Elastosonographic Evaluation of Endometrium in Postmenopausal Bleeding

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ABSTRACT

OBJECTIVE: The aim of this study was to evaluate the elastosonographic changes of endometrium in postmenopausal women with uterine bleeding.

STUDY DESIGN: A total of 80 women in their postmenopausal period were enrolled for the study; 19 with postmenopausal bleeding and 61 normal healthy controls. All patients with a history of previous uterine surgery (including myomectomy) and/or endometrial interventions such as endometrial ablation, polyp removal, hysteroscopic interventions (except solely diagnostic procedures) and endometrial sampling within one year were excluded from the study because of the possibility of endometrial changes that may interfere with elastosonographic starin ratios. B-mode scanning, Doppler and real-time tissue elastography (RTE) were performed by the same single operator, blinded to the study design. The ultrasonographic findings (strain ratio, endometrial thickness, uterine artery Doppler indices) were evaluated between groups.

RESULTS:The means of age were 57.84±5.36 years and 56.34±3.32 years for the study group and the controls respectively. The groups were similar in regard to age (p=0.328). The parity of the postmenopausal bleeding group was significantly higher than the controls (p<0.001). When uterine artery Doppler indices were compared between groups, study group was found to have lower values in regard to controls (p<0.001). The medians of endometrial thickness were 4.30 (IQR=3.80)mm in the study group and 2.60 (IQR=0.90) mm in the control group and the difference was found to be significant (p<0.001). The medians of elastosonographic B/A ratios were 0.98 (IQR=0.18) and 1.27 (IQR=1.78) for the study group and controls respectively. The B/A ratios were found to be significantly lower in the study group (lower tissue elasticity) (p<0.001).

CONCLUSION: Tissue biopsy for histopathologic evaluation is still the gold standart in cases with postmenopausal bleeding. However, the need for a noninvasive method with high sensitivity and specificity is still under search. Some women who had been offered biopsy but did not accept the intervention because of the invasive nature of the procedure will be eft undiagnosed for a possible malignancy. Evaluation of the endometrium with real-time tissue elastosonography is one of the noninvasive methods with this potential and the diagnostic value of RTE could be possible with multicentric studies including more subjects.

Keywords: Elastosonography, Endometrium, Postmenopausal bleeding

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Introduction

Postmenopausal bleeding is a relatively common and serious clinical gynecologic problem. It is a situation of "endometrial cancer until proven otherwise" in classic teaching. The incidence of malignancy was reported within a range of 1% to 14% in various studies. The varying rates depend on the years since the onset of menopause and classical risk factors such as diabetes, obesity, hypertension and low parity.[1] The first-line approach in postmenopausal bleeding is the evaluation of the endometrium with transvaginal sonography. According to the opinion of the American College of Obstetricians and Gynecologists (ACOG), the cutt-off value

of endometrial thickness is accepted as 4mm. Because the risk of malignancy less than 1/917 when endometrium is less than or equal to 4mm, endometrial biopsy is not recommended.[2] Fluid enhancement with saline infusion sonography is an alternative method in cases where endometrial echo could not be visualised adequately such as in coexisting leiomyomas, previous uterine surgery, obesity, adenomyosis. An endometrial thickness <2mm. on each side of fluid is compatible with atrophy.[3] A thin and distinct endometrium on transvaginal sonography (with or without saline infusion) has a high negative predictive value (>99%).

Ultrasound strain imaging is relatively a new technique which is performed using a transducer obtaining radiofrequency echo data during manual freehand compressions of the tissue. This modality images the strain or stiffness distribution throughout an organ in response to an applied stress. The technique is currently being used mainly for differential diagnosis of masses in breast and thyroid imaging. Although preliminary results had been reported for applications in gynecology and obstetrics, the technique is still not in routine clinical practice.[4,5,6,7]

Although the optimal endometrial screening modality still remains controversial, TVUS alone is usually adequate in asymptomatic patients with endometrial thickness ≤4mm. However, a more detailed evaluation is needed in patients with postmenoposaul bleeding and where the endometrial line is irregular or thickness is >4mm. Although it is an invasive procedure, endometrial tissue sampling is used liberally by many gynecologists to rule out a malignancy.

Finding a non-invasive way to accurately diagnose the cause for uterine bleeding in postmenopausal women would avoid the physician to perform unnecessary interventions. In this article, we present preliminary results that illustrate the ability of ultrasound strain imaging to define the elasticity of endometrial tissue in postmenopausal bleedıng cases and normal healthy postmenopausal controls. Adding the modality of real-time tissue elastography to standart B-mode transvaginal sonography may enhance the diagnostic accuracy to differentiate endometrial pathologies (endometrium cancer and endometrial hyperplasia) in regard to changes in tissue stiffness of endometrium in women with postmenopausal period.

Material and Method

Selection of Groups

A prospective case–control study was performed at a tertiary referral hospital between January 2015-April 2015. The study was approved by the scientific and bioethical review board (IRB No. 11.03.2015/735).

Nineteen women with history of uterine bleeding who are in their postmenopausal period were included in the study. Because of probable changes in the elasticity of endometrium and adjacent myometrium, all patients with a history of previous uterine surgery (including myomectomy) and endometrial interventions such as endometrial ablation, polyp removal, hysteroscopic interventions (except diagnostic hysteroscopy), endometrial sampling within one year and those using hormone replacement therapy (HRT) were excluded from the study. The control group was comprised of 61 healthy subjects in postmenopausal period with the same criteria of exclusion. Written informed consents were obtained from all the participants.

Elastosonographic evaluation of endometrium

All ultrasonographic examinations including B-mode scanning, Doppler and real-time tissue elastography (RTE) were performed by using the same commercially available ultrasound equipment (Hitachi RTE, HI VISION, Preirus, Japan) and the same transvaginal transducer (V53W transvaginal probe). The images were acquired by the same single operator (IBG), blinded to the study design and having more than 10 years of experience in obstetrical sonographic imaging. All examinations were performed in dorsal lithotomy position with an empty bladder. Endometrium was visualised in the saggital plane of uterus with a clear view of endometrium and adjacent myometrium. After placing the endovaginal probe in the anterior fornix of vagina, a clear view of endometrium was obtained. RTE was performed by freehand technique (applying light repetitive compressions to the region of interest, each lasting around 1 second). Dual mode screen was used for displaying B-mode and elastography side-by-side on screen. A sinusoidal wave form was obtained after four to five compression-decompression cycles. We selected the most symmetrical waveform and compared the radiofrequency signals at the peak of the compression and at the trough of the decompression in the same cycle. Elastographic color mapped images were translucent and overlapping the gray scale images. A color scale ranging from blue to red representing the degree of tissue elasticity was displaced on the screen; red signals representing the tissues with high elasticity and bluesignals representing tissues with low elasticity. The reference point for elastography was the adjacent myometrial tissue. Circles ranging from 3 to 5 mm. were placed to the region of interests of both the endometrium and the adjacent myometrium. Strain ratios were calculated and displayed automatically by the embedded software of the sonographic equipment (Figure 1).

Statistics

The data was analyzed and the graphics were obtained by the commercially available software, Statistic Package for Social Sciences (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.) The relevance of the distribution of continuous variables such as age and endometrial thickness were evaluated with Shapiro-Wilk test. The continuous variable of age was expressed as mean±standart deviation, the other continuous variable of endometrial thickness was expressed as median (IQ<R: Interquantile Range) and

categorical variables as n (%). Mann-Whitney U test was used to compare the study group with control group in regard to age, parity, endometrial thickness, Doppler indices and B/A ratios. A p-value <0.05 was considered as statistically significant.

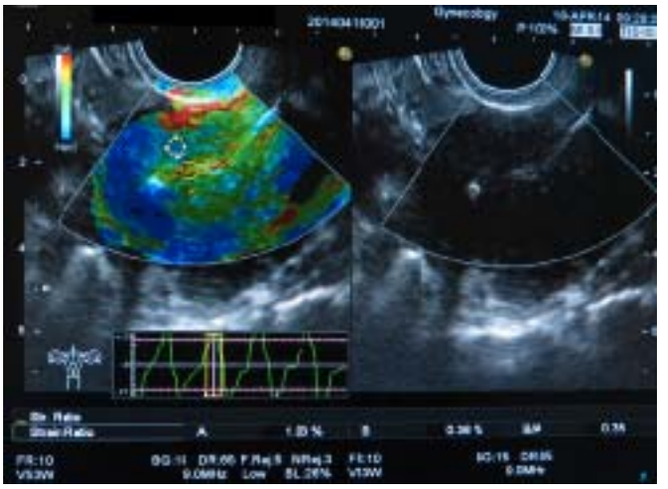

Figure 1: Endometrial elastography and strain ratio calculation in a saggital plane: endometrium (A), adjacent myometrium (B).

Results

Endometrial sampling was performed for all 19 women having the complaint of postmenopausal uterine bleeding/ spotting. The demographic statistics for the study group and the controls were summarized in Table 1. The means of age were 57.84±5.36 years and 56.34±3.32 years for the study group and the controls respectively. The groups were similar in regard to age (p=0.328). The parity of the postmenopausal bleeding group was significantly higher than the controls (p<0.001). When uterine artery Doppler indices were compared between groups, study group was found to have lower values in regard to controls (p<0.001). The medians of endometrial thickness were 4.30 (IQR=3.80)mm in the study group and 2.60 (IQR=0.90)mm in the control group and the difference was found to be significant (p<0.001) (Figure 2). The medians of elastosonographic B/A ratios were 0.98 (IQR=0.18) and 1.27 (IQR=1.78) for the study group and controls respectively. The B/A ratios were found to be significantly lower in the study group (p<0.001) (Figure 3).

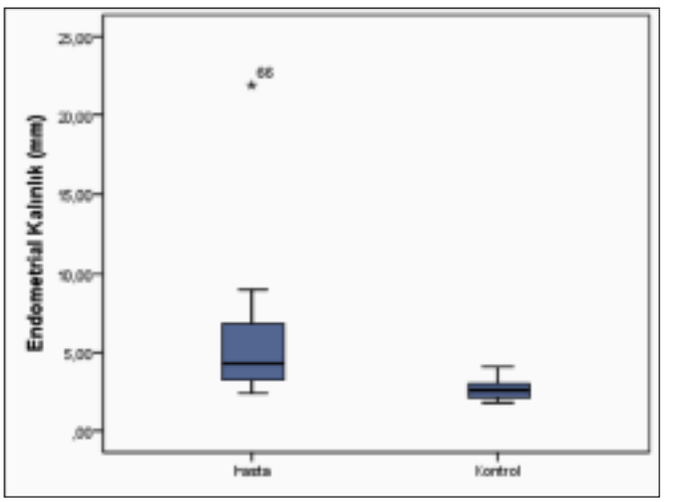

Figure 2: Distibution of endometrial thickness among groups

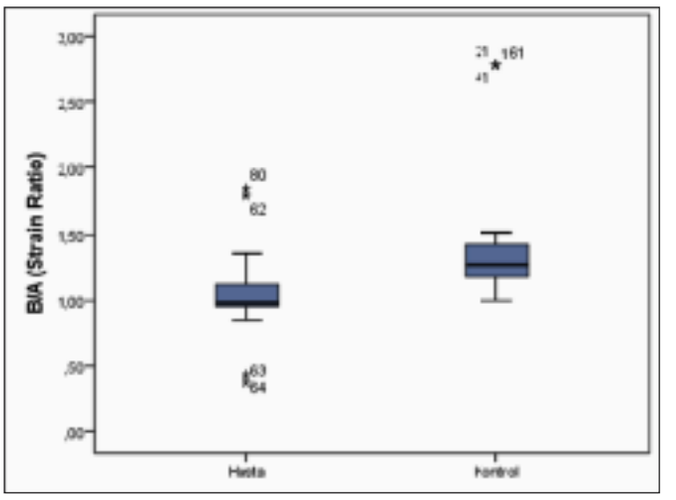

Figure 3: Distribution of elastosonographic strain ratio (B/A ratio) among groups

Table 1: Demographic and ultrasound findings among groups

	Control (n=61)	Postmenopausal Bleeding (n=19)	p
Age[1]	56.34±3.32	57.84±5.36	0.328
Parity	3.00 (1.00)	4.00 (2.00)	**<0.001**
Route of Delivery [n (%)]			-
C/S	3 (4.9)	0 (0.0)	
Vaginal	58 (95.1)	19 (100.0)	
Bleeding&Spotting [n (%)]	0 (0.0)	19 (100.0)	-
Endometrial thickness (mm)	2.60 (0.90)	4.30 (3.80)	**<0.001**
B/A	1.27 (1.78)	0.98 (0.18)	**<0.001**
Doppler PI	7.20 (0.45)	1.98 (0.63)	**<0.001**
Doppler RI	1.21 (0.85)	0.81 (0.10)	**<0.001**
Doppler S/D	8.84 (0.45)	4.28 (1.60)	**<0.001**

Descriptive analysis: Median (Inter Quartile Range-IQR); [1]: mean±standart deviation

After histological examination, among patients of postmenopausal bleeding group, there were 2 patients diagnosed to have simple endometrial hyperplasia without atypia and 17 patients to have normal histopathologic results. The demographic and ultrasonographic findings of the two women with abnormal histopathologic findings were as following: ages of 53 and 54, parity of 5 and 4, vaginal delivery for both, endometrial thickness of 6.8mm and 2.5mm, uterine artery Doppler PI value of 1.18 and 2.11, RI value of 0.69 and 0.72, S/D ratio of 3.21 and 4.87, elastosonographic strain ratio (B/A) of 1.79 and 1.84 respectively. Because of the limited subject size, no statictical analyses could be performed for abnormal histopathology group.

Discussion

The first-line approach for the evaluation of the women with postmenopausal bleeding is transvaginal sonography with or without saline infusion. However there is still debate on the cut-off value for the endometrial thickness to define an abnormality.[8,9,10] There are several studies discussing the cut-off values of endometrial thickness and histopathological endometrial verification. In a recent review of literature by Breijer et al.[11] endometrial thickness cut-off values and histopathologic correlations had been compared. Most frequently used cut-off values were 4, 5 and 6 mm with increasing sensitivity but decreasing specificity as the cut-off value was increased. The 95% confidence intervals (CI) were also very wide. Although the transvaginal sonographic evaluation is still the first-line approach to evaluate the endometrium in postmenopausal bleeding, there is still uncertainty.

There are two modalities of elastosonographic imaging: compressive or strain elastography and shear-wave elastography. Both the imaging method and the force applied for tissue compression are different in these two techniques. While stress is applied by repeated manual compression of the transducer in strain elastography, shear-wave elastosonography uses an acoustic radiation force impulse generated by a focused ultrasound beam instead of manual generation of force. Thus the method is largely dependent on examiner's experience in strain elastography but highly reproducible and with lower intra and inter observer differences in shear-wave elastography.[12,13] Apart from the generation of force applied, the diagnostic performance of elastosonography is largely dependent on the diameter and localization of region of interest (ROI). A wider compression power is exposed on the tissue near to the probe when compared to a region distal to the probe. In a similar manner, laterality of the ROI also results in compression axis to be lower when compared to the central located ROI.[14,15] All these factors should be taken into account both during performing the technique and evaluation process of the results.

The strain ratio labeled as B/A; A as the tissue of interest (endometrium) and B as the reference adjacent tissue (myometrium adjacent to endometrium) were calculated for both the postmenopausal bleeding group and the healthy postmenopausal controls. Higher the B/A ratio, stiffer the tissue is. In our study, the endometrium of the postmenopausal women with bleeding had been found to have lower B/A ratios, hence softer and higher elasticity. This increased elasticity and softening of endometrial tissue may be responsible for the shedding of endometrial tissue, hence causing bleeding.

One of the weakness of this study is the small sample size. As the number of cases is small, possible diagnostic value of elastographic indices and other parameters in differentiation of endometrium cancer and endometrial hyperplasia could not be studied.

Postmenopozal Kanamada Endometriyumun Elastosonografik Değerlendirilmesi

ÖZET

AMAÇ: Bu çalışmamızın amacı postmenopozal kanamalı hastaların endometriyumlarının elastosonografik incelenmesidir.

GEREÇ VE YÖNTEM: Postmenopozal dönemdeki 80 kadın çalışmaya dahil edilmiştir; 19 postmenopozal kanama yakınması olan çalışma grubu ve 61 normal sağlıklı postmenopozal kadın. Geçirilmiş uterin cerrahi (myomektomi dahil) ve/veya endometriyal ablasyon, polip çıkarılması, histeroskopik girişimler (sadece tanısal amaçlı olanlar hariç) gibi endometriyal girişimsel işlemler ve son 1 yıl içerisinde endometriyal örnekleme yapılmış olan hastalar endometriyumda elastosonografik değerlendirmede olası değişiklere neden olabileceklerinden dolayı çalışma dışı tutulma ölçütleri olarak kabul edildi ve çalışmaya dahil edilmedi. Tüm B-mod taramaları, Doppler ve gerçek zamanlı doku elastosonografileri çalışma dizaynına kör, tek bir uygulayıcı tarafından yapıldı. Gruplar arası ultrasonografik parametreler (gerilim oranı, endometriyal kalınlık, uterin arter Doppler parametreleri) karşılaştırıldı.

BULGULAR: Çalışmada bulunan 61 kontrol grubu bireylerin yaş ortalaması 56,34±3,32 yıl, 19 çalışma grubu postmenopozal kanama görülen hastanın yaş ortalaması 57,84±5,36 yıl olarak hesaplandı. Bireylerin yaşlarının benzer olduğu görüldü (p=0,328). Postmenopozal kanama hastalarının parite sayılarının anlamlı düzeyde yüksek olduğu belirlendi (p<0,001). Uterin arter Doppler ölçüm sonuçlarının kontrol grubunda hasta grubuna göre anlamlı düzeyde yüksek olduğu tespit edildi (p<0,001). Kontrol grubu bireylerinin ortanca endometriyal kalınlık değeri 2,60 (ÇAG=0,90)mm, hasta grubu bireylerinin ortanca endometriyal kalınlık değeri 4,30 (ÇAG=3,80)mm olarak ölçüldü. Hasta grubunda endometriyal kalınlık değerlerinin anlamlı düzeyde yüksek olduğu görüldü. B/A oranları değerlendirildiğinde, kontrol ve hasta grubunda ortanca değerler sırasıyla 1,27 (ÇAG=1,78) ve 0.98 (ÇAG=0,18) olarak hesaplandı. Kontrol grubunda B/A oranlarının hasta grubuna göre anlamlı düzeyde yüksek olduğu (daha düşük doku elastisitesi) belirlendi (p<0,001).

SONUÇ: Postmenopozal kanama durumlarında altın standart halen histopatolojik değerlendirme amaçlı doku örneklemesidir. Ancak girişimsel bir yöntem olması ve bazı hastalar tarafından kabul edilmeyerek olası tedavi eksikliklerine yol açması nedeniyle girişimsel olmayan tanısal araç arayışı devam etmektedir. Endometriyal dokunun gerçek zamanlı elastosonografi ile değerlendirilmesi bu konuda kullanılabilecek yöntemlerden biri olma potansiyeli taşımaktadır. Çok merkezli ve yüksek sayıda vaka içeren çalışmalar ile elastosonografik değerlendirmenin olası tanısal potansiyeli ortaya konulabilinir.

Anahtar Kelimeler: Elastosonografi, Endometriyum, Postmenopozal kanama

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