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Uterine peristalsis and junctional zone: correlation with age and postmenopausal status

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Abstract

Background: Although age-related change of junctional zone (JZ) of the uterus has been known, there has been no previous systematic study of age-related changes of uterine peristalsis that is observed as the wave conduction of the thickest or darkest area within the JZ.

Purpose: To examine the age-related changes of uterine peristalsis in pre and postmenopausal women using cine magnetic resonance imaging (MRI), and to determine the correlation between peristalsis and JZ on T2-weighted (T2W) imaging.

Material and Methods: Cine MRI analysis was performed in 64 premenopausal volunteers and in 43 postmenopausal women. The peristaltic frequency, JZ detectability, and JZ thickness were evaluated and compared between the two groups. In the premenopausal group, the correlations between age and each item was examined. In the postmenopausal group, the number of years after menopause was used instead of age. The correlation between peristaltic frequency and JZ detectability or thickness was also analyzed.

Results: Peristaltic frequency and JZ detectability significantly differed between the two groups, while JZ thickness did not. Peristaltic frequency did not vary significantly with age before menopause and no peristalsis was observed after menopause. JZ detectability did not change significantly with age or number of years after menopause, while JZ thickness significantly increased with age before menopause, but did not vary after menopause. A significant moderate correlation was observed between JZ detectability and peristaltic frequency, but not between JZ thickness and peristaltic frequency.

Conclusion: Uterine peristalsis frequency did not change significantly according to age, but observed peristalsis on MRI significantly decreased after menopause.

Keywords

Uterine peristalsis, cine magnetic resonance imaging (MRI), menopause, age-related change, junctional zone

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Introduction

The uterus undergoes dynamic morphological changes under the influence of hormonal stimuli, especially those secreted by the ovaries such as estrogen and progesterone. Morphologically, T2-weighted (T2W) images of magnetic resonance imaging (MRI) depict the uterus as three distinct layers of high intensity (endometrium), low intensity (junctional zone [JZ]), and medium intensity (outer myometrium) (1). Histological analysis has revealed that the JZ corresponds to the most inner layer of the myometrium (1,2). Morphometric studies have also revealed that the myocytes present at the JZ are characterized by a three-fold increase in nuclear area per unit area, by a decreased extracellular matrix per unit volume, and by a lower water content when compared with the myocytes of the outer myometrium (2,3). It is important

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to highlight, however, that histological distinction between the JZ and the outer myometrium is not clearly visualized macroscopically. The JZ undergoes morphological changes depending on hormonal status or age (4,5). In relation to age, the JZ is often indistinct in either premenarchal girls or postmenopausal women. It is also known that its thickness increases until the age of 41–50 years, and then decreases (6,7).

Much faster change of JZ morphology or thickness is observed as uterine peristalsis (8). It is observed as wave conduction of the thickest or darkest area in the longitudinal axis within the JZ accompanied or not by endometrial stripping movements on cine MRI (8). Sonographically, the peristalsis is recognized as a stripping movement of the endometrium caused by subtle, wave-like contractions of the subendometrial myometrium (9). Peristalsis also receive hormonal influence of estradiol released by the dominant follicle and changes its orientation, amplitude, and frequency in direct relationship with the phase of the menstrual cycle (10,11). In regard to age-related changes, only one previous report was found documenting the ultrasound examination of three postmenopausal women (9). Therefore, to the best our knowledge, there has been no previous systematic study on the effect of menopause or age-related changes of uterine peristalsis.

The purpose of our study was thus to examine the age-related changes of uterine peristalsis in premenopausal and postmenopausal women using MRI, and to correlate the kinematic findings with JZ thickness and detectability using conventional static T2W imaging.

Material and Methods

Study population

The protocol used in this prospective study was approved by the ethics committee of our institution. Written informed consent was obtained from all participants prior to MR examinations. From April 2012 to May 2014, a cohort of 43 healthy postmenopausal volunteers (age range, 50–77 years; mean age, 61.7 years) and 64 premenopausal volunteers (age range, 20–51 years; mean age, 33.0 years) with regular menstrual cycles were involved in the study. Postmenopausal women were defined as those with a period of amenorrhea of 1 year or more (12).

The exclusion criteria were defined as individuals with myometrial pathology such as fibroids or adenomyosis, individuals under hormone replacement therapy, and individuals with intrauterine devices. All of those factors have documented effect on uterine peristalsis (11,13–15). Participants having Nabothian cysts or ovarian tumors were included, as these pathologies were considered unlikely to affect uterine peristalsis.

MR scanning protocol

In the premenopausal group, MR scans were performed between the proliferative and the ovulatory phase. It has been reported that peristalsis was observed less frequently in the luteal phase, we thus estimated that the luteal phase was not suitable for the examination of peristalsis (10). The date of ovulation was defined as 14 days prior to the anticipated day one of the subsequent cycle. The mean menstrual cycle duration was 29.0 days and the averaged cycle date was 11.7. All volunteers were asked to make note of the beginning of the subsequent menstrual cycle to allow confirmation of the menstrual cycle phase.

MR studies were performed using a 3 T magnet unit (Toshiba Medical Systems, Otawara, Japan) with a phased-array coil. In addition to a routine protocol on the pelvic area, which included an axial fast spin echo T2W image, a sagittal T1-weighted (T1W) image, and a T2W image of the uterus, 60 serial images were obtained from each patient in Fast Advanced Spin Echo (FASE) acquisition (TR, 5756 ms; TE, 80 ms; field of view, 26×27.5 cm; slice thickness, 6 mm; matrix, 256×288; flip angle (FA), 90°; resolution, 1.0×1.0 mm): one image every 3 s over 3 min in the midsagittal plane of the uterus. The sequence of FASE is equivalent to that of HASTE. The entire MR examination was performed within 45 min in all volunteers. No premedication, including anticholinergic drugs or muscle relaxants, was given to any participant prior to MR scanning.

Image analysis

JZ detectability, JZ thickness, and the peristaltic frequency were evaluated. JZ detectability and JZ thickness were evaluated on conventional T2W imaging, and the peristaltic frequency was measured on the 60 serial images by FASE displayed as cine image.

The JZ detectability and peristalsis frequency were independently evaluated by two radiologists with 18 (reader A) and 7 years (reader B) of experience in gynecological MRI. JZ thickness was measured by reader B.

1. JZ detectability was evaluated on a five-point scale as follows: 1, Definitely not identifiable JZ; 2, Probably not identifiable JZ; 3, Undetermined presence of JZ; 4, JZ is slightly identifiable; 5, JZ is clearly identifiable.
2. JZ thickness was measured only in cases where the JZ was detectable, i.e. detectability scores of 4 or 5 by both readers. The thickness of the JZ was calculated as the average between the thickness values of the JZ of the anterior and the posterior walls at the longitudinal midpoint of the uterine corpus (Fig. 1).

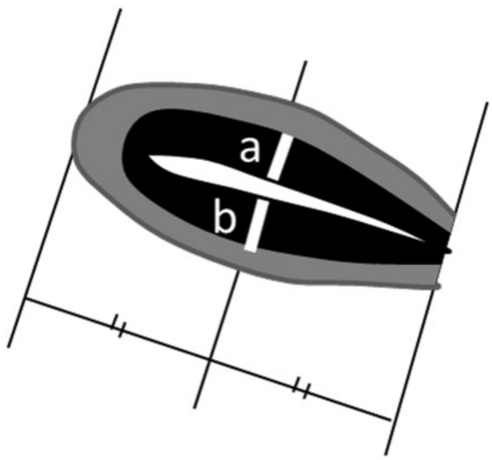

Fig. 1. The way of measuring the JZs. The thickness of the JZ was calculated as the average between the thickness values of the JZ of the anterior wall and that of the posterior wall at the longitudinal midpoint of the uterine corpus.

When the JZ was identified and measurable only at either the anterior or the posterior wall, the JZ thickness of the measurable wall was regarded as the representative JZ thickness value.

3. In relation to the uterine peristalsis, peristaltic frequency was measured as the number of movements occurring every 3 min (number of times per 3 min). The direction of peristalsis was not evaluated in this study. In a previous report, peristalsis was defined as follows: (i) conduction of the thickest or darkest areas of the JZ associated with endometrial stripping movements; (ii) conduction of the thickest or darkest areas of the JZ without endometrial stripping movements; and (iii) endometrial stripping movement alone (8). However, we believe that, in some cases, the intensity of the inner myometrium might not be lower than the outer myometrium. In such cases, it might not be appropriate to use the designation JZ. Therefore, we defined peristalsis as the wave conduction of the thickest or darkest area in the longitudinal axis within "the inner myometrium" accompanied or not by endometrial stripping movement. The third pattern of peristalsis, i.e. the endometrial stripping movement alone pattern, is uncountable because this pattern of peristalsis is not associated with any identifiable direction. Therefore, the number of peristalsis was not counted in cases presenting endometrial stripping movement only (8). These cases were excluded from the calculation of mean peristalsis frequency. Cases without observable peristalsis were assigned a frequency of zero, and included in the calculation of peristaltic frequency.

Statistical analysis

The normality of the JZ thickness data was verified by the Kolmogorov–Smirnov test. As such, the JZ thickness values in the premenopausal and postmenopausal groups were compared with unpaired Student's t-test. The normality of the peristaltic frequency data was rejected. Therefore, comparison of peristaltic frequency and JZ detectability, between the premenopausal and postmenopausal groups, was performed using the non-parametric Mann–Whitney U test.

The age-related changes of the three parameters, JZ thickness, JZ detectability, and peristaltic frequency, were also analyzed. In the premenopausal group, the correlation between age and JZ thickness was analyzed using Pearson's correlation test. The correlation between age and JZ detectability as well as between age and peristaltic frequency were assessed using the Spearman's rank correlation test. In the postmenopausal group, the same analyses were performed using the number of years after menopause instead of the age.

The correlation between peristaltic frequency and JZ detectability, as well as the correlation between peristaltic frequency and JZ thickness, were analyzed using Spearman's correlation test. Those analyses were performed separately in the premenopausal group or in the postmenopausal group.

A P value of less than 0.05 was considered statistically significant.

Concordance of the two readers' results was measured by the weighted kappa coefficient: a kappa value less than 0.00 signified poor agreement; 0.00–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60; moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, almost perfect agreement (16).

Results

Of the 64 premenopausal participants enrolled in the study, 14 were excluded due to the presence of fibroids (n = 13) and adenomyosis (n = 1). As a result, 50 premenopausal women with normal uterine appearance (age range, 20–48 years; mean age, 31.0 years) were included in the study. Of the 43 postmenopausal participants, 15 were excluded because the midsagittal plane of the uterus could not be successfully determined due to too thin endometria (n = 5) and because of the presence of fibroids (n = 10). Thus, 28 postmenopausal women with a normal uterus appearance (age range, 51–77 years; mean age, 62.6 years) were included in the study. The age distribution of the participants included in the study is shown in Table 1.

The averaged frequency of peristalsis was 4.5 per 3 min (as assessed by reader A), and 4.6 per 3 min (as assessed by reader B) in the premenopausal group. In the postmenopausal group, no peristalsis was observed by either reader (Fig. 2). A significant difference was determined in the peristalsis frequency between the premenopausal and the postmenopausal groups by both readers ($P < 0.0001$ for both readers A and B). In the premenopausal group, there was no significant correlation between age and peristaltic frequency ($r = 0.118$, $P = 0.44$ for reader A vs. $r = 0.27$, $P = 0.06$ for reader B) (Fig. 2). The Kappa value was 0.70, thus indicating a substantial inter-observer agreement.

As for the JZ detectability, the average score in the premenopausal group was 4.4 (reader A) and 4.4 (reader B), while that of postmenopausal group was 1.5 (reader A) and 2.1 (reader B) (Figs. 3 and 4). In the premenopausal group, JZ was detected, which means a score of 4 or 5 was assigned, in 44/50 women by reader A and 42/50 by reader B. In the postmenopausal group, the JZ was detected in 3/28 participants by reader A and in 5/28 participants by reader B. A significant difference was observed in the JZ detectability between premenopausal and postmenopausal women by both readers ($P < 0.0001$). No significant correlation was observed between JZ detectability and age in the premenopausal group by either reader ($r = 0.12$, $P = 0.41$ reader A, $r = 0.16$, $P = 0.27$ reader B). In the postmenopausal group, no significant correlation was observed between JZ detectability and number of years after menopause ($r = -0.201$, $P = 0.32$ reader A; $r = -0.15$, $P = 0.45$ reader B). The Kappa value was 0.85, thus indicating a near-perfect inter-observer agreement.

The JZ thickness of either the anterior or the posterior wall was measured in 40/50 women in the

Table 1. Age distribution of the participants included in the study.

Age (years)	20–29	30–39	40–49	50–59	60–69	70–77
Premenopausal*	28	12	10	0	0	0
Postmenopausal*	0	0	0	12	10	6

*Number of participants per age group.

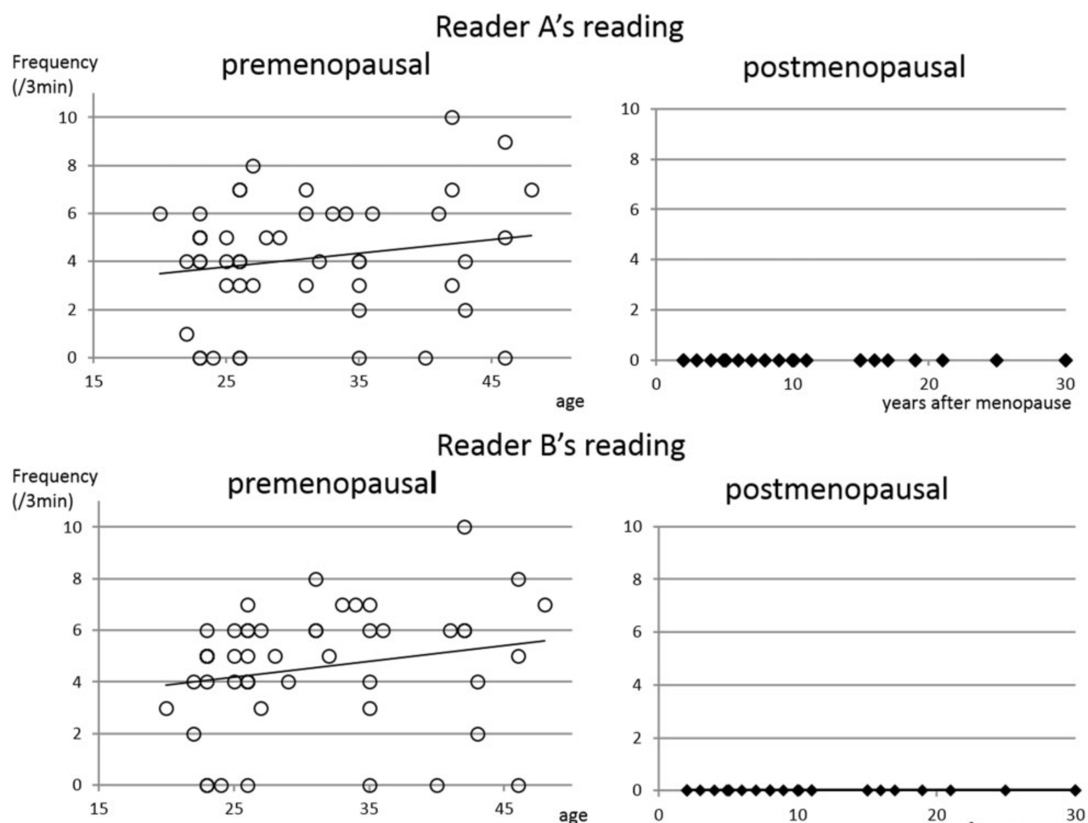

Fig. 2. The correlation between peristalsis frequency and age (or years after menopause). The average frequency of peristalsis (times per 3 min) was 4.5 (reader A) and 4.6 (reader B) in the premenopausal group. In the postmenopausal group, no peristalsis was observed by either reader. A significant difference was observed in the peristaltic frequency between the premenopausal and postmenopausal groups by both readers ($p < 0.0001$ for both readers A and B). There was no significant correlation between age and peristaltic frequency in the premenopausal group.

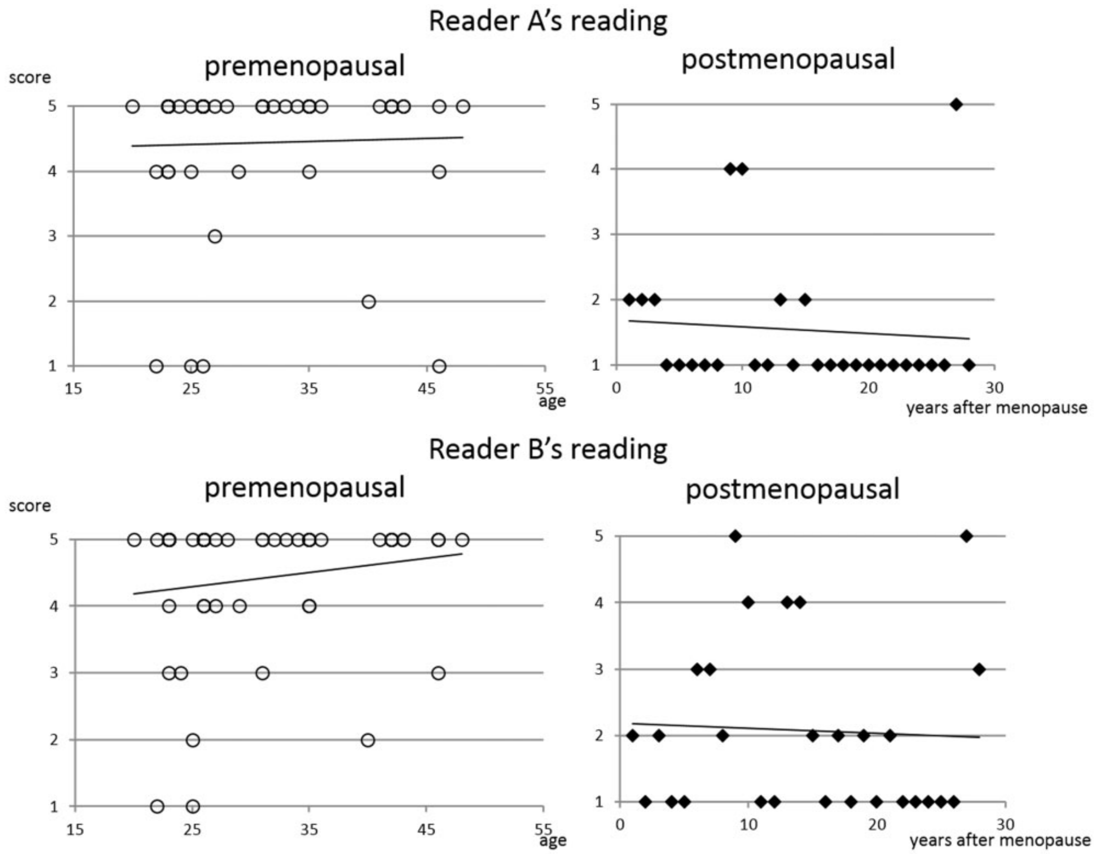

Fig. 3. The correlation between JZ detectability and age. The average score in the premenopausal group was 4.4 (reader A) and 4.4 (reader B), and that of the postmenopausal group was 1.5 (reader A) and 2.1 (reader B). A significant difference was observed in the detectability of the JZ between premenopausal and postmenopausal women by both readers ($P < 0.0001$). No significant correlation was observed between JZ detectability and age or number of years after menopause in either group.

premenopausal group and 3/28 women in the postmenopausal group. The average JZ thickness was equal to 0.45 ± 0.17 cm in the premenopausal group and 0.36 ± 0.03 cm in the postmenopausal group. No significant difference was observed between the premenopausal and the postmenopausal groups ($P = 0.39$). The JZ thickness significantly increased with age in the premenopausal group ($r = 0.36$, $P = 0.02$), while a correlation between the JZ thickness and the number of years after menopause, in the postmenopausal group, was not significant ($r = 0.40$, $P = 0.74$) (Fig. 5).

In the premenopausal group, a correlation between JZ detectability and peristalsis frequency was observed by both readers ($r = 0.33$, $P = 0.03$ reader A; $r = 0.41$, $P = 0.004$ reader B) (Fig. 6). On the other hand, no correlation was observed between JZ thickness and peristalsis frequency in the premenopausal group ($r = -0.02$, $P = 0.88$ reader A; $r = -0.02$, $P = 0.92$ reader B) (Fig. 7).

Since no peristalsis was observed in the postmenopausal group, the correlation between peristalsis and JZ detectability or thickness was not tested in this group.

Discussion

Our results show that there was no significant correlation between age and peristaltic frequency in premenopausal participants, and that no peristalsis was observed in any of the postmenopausal women. It is currently believed that uterine peristalsis is controlled by estradiol released by the dominant follicle (11). Since estradiol levels remain unchanged during the reproductive age period but significantly decrease after menopause, our result agrees with these hormonal changes (17). As for peristalsis during a postmenopausal state, only three cases, as evaluated by transvaginal ultrasound (TVUS), have been reported (9). In two of the three cases, no contraction was observed, while the third case showed a retrograde movement. One possible reason for the discrepancy between their results and ours could be the difference of modality, but further study would be required.

The JZ thickness increased with age in the premenopausal status in our study. Hauth et al. showed that the JZ thickness significantly increased until 41–50

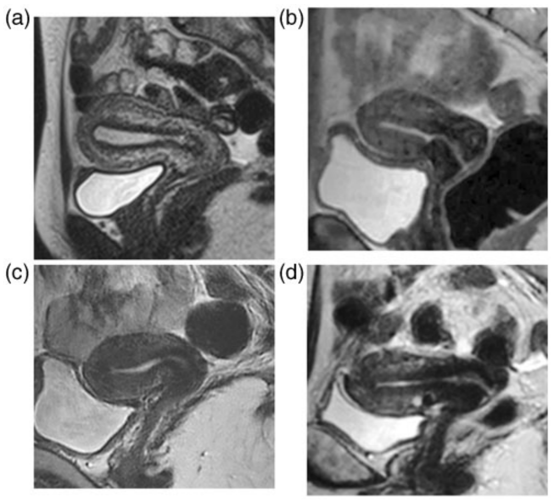

Fig. 4. Examples of premenopausal and postmenopausal uteri. (a) Representative image of the uterus of a premenopausal participant on T2W imaging. The case of a 31-year-old premenopausal woman in her proliferative phase (day 12 of a 28-day menstrual cycle). The three layers of the uterus are clearly distinguishable. (b) Representative image of the uterus of a postmenopausal participant on T2W imaging. A 59-year-old postmenopausal woman, 7 years after menopause. The JZ is indistinct. (c) A 22-year-old premenopausal woman in her proliferative phase (day 9 of a 30-day menstrual cycle). The JZ is indistinct. (d) A 54-year-old postmenopausal woman, 3 years after menopause. The subendometrial myometrium shows a lower signal intensity compared to the outer myometrium.

years of age (7). Although the authors did not separate the participants into premenopausal or postmenopausal, the average age of menopause is known to be around the 50 s (12). Therefore, our results of a significant increase in the JZ thickness in function of age in premenopausal participants, is in line with their results. On the other hand, our results in the postmenopausal women are in contradiction with their observations that JZ thickness decreased after the age of 50 years. One of the reasons behind this discrepancy might be differences in the criteria of defining JZ because the rate of participants with measurable JZ in the study of Hauth et al. was much larger than ours (18). Our results were, however, similar to those reported by Brown et al. suggesting that the JZ thickness was maintained after menopause (19).

Our results further showed that peristaltic frequency was significantly correlated with JZ detectability in the premenopausal group. Peristalsis, a contraction of the inner myometrium, is recognized as a low signal intensity area on cine MRI (8). The underlying mechanism could be the same as sustained uterine contraction (20). That is, a transient decrease in blood volume in an area of contraction of the myometrium results in a decrease in water content, and thus accounts for a lower intensity (20). Images on conventional T2W imaging could be a summary image during the acquisition time on cine MR (21). Therefore, when peristalsis is observed more frequently, the signal intensity of the inner myometrium would be lower, which could result in darker and more distinguishable JZ on conventional

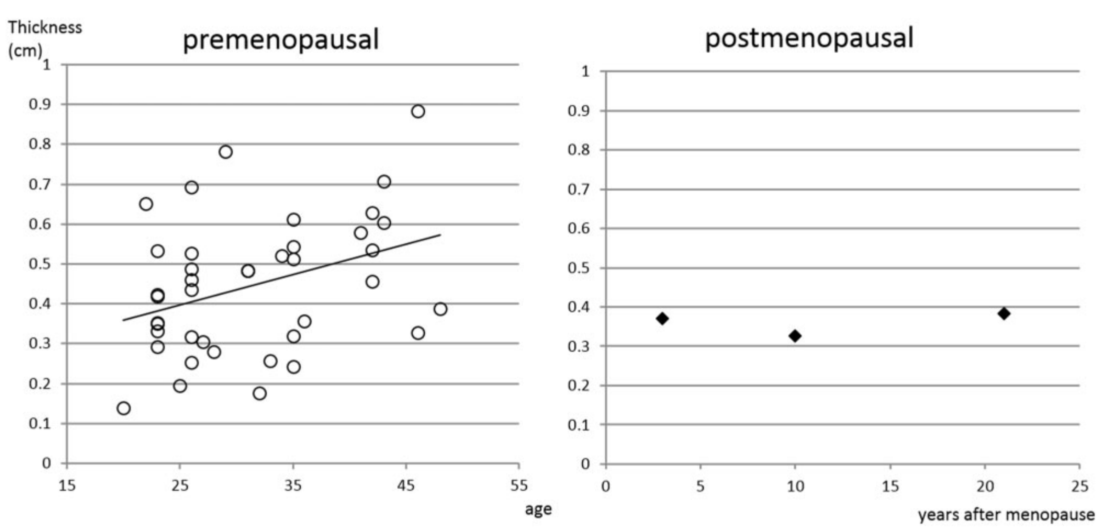

Fig. 5. The correlation between JZ thickness and age or the years after menopause. The mean JZ thickness was 0.45 ± 0.17 cm in the premenopausal group and 0.36 ± 0.03 cm in the postmenopausal group. No significant difference was observed between the premenopausal and postmenopausal groups ($P = 0.39$). JZ thickness significantly increased with age in the premenopausal group ($r = 0.36$, $P = 0.02$), while the correlation between the JZ thickness and the number of years after menopause was not significant ($r = 0.40$, $P = 0.74$).

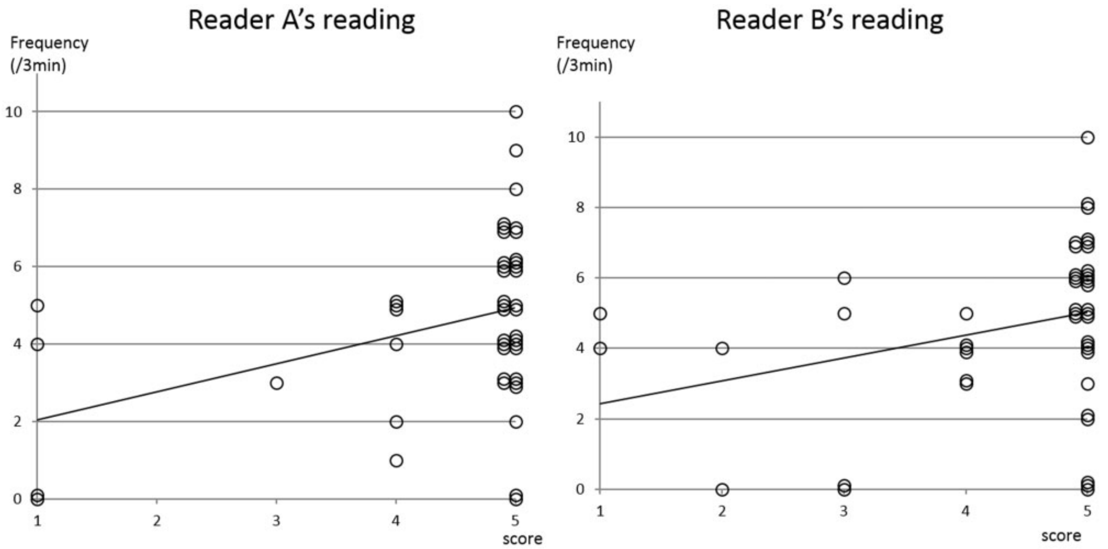

Fig. 6. The correlation between peristalsis frequency and JZ detectability. In the premenopausal group, a positive correlation was observed between JZ detectability and peristalsis frequency for both readers (r = 0.33, *P* = 0.03 for reader A and r = 0.41, *P* = 0.004 for reader B).

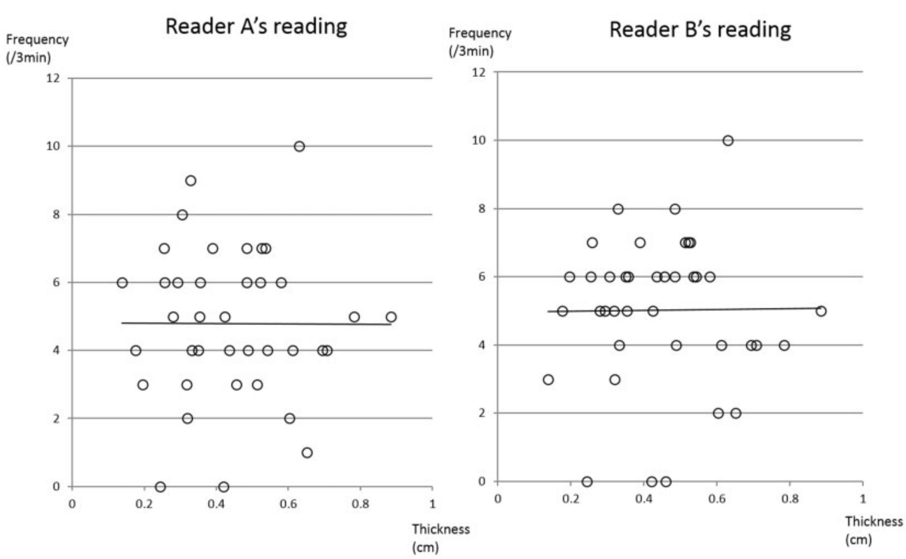

Fig. 7. The correlation with peristalsis frequency and JZ thickness. No correlation was observed between JZ thickness and peristalsis frequency in premenopausal participants (r = −0.02, *P* = 0.88 for reader A and r = −0.02, *P* = 0.92 for reader B).

T2W imaging. In addition to previously found histological reasons of low intensity of JZ (a three-fold increase in nuclear area per unit area, a decreased extracellular matrix per unit volume, and a lower water content compared with the myocytes of the outer myometrium), there might be a functional reason of low intensity of JZ: a myometrium contraction. However, the degree for peristalsis of contributing to low intensity of JZ on T2W imaging might not be considerable, for there were some cases with clearly identifiable JZ but no observable peristalsis.

This study has several limitations. First, ovarian hormone serum levels were not measured in this study and thus, there is a possibility of displacement in the menstrual cycle phase. Nonetheless, we have recorded the beginning of the subsequent menstrual cycle, thus allowing confirmation of the menstrual phase cycle. Second, the number of participants involved in the study was small, and in particular, the number of participants with a measurable JZ thickness was only of three in the postmenopausal group. Therefore, there could be peristalsis, which is existing but non-detectable on

MRI in this group. Further studies including TVUS as well as MRI with a larger number of participants will be required to establish more definitive conclusions. Third, our method of exclusion based on the underlying pelvic pathology may be questioned, as none of the participants underwent any physical examination. Indeed, despite normal MRI, subtle endometriosis cannot be totally ruled out.

In conclusion, this study demonstrates that uterine peristalsis frequency did not significantly change with age, but significantly decreased after menopause. The results are in line with previous reports that uterine peristalsis frequency is controlled by the release of estradiol by dominant follicles. The knowledge of the normal value of uterine peristalsis frequency will be the basis of identification of abnormal uterine peristalsis, which might be related to adenomyosis or infertility. Moreover, a significantly moderate correlation between peristalsis frequency and JZ detectability was observed, while no correlation was determined with JZ thickness.

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Declaration of conflicting interests

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