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The Connection between the Endometrial Thickness and the Risk of Endometrial Malignancy in Postmenopausal Women

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Abstract

BACKGROUND: Postmenopausis is a period that starts one year after the last menstruation. Late menopause, after 70 years, is called senile.

AIM: To examine the correlation between endometrial thickness and the risk of endometrial malignancy in postmenopausal.

MATERIAL AND METHODS: Prospective clinical study involving 120 postmenopausal patients treated at the University Clinic for Gynecology and Obstetrics – Skopje, divided into two groups: control and examination. The control group included 40 postmenopausal patients, hospitalised and operated due to urogenital pathology. The examined group consisted of 80 patients divided into three subgroups according to the ultrasound verified thickness of the endometrium: from 5-8 mm; > 8-11 mm and above 11 mm. A detailed history and intervention were taken in the patients from both groups, and the material was sent for histopathological analysis to determine eventual malignancy.

RESULTS: The probability of endometrial malignancy significantly increased by 1.012 times in the group with a thickness of the endometrium from 5-8 mm, 1.769 times in the endometrial thickness group > 8-11 mm and 4.737-fold in the group over 11 mm compared to the control group.

CONCLUSION: In postmenopausal patients, the likelihood of endometrial cancer significantly increases with the thickness of the endometrium.

Introduction

Postmenopausal is a period that begins one year after the last menstrual period. In this period, a new source of oestrogens is estrone. The average age for menopause in developed countries is 51.4 years [1]. It is divided into early and late menopause. Late menopause, after 70 years, is called senile. In 10-15% of cases, postmenopausal bleeding is caused by endometrial cancer, and usually abnormal uterine bleeding is caused by endometrial polyps or atrophy [2]. The incidence of endometrial cancer in postmenopausal patients is 0.7% but increases in patients with additional risk factors [3]. In this period, abnormal uterine bleeding belongs to polyps, endometrial atrophy, endometrial hyperplasia, endometrial carcinoma, submucosal fibroid, hormone therapy, uterine or uterine infections, use of certain drugs [4], etc.

According to FIGO, the International Federation of Gynecology and Oncology, the stages are subclassified into two pathological types. Type 1-estrogen-dependent [5] in which in 30-80% of cases, the mutation of the PTEN gene is responsible for this type of malignant tumour. It occurs from complex atypical hyperplasia [6]; it is associated with estrogen stimulation and is not aggressive [7]. According to Kurmani's collaborators, this type of cancer is characterized by low malignancy, diagnosed in the early stage, has a superficial invasion of the myometrium and has high sensitivity and good

prognosis, with 85% five-year survival [8], [9]. Type 2-neurosurgeon-dependent [5] endometrial cancer is poorly differentiated, with a deep myometrial invasion, including lymph nodes, low progestin sensitivity and 58% five-year survival [8], [9]. It develops from an atrophic endometrium and is not associated with hormone stimulation [6] metastasizes and grows outside of the uterine hull [7]. Mutations of the P53 gene occur in 50% of cases.

Papillary serous and mesonephrom belongs in this group. This neoplasia is very aggressive.

The purpose of the study was to investigate the predictive role of the thickness of the endometrium in the onset of endometrial malignancy in postmenopausal patients.

Material and Methods

This is a prospective clinical study, including 120 postmenopausal patients treated at the University Clinic for Gynecology and Obstetrics - Skopje. Patients were divided into two groups: a control and examination group. The control group included 40 postmenopausal patients, hospitalised and operated due to urogenital pathology, and ultrasonically detected endometrial thickness less than 5 mm. The examined group included 80 postmenopausal patients hospitalised due to endometrial bleeding with an ultrasound detection of an endometrial thickness greater or equal to 5 mm. According to the thickness of the endometrium, the examinees from the examined group were divided into three subgroups: a) subgroup 1 = 5-8 mm; b) subgroup 2 = 8-11 mm; and c) subgroup 3 => 11 mm. A detailed history and intervention were taken in the patients from both groups, and the received material was sent for histopathological analysis to determine eventual malignancy.

The study excluded patients in generative reproductive age, patients who were not able to do fractional exploratory curettage, patients with a personal history of malignant disease (past or current), patients with a personal anemia for benign or malignant tumors of the ovary , breast cancer patients treated with tamoxifen , patients with any pelvic surgery due to other gynecological pathology.

Statistical analysis

The data during the survey were processed with the statistical package SPSS 20.0. The Pearson Chi-square homogeneity test was used to establish an association between certain attributive dichotomies of the two groups of respondents. The Shapiro-Wilk W test was used to determine the frequency distribution frequency of certain variables. To test the significance of the difference between two and more numerical variables with regular or irregular distribution of frequencies was the Studentov T-test for independent samples, the Mann Whitney U test and the Kruskal-Wallis ANOVA test. A significance level of $p < 0.05$ was used to determine the statistical significance.

Results

Characteristics of the sample

In the investigated group of patients, the average age was 62.3 ± 7.7 years, and in control, it was 64.4 ± 7.5 years (Table 1). The tested difference between the two groups relative to age, $p > 0.05$, did not indicate a significant difference (Mann-Whitney U Test: $Z = -1.3138$; $p = 0.1889$). Patients from the investigated or control group have an average number of years in menopause 11.9 ± 6 v.s. 11.8 ± 4 years difference in significance between groups (Mann-Whitney U Test: $Z = -0.4397$; $p = 0.6601$).

Table 1: Descriptive analysis of the sample according to certain parameters and groups

Group	(Means)	Number	Standard deviation (Std.Dev.)	Minimum (Min)	Maximum (Max)	Median (IQR)
Age						
Examination	62.33	80	7.68	49	84	61 (56-67)
Control	64.37	40	7.51	52	79	65 (57.5-68)
Years in menopause						
Examination	11.97	80	6.01	3	30	10 (7.5-15)
Control	11.85	40	4.03	5	18	11.5 (8-15)
BMI						
Examination	29.46	80	5.42	14.9	42.7	29.7 (26-32.3)
Control	28.66	40	3.85	21.8	41.4	28.2 (26.1-30.3)

In the whole sample, the majority of the respondents were married 115 (95.8%), 1 (0.8%) were single, and 4 (3.3%) divorced (Table 1). For $p > 0.05$, no significant association was found between the group and the marital status of the subjects (Fisher-Freeman-Halton exact test: $p = 0.9999$).

Both the examination and the control group are dominated by the majority of respondents who are non-smokers, and consequently, 52 (65%) v.s. 30 (75%) (Table 1). For $p > 0.05$, there is no statistically significant association between the group to which the examinees belong and the smoking status (Pearson Chi-square test = 0.2323; df = 1; $p = 0.2669$).

Patients in the examined group had an average BMI of 29.5 ± 5.4, and those of the control 28.7 ± 3.8 without a significant difference between the two groups compared to this parameter (Student's t-test for independent sample = 0.8346; df = 118; $p = 0.4056$) (Table 1).

Endometrial analysis

The average thickness of the endometrium in the examined group was 10.8 ± 5.6 mm with a minimum thickness of 6mm and a maximum thickness of 32mm while in the control group it was 2.7 ± 0.8 mm with a minimum thickness of 1mm and a maximum thickness of 4.5 mm (Table 2). According to the median analysis, 50% of the patients in the control or examination group had endometrium thickness greater than the corresponding IQR = 2.8 mm (2-3) v.s. IQR = 9mm (7-12). The analysis, for p < 0.05, indicated a significant difference between the examinees of both groups in terms of endometrial thickness (Mann-Whitney U Test: Z = 8.907235 p = 0.00001) in favour of a significantly thicker endometrium in the assay group.

Table 2: Analysis of the thickness of the endometrium (mm) in the control and examination group

Group	N	X ± sd	Minimum (min)	Maximum (max)	Mediana (iqr)
Examination	80	10.8 ± 5.6	6	32	9 (7 – 12)
Control	40	2.7 ± 0.8	1	4.5	2.8 (2 – 3)

Mann-Whitney U Test: Z = 8.907235; p = 0.00001; ** Significant for p < 0.05.

According to the results of the ultrasound-ultrasound measurement of the thickness of the endometrium, the examination group (N = 80 patients) was divided into three subgroups: (a) 5-8 mm with a total of 36 (45%) patients; (b) < 8-11 mm with a total of 17 (21.25%) patients; and (c) < 11 mm with a total of 27 (33.75%) patients (Table 3).

Table 3: Division in subgroups of the examination group by endometrial thickness

Subgroups by the thickness of the endometrium (mm)	Number	%
5-8	36	45
> 8-11	17	21.2
> 11	27	33.7
Total value	80	100%

In the control group, the average thickness of the endometrium was 2.7 ± 0.8 mm, with a minimum thickness of 1mm and a maximum thickness of 4.5 mm. In the first subgroup with thickness of endometrium 5-8mm, the average thickness of the endometrium was 6.9 ± 0.9 mm with a minimum of 6.0 mm and a maximum of 8.0 mm. According to the media analysis, 50% of patients in this subgroup have an endometrial thickness greater than IQR = 7 mm (5-8 mm). In the second subgroup with an endometrial thickness of 8.0-11.0 mm, the average thickness of the endometrium was 9.4 ± 0.5 mm with a minimum of 9mm and a maximum thickness of 10mm. According to the analysis of the media, 50% of patients in this subgroup have an endometrial thickness greater than IQR = 9 mm (9.0-10.0 mm). In the third subgroup with a thickness of endometrium > 11 mm, the average endometrium thickness was 16.8 ± 5.8 mm with a minimum of 11 mm and a maximum of 32 mm. According to the median analysis, 50% of patients in this subgroup had an endometrial thickness greater than IQR = 14 mm (12.0 -22.0 mm) (Table 3).

Table 4: Thickness of endometrium (mm) in subgroups of the examination group

Subgroups	The thickness of the endometrium (mm)	N	X ± SD	Minimum	Maximum	Median (IQR)
Subgroup 1	5 – 8	36	6.90 ± 0.88	6	8	7 (5 – 8)
Subgroup 2	> 8 – 11	17	9.40 ± 0.49	9	10	9 (9 – 10)
Subgroup 3	> 11	27	16.82 ± 5.82	11	32	14 (12 – 22)

For p < 0.05, a significant difference was found between the three subgroups of the examinated group compared to the thickness of the endometrium (Kruskal-Wallis ANOVA: H = 68.967; p = 0.00001). The individual subgroup analysis, for p < 0.05, indicated a significant difference between the first and second , first and third vs. the second and third subunits for consequently Mann-Whitney U Test: Z = -5.831; p = 0.00001 vs. Mann-Whitney U Test: Z = -6,750; p = 0.00001 vs. Mann-Whitney U Test: Z = -5.532; p = 0.00001 (Table 4).

Table 5: Binary logistic regression analysis of the predictive role of endometrial thickness for prediction of endometrial malignancy

Variable	B	S.E.	Wald	Df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
The thickness of endometrium about unit thickness of endometrium								
endometrium (mm)	0.164	0.052	10.073	1	0.002*	1.178	1.065	1.304
Endometrium thickness - reference category / < 5mm								
5 mm -8 mm	1.897	1.381	2.864	1	0.049*	1.012	1.014	3.549
>8 mm - 11 mm	2.377	1.164	4.167	1	0.041*	1.769	1.099	5.488
>11 mm	2.690	1.098	6.001	1	0.014*	4.737	1.712	12.840

* Significant for p < 0.05.

The thickness of the endometrium is a significant predictor of endometrial malignancy (p < 0.05). With each millimeter an increase in endometrium, the likelihood of endometrial malignancy increases significantly by 1,178 [p = 0.002, 95% CI = 1.065-1.304] times. Compared to patients with a thickness of endometrium < 5 mm, binary logistic regression indicated that the probability of endometrial cancer was for: a) 1.012 [p = 0.049, 95% CI = 1.014-3.549] times greater in endometrial thickness of 5-8 mm; b) 1.769 [p = 0.041, 95% CI = 1.099-5.488] times greater in endometrial thickness > 8-11 mm; and c) 4.737 [p = 0.014, 95% CI = 1.712-12.840] times greater in patients with an endometrial thickness of > 11 mm (Table 5).

Discussion

The results of this study showed that with an increase in unit endometrium, the likelihood of malignancy increased by 1,178. Namely, an increase in the thickness of the endometrium by 1 mm relative to the control group significantly increases the likelihood of endometrial malignancy in patients with endometrial thickness from 5-8 mm in 1,012 times, in

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those with an endometrium thickness of 8-11 mm in 1,769 times, while in patients with endometrial thickness > 11 mm, the likelihood of endometrial cancer is greatest and increases by 4,737 times in relation to control. The results of this study correlate with the relevant literature concerned.

Thus, in the study of Smith-Bindman et al. in which correlation between endometrial thickness and endometrial cancer risk was examined, a 6.7% risk of endometrial malignancy was found in patients with an endometrial thickness of over 11 mm and a 0.002% risk of endometrial thickness below 11 mm (10).

In conclusion, the thickness of the endometrium is a significant predictor of endometrial malignancy. With each millimetre, an increase in the endometrium significantly increases the likelihood of endometrial malignancy for:

-Enlargement for a unit of the endometrium, the risk of endometrial malignancy increases by 1.178 times.

-1.012 times [p = 0.002, 95% CI = 1.065-1.304] in the group with a thickness of the endometrium of 5-8 mm relative to the control.

-1.769 times [p = 0.041, 95% CI = 1.099-5.488] in the endometrial thickness group of 8-11 mm in terms of control.

-4.737 times [p = 0.014, 95% CI = 1.712-12.840] in the group with an endometrial thickness of over 11 mm relative to the control group.

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