women in office gynecology and, as a first step, it was thought to be essential to determine the median ET of general premenopausal women who attend office gynecology. In addition, it was thought to be useful to determine the upper limit of the ET in premenopausal women in clinical practice. However, in the previous studies of TVS that was performed on premenopausal or postmenopausal women, a "normal control" was defined as a woman who had no endometrial disease,^{1,2} but most of these women attended large medical centers for symptoms and were not representative of the general female population in office gynecology.^{1,2} Furthermore, the ET has been investigated in the field of reproductive medicine; however, these studies mainly included infertile women.^{3,4} Some reports included healthy volunteers;^{5–7} however, these reports included only 23–50 cases and it was thought to be not enough to determine the median ET. There are few reports about ET that have included the general female population on a large scale.

The aim of the present study was to determine the median and upper limits of the ET of premenopausal women who attended office gynecology for cervical cancer screening and to evaluate the

relationship between the ET and various risk factors of endometrial cancer on a large scale.

2 | MATERIALS AND METHODS

2.1 | Inclusion criteria

The inclusion criteria included: (1) women attending office gynecology for cervical cancer screening (municipal cervical cancer screening or cervical cancer screening in a medical check-up); and (2) women with vaginitis or prolapse were permitted. All the women provided written informed consent and this study was approved by the institutional review board of Hokkaido Cancer Center, Sapporo City, Japan.

2.2 | Exclusion criteria

The exclusion criteria included: (1) the use of medications with a direct effect on ET, such as sex hormones or tamoxifen; (2) a difficulty in visualizing the endometrium due to uterine fibroids or adenomyosis (an inability to visualize the entire endometrium without deformation); (3) endometrial polyp; (4) endometrial cancer or endometrial hyperplasia (including the subsequent diagnosis of these diseases); (5) during fertility treatment; (6) the use of supplements, such as placental preparations; and (7) women who were considered to be ineligible for other reasons by the attending physician.

2.3 | Ultrasonography

A magnified longitudinal image of the uterus was displayed on the monitor and the uterus was measured on a magnified image that

occupied more than 2/3 of the monitor screen. Then, the endometrium was visualized on a leaf image and the thickest part was measured to one decimal by using the longitudinal image of the uterus.⁸ If an echo-free space was seen, representing the uterine cavity, only the solid portion was measured, excluding this region. The ET always was measured before cervical cytology or a histological examination was performed.

2.4 | Pathological examination

Pathological information was not mandatory in this study because performing endometrial sampling in all women without abnormal genital bleeding who presented for cervical cancer screening (municipal cervical cancer screening or cervical cancer screening in a medical check-up) would be ethically problematic. In addition, endometrial diseases, such as endometrial cancer or hyperplasia, are thought to be very few in number in women without genital bleeding who present for cervical cancer screening and it was considered that there would be little effect on the median value of the ET. However, when a cytological or histological examination was performed, the women who were found to have endometrial polyp, endometrial hyperplasia, or endometrial cancer were excluded from analysis in this study.

2.5 | Investigated clinical factors

The following clinical factors were investigated: age, age of first menstruation, details of the last period, menstrual cycle, height, body weight, complications (diabetes mellitus, hypertension, hyperlipidemia, nulligravidity, infertility, menstrual disorders, and estrogen therapy), a history of breast cancer, current symptoms (abnormal genital bleeding, AGB), obstetric history, and marital history.

2.6 | Sample size estimation

In order to estimate the reference values of the ET, the precision of the 90th percentile and the 95th percentile are required to be high enough. To find the 95% confidence interval for the q th quantile ($q = 0.9$ for the 90th percentile), the nearest integers of the following r_q and s_q values are estimated. The r_q th and s_q th observations in the ranking are the 95% confidence interval for the population q th quantile with sample size n :⁹

$$r_q = nq - 1.96\sqrt{nq(1-q)}, \quad s_q = 1 + nq + 1.96\sqrt{nq(1-q)}$$

The lower 95% confidence limit of the 95th percentile is greater than the upper 95% confidence limit of the 90th percentile with >475 patients. The $r_{0.95}$ is 442 and $s_{0.9}$ is 441 for 475 patients. Therefore, the minimum required sample size is 475. In this study, the total sample size was 849, the $r_{0.95}$ was 792, and the $s_{0.9}$ was 780. Thus, the precisions of the 90th percentile and the 95th percentile were high enough.

2.7 | Data collection

All the data were obtained from the participants' medical records, including the ultrasound images. A correspondence table containing the patient identification numbers and registration numbers was prepared at each participating institution for linkable anonymization of the data. The case report forms were marked with the registration numbers and sent to the data center (Department of Biostatistics, Hokkaido University Graduate School of Medicine, Sapporo, Japan).

2.8 | Participating institutions

The participating institutions were: Sakura Ladies Clinic (Chitose City, Hokkaido), Hokkaido Cancer Society (Sapporo City, Hokkaido), Rhythmic Obstetrics and Gynecology Clinic (Sapporo City, Hokkaido), Hokkaido Cancer Center (Sapporo City, Hokkaido), Sakamoto Tomomi Clinic (Hirosaki City, Aomori), Mami Ladies Clinic (Hachinohe City, Aomori), St. Cecilia Ladies Clinic (Aomori City, Aomori), Azabu Juban Minami Women's Clinic (Minato Ward, Tokyo), Mizuho Women's Clinic (Kokubunji City, Tokyo), Kobiki Women's Clinic (Kawasaki City, Kanagawa), Yokohama First Health Check Place (Yokohama City, Kanagawa), Sutou Ladies Clinic (Osaka City, Osaka), Tasaka Clinic (Toyonaka City, Osaka), Minami-Morimachi Ladies Clinic (Osaka City, Osaka), Kiyu Ladies Clinic (Nara City, Nara), Mio Fertility Clinic (Yonago City, Tottori), Hiroshima Breast Center (Hiroshima City, Hiroshima), Kakinoki Hospital (Kagoshima City, Kagoshima), and Dozono Clinic (Kagoshima City, Kagoshima).

Hokkaido Cancer Center was the only large medical center; however, in this institute, only the cases of Sapporo municipal cervical cancer screening were enrolled. Endometrial cancer is more common in urban areas. Therefore, the ET was analyzed separately for the women from urban areas and rural areas. The following urban areas were selected: Minato Ward (Tokyo), Kokubunji, Kawasaki, Yokohama, Osaka, and Hiroshima; the following rural areas were selected: Chitose, Hirosaki, Hachinohe, Aomori, Nara, Yonago, and Kagoshima. Initially, it was planned to enroll 25 institutions in this study, but four institutions did not participate.

2.9 | Analysis methods

The median, 90%, 95%, and other percentiles of ET with 95% confidence intervals were calculated. Differences in the ET between groups were compared by the t test. In addition, the ET was compared between groups with stratification by various factors and differences in the mean values were tested for 73 items, with a significance level of .000685 (.05/73) by using the Bonferroni method in order to avoid false-positive results. The ET was compared among menstrual cycles and differences in the mean values were tested for 66 items, with a significance level of .00075 (.05/66) by using the Bonferroni method in order to avoid false-positive results.

2.10 | Definition of menstruation

A normal menstrual cycle was defined as a menstrual cycle length of ≥ 25 days and ≤ 38 days, with a variation of < 7 days. "First half" was the first half of the menstrual cycle (within the first half of the cycle). "Second half" was the second half of the menstrual cycle (within the second half of the cycle). Polymenorrhea was defined as a menstrual cycle length of ≤ 24 days. Oligomenorrhea was defined as a menstrual cycle length of ≥ 39 days. An irregular menstrual cycle was defined as a menstrual cycle length of ≥ 25 days and ≤ 38 days, with a variation of no less than 7 days. Amenorrhea was defined as the absence of menstruation for 90 days. The women also were classified into three groups, based on their Body Mass Index (BMI): < 25 , 25–30, and ≥ 30 . The following risk factors for endometrial cancer were investigated: hypertension, diabetes mellitus, hyperlipidemia, obesity (BMI: ≥ 30), a history of breast cancer, and a history of fertility treatment.

3 | RESULTS

3.1 | Geographic data and other baseline characteristics of the participants

Between September 22, 2014 and March 31, 2015, 849 women were enrolled in this study and cytological examination of the endometrium was performed in 135 of them. The endometrial cytology revealed abnormalities in three women (positive in one woman and suspicious in two women). Finally, a histological examination led to a diagnosis of endometrial cancer in one woman and a secretory-phase endometrium in two women; thus, the woman with endometrial cancer was excluded from this study. Furthermore, the clinical information was self-reported by each woman based on a questionnaire; thus, the information about the height of three women, symptoms in seven women, and the menstrual cycle in 17 women were lacking. In addition, 37 women were breastfeeding and these women obviously have a thin endometrium. These women were excluded from the analysis. Finally, 797 women were analyzed.

The participants' median age was 38.5 years (10%/90% quantiles: 27.3/48.1 years old). Table 1 shows the geographic data and baseline characteristics of the women. In the 797 women from whom information about their menstrual cycle could be obtained, the results were as follows: 562 (70.5%) women had normal menstruation, 145 (18.2%) women had irregular menstruation, 19 (2.4%) women had polymenorrhea, 18 (2.3%) women had oligomenorrhea, and 43 (5.4%) women had amenorrhea. The menstrual cycle was normal in $\sim 74.3\%$ (104/140) and 80.0% (245/306) of the women aged under 30 years and aged 30–40 years, respectively, while 63.5% (223/351) of the women aged over 40 years had a normal menstrual cycle. Among the 572 women with a normal menstrual cycle, the median length of the menstrual cycle was 28 days (10%/90% quantiles: 28/30 days) and 372 (65%) of these women answered that their cycle length was 28–30 days.

TABLE 1 Background of the participants

Factor	N
Area	
Rural	469
Urban	328
Age (years)	
< 40	433
≥ 40	364
Body mass index	
< 25	709
25–30	64
> 30	24
Abnormal genital bleeding	
Absent	687
Present	115
Risk factors ^a	
Absent	725
Present	72
Obstetric history	
Nulligravid	317
Parous	480
Menstrual cycle	
Normal	572
Irregular	145
Polymenorrhea	19
Oligomenorrhea	18
Amenorrhea	43

^aRisk factors: Hypertension (17); diabetes mellitus (3); hyperlipidemia (9); obesity (24); history of breast cancer (12); infertility (18).

3.2 | Endometrial thickness

Table 2 shows the menstrual status and ET. In all the women, the median ET was 8.6 (95% CI: 8.3–8.8) mm, with the 90% and 95% quantiles being 13.8 (95% CI: 13.3–14.3) and 15.8 (95% CI: 15.1–17.1) mm, respectively. The investigation of the relationship between the menstrual status and the ET revealed that the median ET was significantly thinner in the women with amenorrhea (5.1 [95% CI: 4.2–7.5] mm) than during the latter half of normal menstruation or in the women with an irregular menstrual cycle or polymenorrhea. In the women with normal menstruation, the median endometrium was significantly thicker during the second half of the menstrual cycle than during the first half. Table 3 displays the relationship between the ET and the participants' age, BMI, AGB, risk factors for endometrial cancer, obstetric history, and regional characteristics. When examined in all of the women, none of these factors showed a relationship with the ET.

TABLE 2 Endometrial thickness and the corresponding menstrual status

Variable	N	Quantile (95% confidence interval)				
		5% Quantile	10% Quantile	50% Quantile: Median	90% Quantile	95% Quantile
All participants	797	2.9 (2.5–3.2)	3.8 (3.5–4.1)	8.6 (8.3–8.8)	13.8 (13.3–14.3)	15.8 (15.1–17.1)
Second half of normal cycle	339	4.1 (3.3–4.8)	5.2 (4.7–6.1)	9.6 (9.3–10.2) ^a	14.2 (13.8–15.4)	16.5 (15.1–18.2)
Irregular cycle	145	2.4 (1.2–3.8)	4.1 (2.3–4.8)	8.9 (7.8–10.1) ^b	15.5 (14.5–19.8)	19.0 (15.7–24.6)
Polymenorrhea	19	3.8 (3.8–24.4)	4.4 (3.8–24.4)	8.8 (7.6–11.7)	14.9 (3.8–24.4)	24.4 (3.8–24.4)
Oligomenorrhea	18	1.7 (1.7–21.7)	2.4 (1.7–4.4)	7.8 (4.9–10.3)	12.4 (10.3–21.7)	21.7 (11.0–21.7)
First half of normal cycle	233	2.8 (2.4–3.1)	3.4 (3.0–3.8)	6.8 (5.9–7.6) ^{a,b}	11.8 (10.8–13.0)	13.2 (12.1–14.0)
Amenorrhea	43	1.4 (0.0–16.2)	2.1 (0.0–2.9)	5.1 (4.2–7.5) ^{a,b}	12.8 (9.4–16.2)	13.4 (0.0–16.2)

^aSecond half, compared to first half, amenorrhea ($P < .0001$).

^bIrregular cycle, compared to first half, amenorrhea ($P < .0001$).

TABLE 3 Clinical background and endometrial thickness

Item	Overall	First half	Second half	Irregular	Polymenorrhea	Oligomenorrhea	Amenorrhea
N	797	233	339	145	19	18	43
All participants (%)	8.6 (3.8/13.8)	6.8 (3.4/11.8)	9.6 (5.2/14.2)	8.9 (4.1/15.5)	8.8 (4.4/14.9)	7.8 (2.4/12.4)	5.1 (2.1/12.8)
Age (years) (%)							
<40	8.5 (3.7/13.4)	6.5 (3.3/10.8)	9.7 (6.2/14.1)	9.8 (4.4/15.2)	9.1 (6.8/11.99)	9.7 (4.4/12.4)	4.4 (1.8/8.4)
>40	8.3 (3.1/13.9)	7.4 (3.5/13.0)	9.6 (4.6/15.1)	8.6 (3.0/16.4)	8.7 (3.9/23.3)	5.7 (1.8/20.6)	5.3 (2.2/12.9)
Body Mass Index (%)							
<25	8.4 (3.6/13.7)	6.8 (3.4/11.8)	9.6 (5.1/14.1)	8.9 (4.6/15.2)	8.8 (4.4/14.9)	8.2 (3.2/13.3)	5.1 (2.2/13.0)
25–30	8.4 (2.8/14.1)	7.0 (2.5/9.7)	10.3 (6.1/14.9)	7.0 (1.8/13.6)	–	2.4 (2.4/2.4)	3.9 (0.0/6.9)
≥30	9.4 (3.0/18.6)	8.3 (4.8/11.7)	9.9 (1.1/13.0)	12.8 (1.2/25.8)	–	–	6.3 (6.0/8.4)
Metrorrhagia (%)							
Present	8.8 (3.8/16)	9.0 (3.1/11.0)	9.5 (3.9/15.6)	8.8 (3.2/20.6)	8.8 (7.5/11.9)	6.9 (4.4/21.7)	5.6 (3.1/13.5)
Absent	8.4 (3.5/13.6)	6.6 (3.5/11.9)	9.6 (5.4/14.1)	9.1 (4.4/14.9)	9.1 (4.2/18.0)	7.8 (2.1/11.6)	5.0 (1.9/10.3)
Risk factors (%)							
Present	7.5 (2.7/13.1)	7.4 (3.8/11.9)	8.3 (4.6/12.9)	7.3 (1.6/21.2)	8.8 (4.4/15.9)	4.1 (2.4/4.4)	6.0 (1.3/13.0)
Absent	8.5 (3.6/13.8)	6.7 (3.4/11.8)	9.6 (5.4/14.3)	9.0 (4.6/15.5)	8.8 (8.8/8.8)	9.2 (2.9/15.2)	4.7 (2.1/12.6)
Obstetric history (%)							
Nulligravid	8.5 (3.8/13.8)	6.0 (3.1/11.0)	9.5 (4.9/14.0)	8.8 (3.8/15.3)	11.1 (3.8/24.4)	10.3 (4.1/12.4)	8.4 (3.2/15.1)
Parous	8.3 (3.3/13.8)	7.5 (3.6/12.6)	9.7 (5.8/14.9)	9.0 (4.0/15.9)	8.7 (4.8/11.5)	6.5 (1.8/19.4)	4.9 (1.8/9.3)
Area (%)							
Urban	8.4 (3.7/13.8)	7.1 (3.2/10.9)	10.3 (5.1/14.3)	7.9 (3.7/15.9)	8.6 (3.8/13.2)	8.8 (4.5/12.2)	5.0 (1.7/11.6)
Rural	8.4 (3.4/13.8)	6.7 (3.5/13.0)	9.6 (5.2/14.2)	9.5 (4.4/15.4)	8.8 (7.1/20.2)	5.2 (1.7/21.7)	5.6 (2.1/13.4)

Median (10%/90% quantile). First half, first half of a normal cycle; irregular, irregular cycle; second half, second half of a normal cycle.

3.3 | Phase of the menstrual cycle at measurement and endometrial thickness

Sixty-six percent of the women had normal menstruation, with a menstrual cycle length of 28–30 days. The relationship between the phase

of the menstrual cycle and the ET was investigated in 375 of these women, in whom the timing of the menstrual cycle at the measurement of the ET was known (Table 4). The length of the menstrual cycle was self-reported by each woman. If a range was reported, the median length was rounded down to the nearest integer. For example, if a

Menstrual cycle (day)	N	Quantile (95% confidence interval)		
		50% Quantile	10% Quantile	90% Quantile
1-6	13	7.0 (2.2-8.6) [†]	1.6 (1.3-14.9)	13.3 (1.3-14.9)
7,8	30	5.4 (4.5-7.5) ^{**}	3.1 (2.4-4.1)	10.8 (7.9-17.6)
9,10	30	5.4 (4.8-6.8) ^{***}	3.1 (2.6-3.9)	10.0 (8.8-11.7)
11,12	39	6.8 (5.7-8.4) ^{****}	3.1 (2.5-5.0)	12.6 (9.2-17.6)
13,14	40	9.2 (7.6-10.6)	4.7 (2.8-5.7)	13.3 (11.8-14.0)
15,16	40	8.5 (8.0-9.6)	5.1 (2.0-6.0)	13.0 (11.4-19.9)
17,18	33	11.1 (9.0-12.3) ^{**,***}	6.5 (4.6-7.5)	17.4 (13.6-20.3)
19,20	24	10.1 (8.6-11.8)	4.5 (1.6-33.8)	15.2 (1.6-33.8)
21,22	52	11.1 (9.7-11.9) ^{*,**,***,****}	7.5 (4.5-8.7)	16.0 (13.9-79.0)
23,24	27	11.0 (9.0-12.8)	3.9 (1.7-17.8)	14.4 (1.7-17.8)
25,26	25	9.2 (7.4-12.2)	3.6 (3.4-25.4)	15.0 (3.4-25.4)
27-30	22	9.4 (7.9-13.7)	5.9 (4.8-17.3)	14.4 (4.8-17.3)

* $P = .00075$, ** $P = .00075$, *** $P = .00075$, and **** $P < .00075$.

woman reported that the menstrual cycle ranged from 28 to 30 days, it was set at 29 days for this study. When the geographic data and baseline characteristics of these 375 women were assessed, the median age was 38.0 years (10%/90% quantiles: 27.8/46.2 years old), 45 (12%) women had AGB, 162 (43.2%) women were nulliparous, and the median BMI was 20.3 (10%/90% quantiles: 17.8/24.4). The ET was 7.0 (10%/90% quantiles: 1.6/13.3) mm on days 1-6 of the menstrual cycle (probably during menstruation), while it was 5.4 (10%/90% quantiles: 3.1/10.8) mm immediately after menstruation (day 7 or 8), and 9.2 (10%/90% quantiles: 4.7/13.3) mm around the ovulatory phase (days 13-14). On days 17-18, the endometrium was significantly thicker than on days 7-8 or 9-10 ($P < .00075$). On days 21-22, the ET was significantly thicker than on days 1-6, 7-8, 9-10, and 11-12 ($P < .00075$). Subsequently, the ET increased to 11.1 (10%/90% quantiles: 6.5/17.4) mm on days 17-18, but it was still thinner than immediately before the start of menstruation (days 25-30).

4 | DISCUSSION

In the present study, the ET was measured in 849 premenopausal women who attended office gynecology for cervical cancer screening. The number of women who attended office gynecology for cervical cancer screening was thought to be similar to the general premenopausal female population. One study reported that the ET increased rapidly during the follicular phase and then showed little change from the ovulatory phase through to the luteal phase.⁵ According to several reports, the peak of the ET is 10-12 mm.^{3,5-7} In the present study, the ET increased until day 18 of the menstrual cycle and the peak of the ET was 9.6 mm in 375 women with a menstrual cycle of 28-30 days. The peak of the ET might differ between office gynecology and large medical centers. However, the results of the present and previous studies cannot be compared directly because of differences in the study design; that is, the ET was measured once per woman in a large group of women in the present study, while the relationship between

TABLE 4 Relationship between the menstrual cycle and endometrial thickness

the ET and follicular diameter was investigated continuously per woman at various times during the menstrual cycle in 23-50 healthy volunteers in previous reports. When the change in the ET during the menstrual cycle is discussed, the ET should be measured several times per woman, as in previous reports. However, these reports included only 23-50 cases, which is not a sufficient number to determine the median ET during the menstrual cycle. In this study, 375 cases were included.

In all the women, the median ET was 8.6 mm, with the 90% and 95% quantiles being 13.8 and 15.8 mm, respectively. The median ET might not be valuable theoretically without considering the menstrual cycle. However, in clinical practice, the information of the date of last menstruation or the menstrual status is sometimes defective. The authors concluded that determining the upper limit of the ET in premenopausal women is useful in the clinical practice of office gynecology. In fact, in some reports that evaluated the efficacy of TVS for endometrial diseases in premenopausal women, the cut-off value of the ET was determined without considering the menstrual cycle.¹⁰⁻¹³ The incidence of endometrial hyperplasia has been reported to be high in women with polycystic ovary syndrome or anovulation and it also has been reported that obesity and hypertension show a positive correlation with the ET. However, the participants' ET was not related to their age, BMI, AGB, risk factors for endometrial cancer, obstetric history, or regional characteristics when assessed in all the women in the present study.

Several reports have been published concerning the efficacy of TVS for endometrial cancer or hyperplasia in premenopausal women.¹⁰⁻¹³ One study performed TVS and dilatation and curettage (D&C) in 111 premenopausal women with AGB and reported that the median ET was 10.5 mm for all the women, while the recommended cut-off value was 8.0 mm, the sensitivity was 83.9%, and the specificity was 58.8%.¹⁰ In addition, another study performed TVS and endometrial cytology in 144 women with AGB and reported that the median ET was 9.4 mm for all the women and that the recommended cut-off value was 8.0 mm, the sensitivity was 83.6%, and the specificity was 56.4%.¹¹ Furthermore, one report analyzed 196 women who

underwent a scheduled D&C and reported that the median ET was 9.1 mm for the women in the proliferative phase and 10.8 mm for the women in the secretory phase, while the recommended cut-off value was 10.0 mm, the sensitivity was 44%, and the specificity was 56%.¹² Another report examined 367 women and reported that the median ET was 12.2 mm in the women with AGB, compared to 9.4 mm in the women without symptoms. In addition, endometrial cancer was detected in four women with an ET of ≥ 20 mm and in a woman with an ET of 17.3 mm.¹³ However, the women in these studies were patients who had been diagnosed at large medical centers and the controls were not necessarily the general population. In this study, the women who attended office gynecology for cervical cancer screening (municipal cervical cancer screening or cervical cancer screening in a medical check-up) and who were enrolled in the study were thought to be similar to the general premenopausal female population. According to the results of the present study, the median ET was 8.6/8.8/8.4 mm in all the women/women with AGB/women without AGB. The median ET might differ between office gynecology and large medical center patients. Further examination will be required to solve this issue.

In all the women/first half of a normal cycle/second half of a normal cycle, the upper limit of the ET was 13.8/11.8/14.2 mm and 15.8/13.2/16.5 mm with 90% and 95% quantiles, respectively, in office gynecology. Careful follow-up might be needed for the women above the upper limit of the ET. Further study will be required to determine the cut-off value of the ET for the screening of endometrial diseases in premenopausal women in office gynecology.

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DISCLOSURES

Conflict of interest: The authors declare no conflict of interest. **Human and Animal Rights:** All the procedures that were followed were in accordance with the ethical standards of the responsible committee and with the Helsinki Declaration. Informed consent was obtained from all the patients. The study received Hokkaido Cancer Center Institutional Review Board approval (26-12, 2014 September). This article does not contain any study with animal participants that has been performed by any of the authors.

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