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Original Article

Sonoelastographic assessment of the normal uterus and ovaries using shear wave elastography according to different menstrual phases

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A B S T R A C T

Objective: In most of the gynecological studies conducted using the Shear Wave Elastography (SWE) method in the literature, the menstrual cycle period was not taken into account. Current study, we aimed to describe the sonoelastographic features of normal myometrium and ovaries in healthy women and to define their variability during the different phases of the menstrual cycle using the SWE method.

Material and methods: All cases were selected from individuals between the ages of 24-31, with regular menstrual cycles and no systemic disease. Each case was called in, 1-5th, 12-16th, 21-24th day of their menstrual cycles and was evaluated by B-mode imaging and SWE in pelvic ultrasonography. The relationship of menstrual phases with uterine and ovarian elasticity was investigated by comparing all measurements made in different menstrual phases.

Results: No statistically significant difference was observed between the volume of right and left ovaries in terms (p> 0.05). There was no statistically significant difference in terms of elastography measurements obtained from the uterus, right and left ovaries for each menstrual phase according to Bonferroni Correction (p> 0.0163).

Conclusion: Although there was a slight decrease in myometrial SWE measurements in the follicular phase, there was no significant difference regarding the SWE measurements of uterus and ovaries in early follicular, peri-ovulatory, and luteal menstrual stages. Further studies with a large number of participants are needed to suggest whether gynecological studies planned to be carried out with the shear wave elastography method should be planned in a specific menstrual phase.

Keywords: myometrium; share wave elastography; ovary; menstrual phases; uterus

Introduction

Ultrasonography is non-invasive imaging that plays an important role in evaluating patients with gynecological diseases [1]. The ultrasonographic Share Wave Elastography (SWE) method provides information about pathological formations by quantitatively measuring tissue flexibility, and has attracted increasing interest in recent years [2, 3]. Pathologies occurring in tissues may cause changes in the stiffness of tissues, many diseases can be detected by the elastography method, in which tissue flexibility is measured, apart from the pathologies that can be detected by palpation in physical examination. SWE is widely used in the diagnosis of thyroid, breast, kidney, liver and uterus, and ovary pathologies diseases in the literature [4-8]. As a result, SWE methods provides important advantages in determining the alterations in soft tissue stiffness resulting from physiological or pathological processes.

Two main types of ultrasound elastography techniques, SWE and strain elastography (SE), have been established in clinical practice. SWE technically provides quantitative information by measuring the acoustic radiation force coming into the tissue or the speed of the waves generated by the mechanical vibration device. SWE has lower operator requirements and higher accuracy compared to Strain Elastography [9].

Elastographic methods provide significant advantages in determining soft tissue stiffness changes caused by physiological or pathological processes.

Elasticity is defined as the ability to return to its original shape after applying deforming force or tension to an organ or tissue. In the early stages of the diseases, even if there are no abnormal findings in pathological and normal tissues by physical examination or conventional ultrasound, elastography may give us additional information by evaluating the tissue elasticity [10]. Nevertheless, most of the studies performed for uterine and ovarian pathologies that use the elastography method were designed disregarding the day of the menstrual cycle [4-6]. Differently, in a study investigating the viscoelasticity of the uterus and cervix using the high-resolution magnetic resonance elastography method in healthy volunteers, it was reported that, regarding the menstrual phases, myometrium stiffness was higher in the proliferative phase than in the secretory phase [11].

It is known that Progesterone (P4) secreted in the luteal period of the menstrual phase causes relaxation in smooth muscles. Progesterone has several effects on uterine smooth muscle.

Progesterone can increase uterine relaxation by non-genomic and genomic mechanisms . The non-genomic

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effects of acute progesterone exposure include inhibition of transmembrane Ca ++ entry and release of Ca ++ from intracellular stores [12].

Our study was designed with the hypothesis that the tissue elasticities of the uterus and ovaries may change between menstrual phases by the effects of progesterone causing myometrial relaxation. The uterine and ovarian flexibility in different menstrual phases (follicular, periovulatory, and luteal) was evaluated and the results were compared. Our hypothesis supported that, if a potentially significant relationship was found between the groups it would be necessary to consider this in the studies to be carried out. If no significant relationship was found, these results would contribute to the literature while designing the studies for gynecological diseases regardless of the day of the menstrual cycle.

To the best of our knowledge, this is the first study on SWE measurements evaluating uterus and ovaries in different menstrual phases in healthy women.

Material and methods

A total of 15 healthy women were enrolled in this cross-sectional study. The study was conducted between June 1st and 1 December 1st, 2020, in the radiology department of a tertiary hospital, Aydın Adnan Menderes University, Turkey. The study was approved by the Institutional Ethics Committee and written informed consent was obtained from all participants. All cases were selected from healthy women between the ages of 20-31 years with regular menstrual cycles without any gynecological pathologies or complaints. Those with any chronic systemic diseases were also excluded from the study. SWE measurements were made for each woman in the early follicular (1-5), periovulatory (12-16), and luteal (21-24) phases of the menstrual cycle.

The transabdominal approach was used to evaluate both ultrasonography and SWE measurements were calculated with a Samsung RS80 ultrasonography device using a 6 MHz convex probe by a radiologist. First, grayscale ultrasound was used to evaluate the myometrium (corpus) of the uterus and ovarian morphology. Then, SWE measurements were performed to assess ovarian stroma and uterine myometrium, with at least 10 consecutive measurements for each ovary and uterus (Figure 1).

Figure 1. Shear Wave Elastography measurements of ovarian stroma and uterine myometrium.
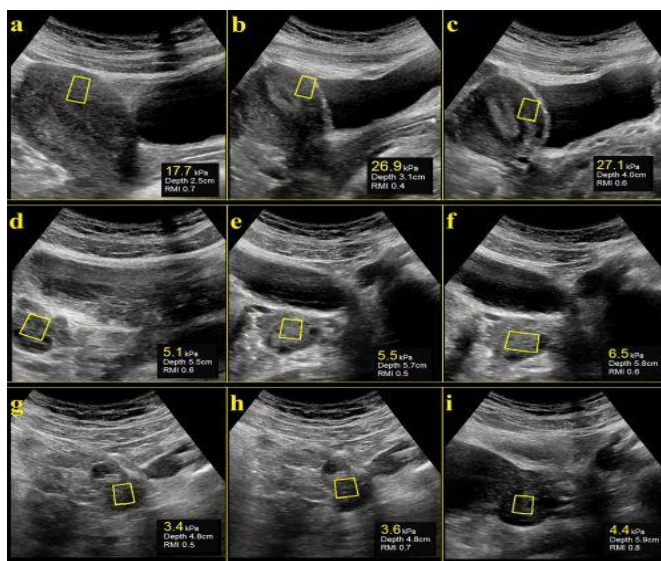
The quality factor (RMI), provided automatically by the device, between 0.4-1.0. Kilopascal (kPa), was used as the unit of SWE measurement, to improve the SWE measurement quality. The elasticity parameters (in kilopascals) of the normal myometrium, and ovaries were recorded. The effects of menstrual phases on uterine and ovarian elasticity were evaluated by comparing all measurements performed in different menstrual phases.

Statistical Analysis

Data analysis was performed using IBM SPSS Statistics version 17.0 software (IBM Corporation, Armonk, NY, USA). Whether the distributions of continuous variables were normally or not being determined Shapiro-Wilk test. Categorical data were expressed as numbers (n) and percentage (%) while quantitative data were given as mean ± SD and median (IQR: 1st quartile – 3rd quartile). While the differences in physiological elastography measurements between left and right side of ovarian were compared Wilcoxon Sign Rank test, otherwise Friedman test was applied for determining the differences among mensuration phases. Spearman's rank-order coefficient of correlation was calculated to examine degrees of association between continuous variables. $p < 0.05$ was considered statistically significant. However, for all possible multiple comparison, the Bonferroni Correction was applied for controlling Type I error.

Results

Descriptive statistics on the demographic and clinical characteristics of the participants included in the study are shown in Table 1.

Table 1. Demographic and clinical characteristics of the cases

	n=15
Age (years)	26.9±2.2
Age range (years)	24-31
Body weight (kg)	62.1±6.8
Length of height (m)	1.69±0.061
Body mass index (kg / m2)	21.6±1.97
Age of menarche (years)	13.3±1.7
Menarche age range (years)	11-17
A history of smoking	8 (53.3%)
A history of alcohol	8 (53.3%)

When ovarian volume and dimensions are examined, there were no statistically significant differences between the ovarian width, ovarian length, and ovarian volume of right and left sides ($p > 0.05$).

Table 2. Elastography measurements of uterus and ovaries according to menstruel phases

Ovary	Right (n=15, kPa)	Left (n=15, kPa)	p-value †
Early follicular	6.5 (5.2-8.2)	7.3 (6.4-8.7)	0.105
Periovulatory	6.0 (5.2-6.6)	6.7 (5.3-7.6)	0.155
Luteal	6.5 (5.5-8.5)	7.5 (5.7-11.4)	0.733
p-value ‡	0.356	0.247	
Uterus	Elastography measurements (kPa)		
Early follicular	17.6 (9.3-32.7)		
Periovulatory	22.0 (5.2-34.7)		
Luteal	20.2 (11.8-45.2)		
p-value †	0.321		

Descriptive statistics; It was expressed as the median (1st quarter - 3rd quarter), † Comparisons made between right and left side within each phase, According to the Wilcoxon Sign test, Bonferroni Correction, the results for p <0.0167 were considered statistically significant, ‡ The results for p <0.025 were considered statistically significant according to the comparisons between phases in the right and left ovaries, Friedman test, Bonferroni Correction.

Table 2 represents Elastography measurements of uterus and ovaries according to menstruel phases. There were no statistically significant differences in terms of elastography measurements obtained from the right and left sides in each menstrual phase according to the Bonferroni Correction (p> 0.0163).

Besides, although elastography measurements performed on both right and left ovaries showed some variation between phases, these changes were not statistically significant according to the Bonferroni Correction (p> 0.025). Similarly, there was no statistically significant difference between the menstrual phases in terms of elastography measurements made from the uterus (p = 0.321). According to Bonferroni Correction, no statistically significant correlation was detected between ovarian volume and the changes in elastography measurements and elastography measurements according to phases in each phase measured from the right and left ovaries (p> 0.0083).

Table 3 represents the correlation coefficients and significance levels between the age and body mass index, and the elastography measurements in each phase, and the changes of elastography measurements according to phases. No statistically significant correlation was found between the age and the elastography measurements performed on the right and left ovaries in each phase according to the Bonferroni Correction (p> 0.0083).

Table 3. Correlation coefficients and significance levels between age and body mass index and elastography measurements in each phase (n=15)

		Age		Body Mass Index	
		$r*$	p-value †	$r*$	p-value †
Elastography measurements	Right ovary				
	Early follicular	0.069	0.808	0.107	0.704
	Periovulatory	0.051	0.856	0.132	0.638
	Luteal	0.153	0.586	-0.086	0.761
	Left ovary				
	Early follicular	-0.051	0.856	0.358	0.190
	Periovulatory	0.212	0.449	0.341	0.213
	Luteal	0.155	0.581	0.082	0.771
Change in elastography measurements between phases	Right ovary				
	Periovulatory - Early follicular	-0.161	0.566	0.050	0.859
	Luteal - Early follicular	0.178	0.527	-0.096	0.732
	Luteal – Periovulatory	0.233	0.404	-0.198	0.478
	Left ovary				
	Periovulatory - Early follicular	0.414	0.125	0.093	0.742
	Luteal - Early follicular	0.055	0.846	-0.325	0.237
	Luteal – Periovulatory	-0.103	0.716	-0.270	0.331

*r: Correlation coefficient, † Results were considered statistically significant for p <0.0083 according to Spearman's correlation test, Bonferroni Correction

In addition, when the ovarian localization was kept constant, no statistically significant correlation was found between the changes of elastography measurements between menstrual phases and age according to the Bonferroni Correction (p> 0.0083).

Discussion

The current study aimed to evaluate if the elastography measurements have changed during menstrual phases due to hormonal changes, in order to contribute to future elastography studies in gynecology. In our study, although the myometrial elastography measurements were lowest in the early follicular phase, SWE measurements for the uterus and ovaries did not differ significantly in the early follicular, peri-ovulatory and luteal periods of the uterus.

Acar et al. reported the SWE value of 24.4 (17.9-32.4) kPa for normal myometrium in their study without considering the menstrual cycle day, which was above the mean swe value that we found [6]. It was thought that the difference in the measurements of SWE values compared to our study could be related to the difference in the patients' ages in both studies (26.9 years, 30.0 years, respectively) and the other study being conducted without considering the menstrual cycle day. In two different studies by Soliman [13] and Manchanda [14] et al., no difference was found between the SWE measurements of menstrual phases, similar to our results. However, these studies diverged from our study because SWE measurements were made in different menstrual phases of different patients. We thought that because of the same patient was called in three different phases of the same menstrual cycle for SWE measurements in our study, the changes occurring throughout the cycle could better reflect the effect on tissue SWE values.

Most of the studies evaluating the uterus and ovary with the SWE method in gynecological diseases were planned independently of the day of the menstrual cycle [4-6]. In the magnetic resonance elastography (MRE) study, which was planned differently from these studies, uterine elasticity was calculated by considering the menstrual phases. In this study investigating the visco-elasticity of the uterus and cervix in sixteen healthy volunteers using the MRE method, significant changes were reported in the uterine corpus myometrium between menstrual phases [11].

Between the phases, the stiffness of the myometrium is higher in the proliferative phase than in the secretory phase. Therefore, they reported that high-resolution MRE can provide functional information of uterine tissue. A different method, the ultrasound SWE method, was used in our study. Although there was no significant difference, we also found the lowest myometrial SWE measurements in the early follicular phase and higher in the periovulatory and luteal phases in the uterine corpus. These results were thought to be due to the progesterone hormone secreted from the corpus luteum as a result of ovulation. Because, progesterone has many effects on uterine smooth muscle. It has been reported that progesterone can cause uterine relaxation by non-genomic and genomic mechanisms (inhibition of transmembrane Ca ++ entry, Ca ++ release from intracellular stores) [12]. It is tempting to speculate from these observations that progesterone might increase tissue elasticity.

In our study, no significant difference was found between the menstrual phases in terms of ovarian SWE values. No other studies exist in the literature except the aforementioned studies, that are comparing the phases of the menstrual cycle with the SWE values of the ovary. We therefore hypothesize from these observations that the ovaries may have been less affected by hormonal changes during the

menstrual phases for structural reasons, such as the lack of myometrial tissue.

SWE is used in the diagnosis of thyroid, breast, kidney, liver and uterus, and ovary pathologies diseases in the literature [4-8]. Currently, SWE is also used in obstetrics and gynecology practice such as prediction of labor induction [15], placental pathologies [16], uterine adenomyosis and leiomyomas[17], and ovarian pathologies [3]. Therefore, SWE should be considered as a non-invasive method that can be used in gynecology and obstetric practice. Although the number of cases in the other MRE study was similar to our study, we thought that the major limitation of our study is the small number of cases.

In conclusion, although myometrial elastography measurements were lowest in the early follicular phase, this difference was not statistically significant. Further studies with a large number of participants are needed in order to suggest whether elastography studies planned to be carried out should be performed in a certain cycle phase.

Disclosure

Authors have no potential conflicts of interest to disclose.

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