

The Predictive Value of Endometrial Thickness in Endometrial Pathologies in Premenopausal Women with Abnormal Uterine Bleeding

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Abstract

Background: Abnormal uterine bleeding (AUB) is one of the most common complains in women of any age seeking gynecologic health care and needs early diagnosis and proper management due to its impacts on the quality of life. This study was conducted to investigate the cut-off value of endometrial thickness (ET) by trans-vaginal ultra-sonography (TVUS) and evaluate its accuracy in the diagnosis of the endometrial abnormalities in premenopausal women with AUB. **Materials and Methods:** In this descriptive study, 64 married women between 35-50 years old were evaluated due to AUB during 2011-2012; TVUS and fractional curettage were done. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of the ET were calculated in different cut-off values. **Results:** The pathological evaluations of the biopsies were normal in 37 (57.8%) patients and were abnormal in 27 (42.2%) patients, 19 endometrial polyps, 6 hyperplastic lesions and 2 endometrial cancers. ET=4 mm had 100% sensitivity, 100% NPV, 10% specificity and 28% PPV in the detection of endometrial abnormalities. ET<10 mm had a proper sensitivity (67%-100%) and NPV (78.6%-100%) but specificity was low (%10-%44). ET=10 mm with sensitivity=63%, specificity=60%, NPV=65.8% and PPV=48.2% was introduced as the cut-off point with the best area under curve (LR+=2.22 LR-=0.77). **Conclusion:** Although an ET<10 mm was less likely to be associated with an endometrial abnormality, the low PPV of ET and low area under ROC curve shows sonography has high false positivity in premenopausal women. ET≤4 mm was more reliable and could reduce unnecessary biopsies. [GMJ. 2013;2(4):141-5]

Keywords: Uterine Bleeding; Pre-menopause; Vaginal ultrasonography; Dilatation; Curettage

Introduction

Abnormal vaginal bleeding (AUB) is one of the most common presenting gynecologic complaints in women seeking gynecologic health care regardless of age. AUB may have some complications which can affect the

quality of life [1]. Although the differential diagnosis includes a wide range of pathologies such as endometrial and endocervical polyps, myomas, synechiae, uterine malformations, endometrial hyperplasia and endometrial cancer, the vast majority had benign causes. This complaint is taken more seriously when it oc-

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curs in women of late reproductive age due to higher possibility of malignancies. Dilatation and curettage (D&C), office endometrial biopsy and recent hysteroscopy have been the gold standard methods for AUB evaluation [2,3]. D&C is an invasive procedure, and it should be performed in the operating room under anesthesia. TVUS has been used to evaluate AUB. It can demonstrate subserosal lesions, intra-myometrial fibroids, endometrial thickness (ET), and can detect ovarian neoplasms (functional cysts or tumors) but cannot reliably distinguish between polyps, sub mucosal and intra-cavitary fibroids, adenomyosis and neoplastic changes [4].

ET measured by TVUS has been shown as an effective procedure for evaluation of AUB in postmenopausal women. In women with postmenopausal bleeding, an ET equal or less than 4-5 mm is associated with a low risk (1%) of endometrial disease [1,4-7]. An ET >4-5 mm is accepted to be a safe cut-off level to differentiate malignant lesions in postmenopausal women who are not on hormonal therapy [8-10]. In contrast with postmenopausal women, the utility of TVUS for excluding endometrial abnormalities in premenopausal women has not been established [6,7]. Ultrasound cannot discriminate between proliferative endometrium, benign endometrial disease, and cancers, all of which cause an increase in endometrial thickness. Because premenopausal hormones may cause proliferation of the endometrium, TVUS is less specific in premenopausal women [8,9]. Considering the lack of data about accuracy of TVUS in diagnosis of the endometrial pathologies in premenopausal women, this study was conducted to investigate a cut-off point of ET in women above 35 years old with AUB for the first time in Iran.

Materials and Methods

This descriptive-diagnostic study was performed on 64 married women scheduled for endometrial sampling or fractional D&C due to AUB in Bouali hospital, Tehran, Iran from May 1st 2011 to May 30th 2012. The study was approved by the ethical committee of Tehran Azad University and informed consents were filled by the participants in the

study after being presented to the methods and procedures.

The study included 64 premenopausal women 35-50 years old who were visited due to AUB. Women with an underlying medical problem such as hypertension, diabetes, thyroid disease, premature ovarian failure (POF), evidence of pelvic inflammatory disease (PID), users of intrauterine devices or oral contraceptive pills, were excluded from the study. After a complete history taking and physical examination, patients were evaluated with TVUS to measure ET and to assess other pelvic pathologies. ET was measured in the sagittal plane of the uterus at its thickest part near the fundus. Then fractional curettage was performed in the operating room, and the specimens were sent for pathological evaluation; all the specimens were evaluated and confirmed by two pathologists of the center. The patients' data include age, gravidity, parity, body mass index (BMI), ET in TVUS and histopathological findings were recorded. Histopathological findings of proliferative and secretory endometrium were considered as normal. Also, polyp, hyperplasia and adenocarcinoma were considered as abnormal pathological lesions. The patients' data were analyzed by SPSS software (Ver. 14.0). The accuracy of TVUS in the detection of endometrial pathologies was calculated in different thicknesses and to assess the cut-off point we used receiving operating characteristic (ROC) curve. The area under the ROC curve reflects the accuracy of ET, incorporating sensitivity, and false-positive error rate (1-specificity). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of the ET were calculated in different cut-off values.

Results

The mean age of participants was 45.2 ± 5.25 years. The mean BMI was 30 ± 3.6 Kg/m². The mean gravidity was 3 (range 0-9) and the mean parity was 3 (range 0-8). The mean ET in TVUS was 11.5 ± 5.5 mm with a range of 4-35 mm.

The distributions of endometrial lesions with ET are shown in Table-1. Thirty-seven of the

patients (57.8%) had normal pathological findings, 22 (34.4%) had proliferated endometrium and 15 (42.2%) had secretory endometrium. Abnormal pathologies were detected in 27 (42.2%) patients. Of them, 29.7% had endometrial polyps, 9.4% had endometrial hyperplasia and 3.1% were reported as endometrial cancer. ET was higher in patients with endometrial cancer (18.6 ± 2.12 mm) and there were no pathological findings in ET lower than 4mm. There were no correlation between ET and endometrial pathology, age, and BMI. The sensitivity, specificity, PPV, NPV, positive and negative likelihood Ratio (L.R+ and L.R-) calculated at each cut-off point of ET are displayed in Table-2. ET=10 mm with sensitivity 63%, specificity 60%, NPV 65.8%, PPV 8.2% with L.R+=2.22 and L.R- =0.77 was introduced as the cut-off point with an area under the curve of 0.614 (Figure-1).

Discussion

AUB is the most presenting symptom of endometrial cancer and it can be observed in 80% to 90% of pre and postmenopausal women with endometrial cancer [1,2,11]. Because of this, careful diagnostic evaluation is advisable. There are limited studies about the diagnostic value of ET in TVUS in premenopausal women with AUB and determination of its cut-off;

hence, we designed this study due to the present controversies. Mortakis et al. conducted a study involving 122 premenopausal and 78 menopause women. Sonography is a sensitive method and in $ET > 5$ mm in premenopausal and > 4 mm in menopause women hysteroscopy is necessary [8]. Soares et al. reported that TVUS had both sensitivity and PPV of 75% in the detection endometrial abnormalities. Also, Sonohysterography had a sensitivity of 75% in the detection of intrauterine adhesions while TVUS was unable to detection these lesions [9]. Ozdemir et al. designed a study and investigated the accuracy and cut-off point of ET by TVUS. They measured ET by TVUS in 144 premenopausal women with AUB prior to endometrial biopsy. $ET = 8$ mm with sensitivity of 83.6%, specificity of 56.4% and NPV of 95.6% was proposed as the cut-off point for detection of the abnormal endometrium [10]. In the present study, $ET \geq 10$ mm with sensitivity of 63%, specificity of 60%, NPV of 65.8% and PPV of 48.2% was introduced as the cut-off point.

In a study on 213 patients with AUB, Abe et al. reported that sonography had 94.6% sensitivity and 77.2% specificity. Moreover, they noticed that TVUS could reduce up to 25% of unnecessary biopsies [12]. In the previous studies, $ET \geq 8$ mm was introduced as the cut-off point in premenopausal women [13,14]. In

Table 1. Predictive Value of Endometrial Thickness in Abnormal Uterine Bleeding in Premenopausal Women; Endometrial Thickness (ET) in Various Endometrial Pathologies.

Histopathology	Number (%)	ET (mean± S.D)
Normal	37(57.8)	10.8±5.93
Proliferative	22(34.4)	13.08±6.47
Secretory	15(23.4)	7.6±2.9
Abnormal	27(42.2)	12.36±4.88
Endometrial polyp	19(29.7)	10.51±3.38
Hyperplasia	6(9.4)	16.17±6
Endometrial cancer	2(3.1)	18.6±2.12

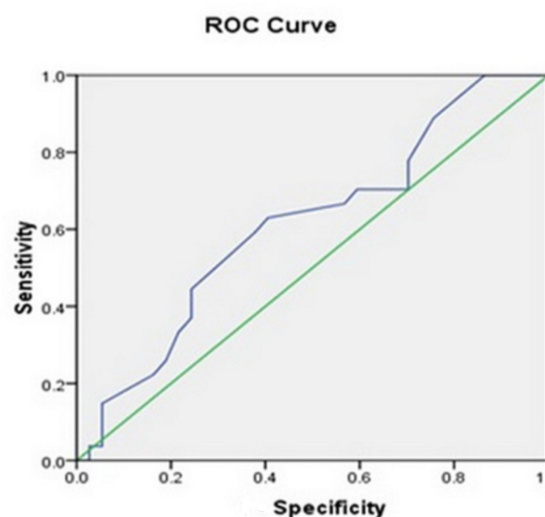


Figure 1. Predictive Value of Endometrial Thickness in Abnormal Uterine Bleeding in Premenopausal Women; ROC Curve of Endometrial Thickness, Area Under the Curve is 0.614.

Table 2. Predictive Value of Endometrial Thickness in Abnormal Uterine Bleeding in Premenopausal Women; Sensitivity, Specificity, Positive Predictive Value (PPV), Negative Predictive Value (NPV), Likelihood Ratios (L. R+, L.R-) of ET at Each Cut-Off Point.

ET (mm)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	L.R +	L.R -
3	100	0	27.9	100	1	0
4	100	10	28	100	1.04	0
5	100	10	28.1	87.5	1.05	0.36
6	89	24	29.7	84.6	1.13	0.48
7	74	30	32.6	82.1	1.29	0.58
8	70	40	34.6	80.8	1.41	0.63
9	67	44	35.4	78.6	1.46	0.72
10	63	60	48.2	65.8	2.22	0.77
11	60	63	45.4	77.7	1.95	0.77
12	44	76	37	74.8	1.57	0.9
13	40	76	40.9	75	1.84	0.89
14	33	78	35.3	73.7	1.46	0.95
15	26	80	33	72.9	1.15	0.99
16	22	84	42	77.7	1.37	0.93
17	15	95	60	77.7	2.77	0.89
18	17	95	60	77.7	2.05	0.95
19	70	95	39	98	1.37	0.98
20	40	95	25	93	0.68	0.99
21	-----	-----	-----	-----	-----	-----
22	40	97	37	93	1.37	0.99
>29	0	97	0	93	0	1.03
>36	0	100	0	100	0	1

Smith *et al.* study, TVUS had a sensitivity of 67% and specificity of 75% [13]. Moreover, Getpook *et al.* showed that TVUS had 83.9% sensitivity and 58.8% specificity [14]. Goldmich *et al.* reported that $ET \leq 5$ mm had 100% diagnostic values in menopausal women and had 92% sensitivity and 96% specificity for rule out endometrial pathologies in premenopausal women [15]. Weber *et al.* showed the positive correlation between increased ET in TVUS and abnormal findings in endometrial biopsies [16]. However, Dueholm *et al.* investigated the cut-off point of ET by TVUS, but they were unable to introduce an optimal point [17].

In our study $ET=4$ mm had a sensitivity of 100%, a specificity of 10%, 100% NPV and 28% PPV in detection of abnormal endometrium. ET less than 10mm had proper sensitiv-

ity (ranging 67-100 percent) and NPV (ranging 78.6-100 percent), but specificity was low (ranging 10-44 percent). $ET=10$ mm was introduced as the cut-off point (L.R+=2.22, L.R-=0.77). One limitation of our study was the small sample size. Hence, we suggest prospective studies to be conducted with more patients in separated age groups and different types of AUB.

Conclusion

According to our findings, an ET less than 10 mm is less likely to be associated with endometrial pathology, low PPV of ET in TVUS and area under ROC curve equation (0.614) showed that TVUS in premenopausal women has high false-positivity, so is not a proper diagnostic method, but $ET < 4$ mm in TVUS was

reliable for initial evaluation of AUB and can reduce unnecessary biopsies.

We recommend TVUS as the first step of evaluation, but the sonographers and clinicians

should pay attention to other findings such as the regularity or irregularity of the endometrium as well.

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