THE ROLE OF ENDOMETRIAL THICKNESSES A RISK FACTOR IN ENDOMETRIAL PATHOLOGIES

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ABSTRACT

Aim: This study aimed to investigate the role of endometrial thickness in endometrial pathologies and compare transvaginal ultrasonography (TvUSG) and histopathological results in pre- and post-menopausal women with abnormal uterine bleeding. **Methods:** We retrospectively reviewed the records of 1882 women with abnormal uterine bleeding between 2018 and 2020. After exclusions, the final study population consisted of 1088 women. The primary variable was the endometrial thickness. Secondary variables examined were the final diagnosis, age, gravidity, parity, and menopausal status. **Results:**Results for 653 women (60.0%) with normal endometrium, 26 women (2.4%) with endometrial carcinoma, and 409 women (37.6%) with other endometrial pathology were analyzed. The mean endometrial thickness of the women with normal endometrium was 11.38±5.80 mm (range: 3-45 mm), while the mean endometrial thickness of the women with other endometrial pathology and endometrial carcinoma were 12.27±5.15 mm (range: 3-33 mm), and 17.24±7.19 mm (range: 5-33 mm), respectively. A statistically significant difference was detected between the groups concerning endometrial thickness ($F=15.464$, $p<0.001$). On the other hand, logistic regression analysis was used to identify the risk factors for endometrial carcinoma. Age ($p=0.003$) and endometrial thickness ($p=0.002$) were the risk factors in predicting endometrial carcinoma. **Conclusion:**Women admitted to the hospital with pre-menopausal or post-menopausal bleeding should undergo detailed gynaecological examination, and the endometrium should be evaluated with TvUSG. If an increased endometrial thickness is detected, an endometrial biopsy should be performed. Even TvUSG is not a definitive diagnostic method; it is a non-invasive, cost-effective, and guiding technique for endometrial pathologies.

KEYWORDS Endometrial thickness, menopause, curettage, transvaginal ultrasonography, endometrial cancer

Introduction

Background/rationale

Abnormal uterine bleeding in women is closely related to age and reproductive status. The most common causes of abnormal uterine bleedings in women at the early stages of the reproductive period are pregnancy and its complications, infections, and endocrine disorders. However, endometrial pathologies, including atrophic vaginitis, cervicitis, endometritis, endometrial atrophy, endometrial hyperplasia, endometrial polyps, as well as cancers of the endometrium, vulva, vagina, and cervix are most common among women in the peri-menopausal and post-menopausal ages (1-3). Additionally, endometrial hyperplasia and endometrial/cervical polyps are a series of lesions that are important for the progression of endometrial cancer (EC) (4). Approximately 75% of all ECs occur in post-menopausal women and progressively worsen with age (2, 5). For this reason, it is especially necessary to evaluate the complaints of patients over 40 years of age with abnormal uterine bleeding in both the pre-menopausal and post-menopausal period and to make a rapid diagnosis(6).

Due to the lack of screening tests for early detection of precancerous pathologies, the diagnosis of endometrial cancer is generally made after the emergence of symptoms. A screening program for the determination of EC that can be applied in practice has not been developed yet(2, 7). Therefore, diagnosis and treatment are usually delayed in patients with asymptomatic endometrial cancer. Nowadays, an endometrial biopsy is the most reliable and the most common diagnostic method used in patients with post-menopausal bleeding to demonstrate endometrial pathologies(8, 9). Although probe curettage is the gold standard diagnostic method, it may have serious complications (10, 11).

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For the early detection of malignant, premalignant, and other pathologies of the endometrium, less invasive and more accessible methods are being searched for. Due to the increase in resolution provided by ultrasonography devices and the ease of use resulting from their computations, ultrasound offers detailed and accurate information, and, thus, has become indispensable in gynecological practice(2, 12).Several studies are showing the relationship between endometrial thickness and endometrial pathologies measured by transvaginal ultrasonography (TvUSG), which is an easily applied non-invasive method for evaluating endometrial pathologies (11, 13-15).

Objectives

This study aimed to investigate the role of endometrial thickness on endometrial pathologies and compare the TvUSG and histopathological results in both pre- and post-menopausal women with abnormal uterine bleeding.

Materials and Methods

Study design

Ethical approval for this retrospective study was obtained from the Research Council and Ethical Committee of Kharkiv Medical Academy of Postgraduate Education, No 29.0417p. Patient consent was not deemed necessary because of the retrospective study design. Study reporting was done following the STROBE guidelines(16).

Participants

During the study period, 1882 women with abnormal uterine bleeding (AUB) had undergone probe curettage and transvaginal USG. Women without a pathology report , and those with no recorded endometrial thickness were excluded. The final study population consisted of 1088 women, of whom the pathology reports indicated normal endometrium in 653cases, endometrial carcinoma, another endometrial pathology in 409 cases in 26 cases.

Variables

The primary study variable was endometrial thickness measured as mm. The secondary variables examined were the final diagnosis, age, gravidity, parity, and menopausal status of the women.

Statistical methods

All statistical analyses were performed with the Statistical Package for Social Sciences version 22 (SPSS, IBM, Armonk, NY, USA). Number (n), percentage (%), mean, standard deviation (SD), minimum, and maximum values were given as descriptive statistics. The one-way ANOVA test was used to compare more than two groups, and Pearson Chi-Square or Fisher's exact tests were used to analyzing categorical data. A logistic regression analysis was performed to determine the independent risk factors of endometrial pathologies. The results were evaluated with a confidence interval of 95%, and the level of significance, p, was set at 0.05.

Results

Descriptive data

Results for 1088 women were analyzed. The mean age of the patients was 48.05±8.53 years (range: 18-95). Of the patients, 653 (60.0%) had normal endometrium, 26 (2.4%) had endometrial carcinoma, and 409 (37.6%) had some other endometrial pathology. The mean (±SD) age of the women with normal endometrium was 47.26±8.39 years (range: 18-81 years), the mean age of women with other endometrial pathology was 48.42±7.52 years (range: 28-74 years), and the mean age of women with endometrial carcinoma was 62.23±13.47 years (range: 45-95 years). There was a statistically significant difference between the groups concerning age (F=41.986, p<0.001). Of the patients with a diagnosis of other endometrial pathology,190 (46.5%) had typical/atypical endometrial hyperplasia, 162 (39.6%) had endometrial polyps, 20 (4.9%) had endocervical polyps, and 37 (9.0%) had chronic endometritis. On the other hand, 26 patients had endometrial carcinoma. There was a statistically significant difference between women with other endometrial pathology and carcinoma concerning age (T=-8.550, p<0.001). The mean gravidity values of women with normal endometrium, other endometrial pathology, and endometrial carcinoma were 3.51±1.93, 3.76±2.35, and 2.71±1.25, respectively. Additionally, the mean parity values of women with normal endometrium, endometrial pathology, and endometrial carcinoma were 2.94±1.68, 3.10±1.42, and 1.80±1.30, respectively.No significant differences were detected between women concerning gravidity and parity (F=1.271, p=0.282; and F=1.865, p=0.156, respectively). A total of 678 (62.3%) participants were pre-menopausal. Of the women with normal endometrium, 229 (33.8%) were post-menopausal, 158 (38.6%) of the women with endometrial pathology were post-menopausal, and 23 (88.5%) of those with endometrial carcinoma were post-menopausal. A significant difference was detected between women concerning menopause status (χ=30.605, p<0.001).

Outcome data

The mean endometrial thickness of the women with normal endometrium was 11.38±5.80 mm (range: 3-45 mm), the mean endometrial thickness of the women with other endometrial pathology was 12.27±5.15 mm (range: 3-33 mm), and the mean endometrial thickness of the women with endometrial carcinoma was 17.24±7.19 mm (range: 5-33 mm). A statistically significant difference was detected between women concerning endometrial thickness (F=15.464, p<0.001) (Table 1). Additionally, the endometrial thickness of 6-10 mm and 11-15 mm intervals were detected in most women with other endometrial pathology (n=151 and n=113, respectively), normal endometrium (n=248 and n=186, respectively), while the endometrial thickness of 11-15 mm and 16-20 mm intervals was detected in most women with endometrial cancer (n=8 and n=9, respectively). The comparison of endometrial thicknesses is given in Table 2. A logistic regression analysis with the enter method was used to identify the weighted risk factors for any endometrial pathology (including cancer) (Table 3). The variables entered into the model were age (year), menopause status (absent/present), and endometrial thickness (mm). Age(p=0.003) and endometrial thickness (p=0.002)were the risk factors in our study for detecting any endometrial pathology. This model had a sensitivity of 93.1% and a specificity of 60.6%.

Table 1 Descriptive characteristics and comparison of findings between the different groups

	Final histologic diagnosis											
	Types of Endometrial pathologies					Significance		Main Study Groups			Significance	
	Endometrial hyperplasia (n=190)	Endometrial polyp (n=162)	Cervical polyp (n=20)	Chronic endometritis (n=37)	Endometrial carcinoma (n=26)	F / χ2	p	Normal endometrium (n=653)	Other pathology (n=409)	Endometrial Carcinoma (n=26)	F / χ2	p
Age (year) (mean±SD)	48.41±6.87	48.76±8.29	52.25±6.93	44.92±6.19	62.23±13.47	21.730	**0.000**	47.26±8.39	48.42±7.52	62.23±13.47	41.986	**0.000**
Gravidity (mean±SD)	3.45±1.49	3.97±3.09	3.73±1.79	4.21±2.15	2.71±1.25	0.861	0.489	3.51±1.93	3.76±2.35	2.71±1.25	1.271	0.282
Parity (mean±SD)	3.07±1.31	3.08±1.59	3.18±1.25	3.25±1.35	1.80±1.30	1.038	0.390	2.94±1.68	3.10±1.42	1.80±1.30	1.865	0.156
Menopause												
Present n (%)	71 (37.4)	68 (42.0)	12 (60.0)	7 (18.9)	23 (88.5)	35.531	**0.000**	229 (35.1)	158 (38.6)	23 (88.5)	30.605	**0.000**
Absent n (%)	119 (62.6)	94 (58.0)	8 (40.0)	30 (81.1)	3 (11.5)			424 (64.9)	251 (61.4)	3 (11.5)		
Thickness (mm, mean±SD)	12.73±5.30	12.47±5.05	11.45±5.96	9.46±3.17	17.24±7.19	8.738	**0.000**	11.38±5.80	12.27±5.15	17.24±7.19	15.464	**0.000**

Standard deviation

Table 2 Comparison of the endometrial thickness between different pathological outcomes

Histologic Diagnosis		Endometrial Thickness						Total
		≤5 mm	6-10 mm	11-15 mm	16-20 mm	21-25 mm	>25 mm	
Types of Endometrial pathology	**Endometrial hyperplasia**	14 (7.4%)	64 (33.7%)	48 (25.2%)	52 (27.3%)	11 (5.9%)	1 (0.5%)	190
	Endometrial polyp	10 (6.1%)	61 (37.7%)	45 (27.8%)	36 (22.3%)	10 (6.1%)	0 (0%)	162
	Cervical polyp	3 (15.0%)	6 (30.0%)	8 (40.0%)	1 (5.0%)	2 (10.0%)	0 (0%)	20
	Chronic endometritis	5 (13.5%)	20 (54.1%)	12 (32.4%)	0 (0%)	0 (0%)	0 (0%)	37
	Endometrial carcinoma	1 (3.8%)	3 (11.6%)	8 (30.8%)	9 (34.6%)	1 (3.8%)	4 (15.4%)	26
Main study groups	**Other endometrial pathology**	(n=32)	(n=151)	(n=113)	(n=89)	(n=23)	(n=1)	(n=409)
	Pre-menopausal	18 (56.2%)	92 (60.9%)	61 (54.0%)	68 (76.4%)	11 (47.8%)	1 (100%)	251 (61.3%)
	Post-menopausal	14 (43.8%)	59 (39.1%)	51 (46.0%)	20 (33.6%)	14 (52.2%)	0 (0%)	158 (38.7%)
	Normal Endometrium	(n=82)	(n=248)	(n=186)	(n=94)	(n=29)	(n=14)	(n=653)
	Pre-menopausal	44 (50.5%)	161 (64.9%)	129 (69.3%)	64 (68.0%)	19 (65.5%)	7 (50.0%)	424 (64.9%)
	Post-menopausal	38 (49.5%)	87 (35.1%)	57 (30.7%)	30 (32.0%)	10 (34.5%)	7 (50.0%)	229 (35.1%)
	Endometrial carcinoma	(n=1)	(n=3)	(n=8)	(n=9)	(n=1)	(n=4)	(n=26)
	Pre-menopausal	0 (0%)	0 (0%)	2 (25.0%)	0 (0%)	0 (0%)	1 (25.0%)	3 (63.9%)
	Post-menopausal	1 (100%)	3 (100%)	6 (7.0%)	9 (100%)	1 (100%)	3 (75.0%)	23 (36.1%)

Table 3 The risk factors of endometrial pathologies including endometrial carcinoma

Risk Factors	Beta	Wald	p	Exp (B)	95% CI for Exp (B)	
					Lower	Upper
Age (year)	0.034	8.591	0.003	1.035	1.011	1.059
Menopause (reference: absent)	-0.169	0.703	0.402	0.845	0.569	1.253
Endometrial thickness (mm)	0.035	9.957	0.002	1.036	1.013	1.059

Discussion

Key results

The study findings supported the use of TvUSG technique on women with pre- or post-menopausal bleedings before the curettage had been applied. The endometrial thickness measured by TvUSG of women with abnormal endometrium was statistically significant from those with normal endometrium.

Limitations

Our study has some limitations. First, due to its retrospective nature, 794 patients were excluded as a result of missing data. Second, the underlying medical problems such as obesity, diabetes, hypertension, as well as some descriptive characteristics including body mass index, complaints, the presence of hormone replacement therapy, and the use of oral contraceptives would have contributed to interpreting the outcomes and helped to find other risk factors for endometrial pathologies.

Interpretation

Abnormal uterine bleeding (AUB) is a crucial problem for both pre- and post-menopausal women. In the case of AUB, the patient should be investigated for endometrial pathologies or endometrial cancer (EC). The recommended method for this purpose is probe curettage. However, there is a particular risk of morbidity and mortality concerning its invasive nature and the necessity of hospital conditions, including general anaesthesia (14). The main complications are the spread of malignant cells to the uterine wall during dilatation, perforation, haemorrhage, and infection (17). Although many publications are suggesting that TvUSG should be performed as the first test in the investigation of endometrial lesions, some clinicians still recommend doing an endometrial biopsy. There are reports that probe curettage has a high false-negative rate (10-15%) in detecting endometrial lesions(13, 18). In one study, it was found that less than half of the uterine cavity was curated in 60% of all applied curettages, and it was reported that the use of TvUSG reduced the need for invasive methods such as endometrial curettage by 40% (19).On the other hand, it has been shown that the sonographic and histopathological findings of endometrium correlate well with each other (2). The sensitivity and specificity rates of the TvUSG were detected in some studies. Our regression model had 93.1% sensitivity and 60.6% specificity. The specificity rates in most of the related studies were quite similar to our results. Howeverour sensitivity rate was quite high when compared to the current literature. Amit et al. (20) performed a survey of 60 post-menopausal women and reported the sensitivity and specificity rates as 78% and 45.6%, respectively. Another study conducted by Dorum et al. (17) on 100 women detected the sensitivity and specificity rates as 80% and 60%, respectively. Moreover, Yumru et al. (21)identified those rates as 78.9% and 88.6%, respectively. However, Weiner et al. (22) found a decreased sensitivity (68%) for TvUSG and stated that endometrial thickness measurement was not a reliable method for determining malignancies (23). According to our findings, we can say that the depth of endometrial thickness measured by TvUSG may be an alternative and non-invasive technique for detecting endometrial pathologies. On the other hand, the endometrial thickness is the most critical risk factor for endometrial pathologies. Tongsong et al. (24) reported that the mean values of endometrial thickness in women with abnormal and normal endometrium were 13.2$\pm$3.6 and 8.2$\pm$4.8, respectively. Minagawa et al. (25) detected the mean values of endometrial thickness in post-menopausal and pre-menopausal women as 12.6$\pm$5.4mm and 7.2$\pm$5.6mm, respectively. Furthermore, another study reported the same values as 13.5$\pm$.7.7 and 6.3$\pm$4.2 (26). From this point, our results were parallel with the current literature. The mean values of endometrial thickness in women with abnormal and normal endometrium were 12.27$\pm$5.15 mm and 11.38$\pm$5.80 mm, respectively. Additionally, the mean values of endometrial thickness in women with endometrial carcinoma were 17.24$\pm$7.19 mm.

Conclusion

Typical/atypical endometrial hyperplasia and endometrial polyps are the common pathological findings in patients with increased endometrial thickness. Women admitted to the hospital with peri-menopausal, or post-menopausal bleeding should undergo a detailed gynaecological examination, and the endometrium should be evaluated with TvUSG.If an increased endometrial thickness is detected via TvUSG, an endometrial biopsy should then be performed. Even though TvUSG is not a definitive diagnostic method, it is non-invasive, cost-effective, and has relatively high sensitivity and specificity for guiding the diagnosis of endometrial pathologies.

Conflict of Interest

The authors have no conflict of interest in this study.

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