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Investigation of risk factors for benign or malignant endometrial pathology in patients presenting with abnormal uterine bleeding

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ABSTRACT

Aims: The aim of this study was to determine the risk factors associated with benign or malignant endometrial pathologies by comparing endometrial biopsy results of women presenting with abnormal uterine bleeding (AUB).

Methods: In this cross-sectional study using retrospective record review method, 100 women over 18 years of age who presented to the gynecology and obstetrics clinic with AUB and underwent endometrial biopsy were included. Age, body mass index (BMI), obstetric and gynaecological history, medical history and pathology results were recorded. Endometrial pathology results were classified as normal, benign and malignant. The effects of demographic and clinical characteristics of the patients on the risk of benign and malignant pathology were analysed.

Results: The mean age and BMI of the participants were 48.7±7.7 and 29.3±5.9 kg/m2, respectively. 59 (59.0%) of the patients were in the premenopausal period and 41 (41.0%) were in the postmenopausal period. Ultrasonographic endometrial thickness was below 8 mm in 23 patients (23.0%), between 8-11 mm in 27 patients (27.0%) and 12 mm or more in 50 patients (50.0%). Pathological results were normal in 35 patients (35%), benign pathology in 45 patients (45.0%) and malignant pathology in 20 patients (20.0%). In multivariate analyses, each 1 year increase in the age of the patients increased the risk of developing malignant endometrial pathology 1.17 times and each 1 mm increase in ultrasonographic endometrial thickness increased the risk of developing malignant endometrial pathology 1.16 times. The cut-off point for ultrasonographic endometrial thickness was found to be >12 mm. According to this cut-off point, the sensitivity and specificity of ultrasonographic endometrial thickness in predicting endometrial pathology were found to be 70% and 62.9%, respectively.

Conclusion: It is important to determine the risk factors of malignant disease in women presenting with AUB and to perform invasive methods such as endometrial biopsy in the early period in women with risk factors to affect the success of treatment directly.

Keywords: Abnormal uterine bleeding, endometrial biopsy, benign pathology, malignant pathology, endometrial cancer

INTRODUCTION

Abnormal uterine bleeding (AUB) is one of the most common clinical conditions requiring gynaecological evaluation worldwide.[1] It constitutes one-third of the admissions to gynecology outpatient clinics, and women in premenopausal, perimenopausal and postmenopausal periods may present with AUB.[2] From menarche to menopause. 9 to 14 per cent of all women have a clinical picture of ACS, which has significant effects on the quality of life of patients and may lead to economic losses.[3]

It has been reported that AUB may occur as a result of structural or non-structural uterine diseases. In 2011, the International Federation of Gynecologists and Obstetrics (FIGO) established the PALM-COEIN classification to define AUB pictures and prevent inconsistencies in terminology in the literature.[4] With this classification, PALM refers to structural causes such as polyps, adenomyosis, leiomyoma and malignancy, while COEIN refers to coagulopathy, ovulatory dysfunction, endometrial causes, iatrogenic causes and unclassified pathologies.[4,5] It has been found that most AUBs are not associated with a premalignant or malignant lesion. However, it is reported that AUBs especially in the postmenopausal period and premenopausal AUBs with additional risk factors may be associated with endometrial cancer. Therefore, women presenting with AUB require additional evaluation for endometrial cancer.[6]

AUB is an important clinical presentation seen in premenopausal, perimenopausal and postmenopausal women and constitutes a significant proportion of

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admissions to gynecology outpatient clinics.[7] Studies have shown that most AUBs are not associated with a premalignant or malignant lesion. However, it has been reported that especially postmenopausal women with AUB and premenopausal women with AUB with additional risk factors should be evaluated for endometrial cancer.[6] In the literature, many studies aim to determine the aetiology of bleeding in women presenting with AUB. In these studies, the PALM-COIN classification was created to eliminate the terminology confusion and to create a common language and the etiological factors were revealed with this classification.[8,9] However. studies investigating the risk factors associated with benign or malignant lesions in women presenting with AUB are limited. Our aim was to determine the risk factors associated with benign or malignant endometrial pathologies by comparing endometrial biopsy results of women presenting to a university hospital with AUB.

METHODS

Ethical Aspects of the Study

Ethics committee approval was obtained from Adıyaman University Non-interventional Clinical Researches Ethics Committee (Date: 22.09.2020, Decision No: 2020/08-21) and institutional permission was obtained from the institution where the study was conducted before the study was started. The research was conducted by the Declaration of Helsinki at all stages from design to reporting. The data and information obtained in the study were not used for other than scientific purposes.

Objective

This study aimed to determine the risk factors associated with benign or malignant endometrial pathologies by comparing the results of endometrial biopsy of women presenting to a university hospital with AUB.

Study Methodology

This cross-sectional epidemiological study using a single-centre retrospective record review method was conducted in a university hospital's Gynecology and Obstetrics Clinic. The study data was screened so that the timeline will be between 01.11.2020-10.05.2021.

Population and Sample of the Study

The population of the study consisted of women over the age of 18 who applied to our clinic with the complaint of AUB and underwent endometrial biopsy. In this hospital, approximately 62.000 outpatient obstetrics and gynecology patients were admitted to the Obstetrics and Gynecology Clinic annually, 9.700 inpatients were followed up, approximately 2.000 gynaecological operations. 3.600 deliveries and 2.700 caesarean sections were performed between 01.12.2007-31.10.2020.

The sample size was not calculated before the study. and all women who met the inclusion and exclusion criteria between the study dates were included in the study between 01.11.2020-10.05.2021. During the study period, 350 patients were examined for participation in the study. 150 patients did not meet the inclusion criteria. 48 met the exclusion criteria and 52 patients were excluded due to missing data. As a result, data from 100 patients were included in the analysis.

The inclusion criteria were being 18 years of age or older, presenting with the complaint of AUB, having endometrial biopsy, not being pregnant, and having no cervical pathology, while the exclusion criteria were previous removal of the uterus, having a known history of gynaecological cancer before probe curettage, and having missing data for the study variables.

Data Collection

The data collection form used in the study consisted of 15 questions including age, body-mass index (BMI), obstetric and gynaecological history, medical history and pathology results.

Those who had a history of hereditary breast cancer. ovarian cancer. endometrial cancer and colon cancer in themselves and/or in their family were considered to have a positive cancer history and/or a positive family history of cancer.

Participants were grouped as underweight if their BMI values were below 18.5 kg/m^2, normal weight if they were between 18.5-25 kg/m^2, overweight if they were between 25.0-30.0 kg/m^2, and obese if they were 30.0 kg/m^2 and above.

GE Voluson P8 USG system (GE Healthcare, USA) was used for ultrasonographic endometrial thickness measurement. In the literature. in studies examining the relationship between ultrasonographic endometrial thickness and malignant pathologies in symptomatic or asymptomatic women, the cut-off point was taken at values ranging between 8-15 mm in premenopausal women[10], while it was taken at values ranging between 3-8 mm in postmenopausal women.[11] Since we included premenopausal and postmenopausal women in our study, ultrasonographic endometrial thickness was grouped as less than 8 mm, 8-12 mm and 12 mm or more in descriptive statistics.

Endometrial pathology results were classified as normal, benign and malignant. Pathological examination of the preparations obtained from endometrial biopsy was analysed in the laboratories of the Department of Medical Pathology of the university. Pathological examination was performed with 40X and 100X magnification

using Olympus BX53. Olympus CX41 and Olympus CX31 (Olympus Corporation, Japan) microscopes after hematoxylin-eosin staining.

Procedure

In the study. a retrospective archive search was performed by the researcher himself between 01.12.2007-31.10.2020.

Statistical Analysis

SPSS version 20.0 and MedCalc version 15 statistical package programs were used for data analysis. Mean±standard deviation. median and minimum-maximum values were used for continuous numerical variables and number and percentage were used for categorical variables. The conformity of the numerical variables to normal distribution was checked by Kolmogorov-Smirnov and Shapiro-Wilk tests. Univariate and multivariate logistic regression analysis was used to analyse the risk of benign and malignant endometrial pathology. In regression analysis, univariate analysis was used first. Multivariate analysis was performed with the factors found to be statistically significant in univariate analyses. Odds Ratio (OR) and 95% confidence interval (95% CI) were calculated to evaluate the risk. ROC analysis was used to determine the cut-off point for ultrasonographic endometrial thickness to predict the development of endometrial pathology. The statistical significance limit value $p<0.05$ was accepted.

RESULTS

Among the women in the study. 8 (8.0%) were under 40 years of age, 55 (55.0%) were between 40-49 years of age. 30 (30.0%) were between 50-59 years of age and 7 (7.0%) were 60 years of age or older. and the mean age was 48.7±7.7 years. While 29 (29.0%) of the women were normal weight. 36 (36.0%) were overweight and 35 (35.0%) were obese, the mean BMI was 29.3±5.9 kg/m^2 (**Table 1**).

Hypertension was found in 20 (20.0%). DM in 14 (14.0%). cancer history in 13 (13.0%) and family history of cancer in 18 (18.0%) of the women (**Table 1**).

While 2 (2.0%) of the women had never been pregnant. the median number of pregnancies was found to be 4. In addition. the parity was 0 in 3 patients (3.0%) and the median parity was 4 (**Table 1**).

59 (59.0%) of the patients were in premenopausal period and 41 (41.0%) were in the postmenopausal period. In addition. 1 patient (1.0%) had polycystic ovary syndrome, 22 patients (22.0%) had myoma uteri, 9 patients (9.0%) had intrauterine device and 11 patients (11.0%) had infertility. Ultrasonographic endometrial thickness was below 8 mm in 23 patients (23.0%), between 8-11 mm in 27 patients (27.0%) and 12 mm or more in 50 patients (50.0%). The mean endometrial thickness was 12.9±6.1 mm (**Table 1**).

Pathology results were normal in 35 patients (35%). benign pathology in 45 patients (45.0%) and malignant pathology in 20 patients (20.0%). 15 (42.9%) of 35 patients with normal pathology results had irregular proliferative endometrium. 12 (34.3%) had endometrial destruction findings and 8 (22.9%) had secretory endometrial findings. Of 45 patients with benign pathology. 18 (40.0%) had endometrial polyps. 16 (35.6%) had endometritis. 10 (22.2%) had simple atypical hyperplasia and 1 (2.2%) had myoma uteri. Of the 20 patients with malignant pathology, 11 (55.50%) had endometrioid adenocarcinoma, 5 (25.0%) endometrioid intraepithelial neoplasia. 1 (5.0%) carcinosarcoma. 1 (5.0%) metastasis, 1 (5.0%) serous cystadenoma and 1 (5.0%) clear cell carcinoma (**Table 1**).

Accordingly, age, BMI, presence of hypertension. presence of DM, history of cancer, family history of cancer, number of pregnancies, number of parities, menopausal status, presence of PCOS, presence of myoma uteri, presence of IUD, presence of infertility and USG endometrial thickness had no statistically significant effect on the risk of benign pathological development (**Table 2**).

Each year increase in the age of the patients statistically significantly increased the risk of malignant pathology development by 1.16 times (p=0.002). In addition, the presence of DM statistically significantly increased the risk of malignant pathology by 7.07 times (p=0.026). Past cancer history of the patient statistically significantly increased the risk of developing malignant endometrial pathology by 4.17 times (p=0.044). Postmenopausal patients are statistically significantly 4.33 times more at risk of developing malignant pathology than premenopausal patients (p=0.014). In addition, each 1 mm increase in ultrasonographic endometrial thickness statistically significantly increased the risk of developing malignant endometrial pathology by 1.13 times (p=0.019). BMI, presence of hypertension. history of cancer. family history of cancer, pregnancy, parity, history of PCOS, myoma uteri, IUD and infertility were not found to be associated with the risk of developing malignant pathology (**Table 3**).

In the multivariate logistic regression analysis performed with the risk factors found statistically significant in univariate analyses. age and ultrasonographic endometrial thickness were found statistically significant in terms of the risk of developing malignant endometrial pathology. Accordingly, each 1-year increase in the age of the patients increased the risk of developing malignant endometrial pathology by 1.17 times (p=0.025). which was statistically significant and independent of the

Table 1. The demographic. anthropometric. medical. obstetric. gynaecological and pathological characteristics of women					
Feature		**n**	**%**	**$\bar{X}$±SD Med**	**Min-Max**
Demographic and anthropometric characteristics of women					
Age (year)	Under 40 years old	8	8.0		
	40-49 years old	55	55.0	48.7±7.7	33.0-76.0
	50-59 years old	30	30.0	47.5	
	60 years and over	7	7.0		
BMI	Normal weight	29	29.0		
	Overweight	36	36.0	29.3±5.9	20.0-49.0
	Obese	35	35.0	29.0	
		100	100.0		
Women's medical history					
Hypertension	None	80	80.0		
	There is	20	20.0		
DM	None	86	86.0		
	There is	14	14.0		
History of cancer	None	87	87.0		
	There is	13	13.0		
Family history of cancer	None	82	82.0		
	There is	18	18.0		
		100	100.0		
Obstetric characteristics of women					
Pregnancy	0	2	2.0		
	1	3	3.0		
	2	7	7.0	4.9±2.4	0.0-11.0
	3	18	18.0	4.0	
	4 and over	70	70.0		
Parity	0	3	3.0		
	1	3	3.0		
	2	10	10.0	4.2±2.1	0.0-10.0
	3	30	30.0	4.0	
	4 and over	64	64.0		
		100	100.0		
Gynaecological characteristics of women					
Menopausal status	Premenopausal	59	59.0		
	Postmenopausal	41	41.0		
History of polycystic ovary syndrome	None	99	99.0		
	There is	1	1.0		
Myoma uteri	None	78	78.0		
	There is	22	22.0		
Intrauterine device	None	91	91.0		
	There is	9	9.0		
History of infertility	None	89	89.0		
	There is	11	11.0		
Ultrasonographic endometrium thickness (mm)	Under 8 mm	23	23.0		
	between 8-11 mm	27	27.0		
	12 mm and above	50	50.0		
Ultrasonographic endometrium thickness (mm)				12.9±6.11.5	15.0-34.0
Results of pathology of women		100	100.0		
Pathological result (n=100)	Normal	35		35.0	
	Benign	45		45.0	
	Malignant	20		20.0	
Normal pathology (n=35)	Irregular proliferative endometrium	15		42.9	
	Signs of endometrial destruction	12		34.3	
	Secretory endometrium	8		22.9	
Benign pathology (n=45)	Endometrial polyp	18		40.0	
	Endometritis	16		35.6	
	Simple atypical hyperplasia	10		22.2	
	Myoma uteri	1		2.2	
Malignant pathology (n=20	Endometrioid adenocarcinoma	11		55.0	
	Endometrioid intraepithelial neoplasia	5		25.0	
	Carcinosarcoma	1		5.0	
	Metastasis	1		5.0	
	Serous cystadenoma	1		5.0	
	Transparent cell carcinoma	1		5.0	

SD: Standard deviation, BMI: Body-mass index, Med: Median, Min: Minimum, Max: Maximum

Table 2. Univariate analysis of factors affecting the development of benign endometrial pathology

Feature (n=80)		Risk of benign pathology OR (95% GA)	p*
Age (years)		**1.02 (0.94-1.10)**	**0.648**
BMI (kg/m²)		0.99 (0.92-1.07)	0.779
Hypertension	None	-	0.370
	There is	1.71 (0.53-5.57)	
DM	None	-	0.273
	There is	2.54 (0.48-13.43)	
History of cancer	None	-	0.256
	There is	0.36 (0.06-2.09)	
Family history of cancer	None	-	0.433
	There is	1.67 (0.46-6.10)	
Pregnancy		0.94 (0.77-1.15)	0.551
Parity		0.91 (0.72-1.16)	0.448
Menopausal status	Premenopausal	-	0.087
	Postmenopausal	2.31 (0.89-6.03)	
History of polycystic ovarian dysplasia	None	-	n.a.
	There is	n.a.	
Myoma uteri	None	-	0.225
	There is	0.51 (0.17-1.52)	
Intrauterine device	None	-	0.270
	There is	0.43 (0.09-1.93)	
History of infertility	None	-	0.245
	There is	2.31 (0.56-9.43)	
USG endometrium thickness (mm)		0.98 (0.90-1.07)	0.668

* Multivariate logistic regression analysis was performed, OR: Odds Ratio, BMI: Body-mass index

Table 3. Univariate analysis of factors affecting the development of malignant endometrial pathology

Feature (n=55)		Risk of malignant pathology OR (95% GA)	p*
Age (years)		1.16 (1.06-1.27)	0.002
BMI (kg/m²)		1.03 (0.95-1.11)	0.527
Hypertension	None	-	0.327
	There is	2.00 (0.50-7.99)	
DM	None	-	0.026
	There is	7.07 (1.27-39.41)	
History of cancer	None	-	0.044
	There is	4.17 (1.04-16.73)	
Family history of cancer	None	-	0.096
	There is	3.32 (0.81-13.66)	
Pregnancy		0.94 (0.77-1.15)	0.551
Parity		0.91 (0.72-1.16)	0.448
Menopausal status	Premenopausal	-	0.014
	Postmenopausal	4.33 (1.34-13.99)	
History of polycystic ovarian dysplasia	None	-	n.a.
	There is	n.a.	
Myoma uteri	None	-	0.836
	There is	1.17 (0.26-5.31)	
Intrauterine device	None	-	0.309
	There is	0.32 (0.03-2.92)	
History of infertility	None	-	n.a.
	There is	n.a.	
USG endometrium thickness (mm)		1.13 (1.02-1.25)	0.019

* Multivariate logistic regression analysis was performed, OR: Odds Ratio, BMI: Body-mass index

presence of DM, menopausal status and ultrasonographic endometrial thickness. In addition, each 1 mm increase in ultrasonographic endometrial thickness increased the risk of developing malignant endometrial pathology by 1.16 times (p=0.043), which was statistically significant and independent of age. DM status and menopausal status (**Table 4**).

The cut-off point for ultrasonographic endometrial thickness was found to be >12 mm. According to this cut-off point. the sensitivity and specificity of ultrasonographic endometrial thickness in predicting endometrial pathology were found to be 70% and 62.9%. respectively (**Table 5** and **Figure 1**).

Table 4. Multivariate analysis of factors affecting the development of malignant endometrial pathology

Feature (n=55)		Risk of malignant pathology Adjusted OR (95% GA)	p*
Age (years)		1.17 (1.02-1.33)	0.025
DM	None	-	0.194
History of cancer	There is	5.09 (0.44-59.41)	
Menopausal status	None	-	0.100
USG endometrium thickness (mm)	There is	4.87 (0.74-32.21)	
Age (years)	Premenopausal	-	0.745
DM	Postmenopausal	0.747 (0.13-4.31)	
History of cancer		1.16 (1.01-1.33)	0.043

* Multivariate logistic regression analysis was performed, OR: Odds Ratio

Table 5. ROC analysis and cut-off point of ultrasonographic endometrial thickness values in the detection of malignant endometrial pathology

Criterion	Ultrasonographic endometrial thickness (mm)
Area under the curve (95% CI)	0.680 (0.540-0.799)
Cut-off point	>12
Sensitivity (95% CI)	70.0 (45.7-88.1)
Specificity (95% CI)	62.9 (44.9-78.5)

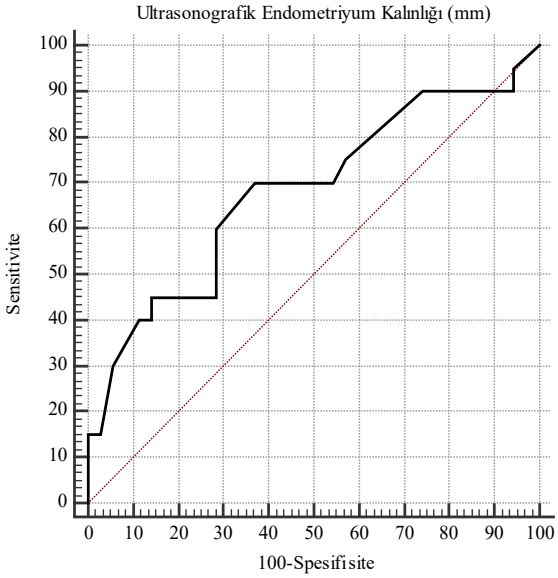

Figure 1. ROC curve of ultrasonographic endometrial thickness in the detection of malignant endometrial pathology

Multivariate logistic regression analysis was performed again according to the risk factors which were found to be statistically significant in univariate analyses and according to being below or above the 12 mm cut-off point found in the ROC analysis for USG endometrial thickness. Accordingly. those with USG endometrial thickness above 12 mm had a statistically significant 5.73-fold higher risk of developing malignant endometrial pathology than those with USG endometrial thickness of 12 mm and below (p=0.034) (**Table 6**).

Table 6. Multivariate analysis of factors affecting the development of malignant endometrial pathology

Feature (n=55)		Risk of malignant pathology Adjusted OR (95% GA)	p*
Age (years)		1.13 (0.99-1.27)	0.063
DM	None	-	0.215
History of cancer	There is	4.78 (0.40-56.46)	
Menopausal status	None	-	0.131
USG endometrium thickness	There is	4.35 (0.65-29.31)	
Age (years)	Premenopausal	-	0.683
DM	Postmenopausal	1.42 (0.26-7.77)	
History of cancer	12 mm and below	-	0.034
	Over 12 mm	5.73 (1.14-28.73)	

* Multivariate logistic regression analysis was performed.

DISCUSSION

According to our study results. each year increase in the age of the patients statistically significantly increased the risk of developing malignant pathology. The presence of DM and past cancer history statistically significantly increased the risk of malignant pathology. Postmenopausal patients were found to be at statistically significantly higher risk of developing malignant pathology than premenopausal patients. Each 1 mm increase in USG endometrial thickness significantly increased the risk of developing malignant endometrial pathology. In multivariate logistic regression analysis. age and ultrasonographic endometrial thickness were found to be statistically significant for the risk of developing malignant endometrial pathology. Each 1 mm increase in USG endometrial thickness increased the risk of developing malignant endometrial pathology. The risk of developing malignant endometrial pathology was found to be statistically significantly higher in women with USG endometrial thickness above 12 mm than in women with USG endometrial thickness of 12 mm or less.

In the multivariate analyses performed according to the findings of the study. each 1 year increase in the age of the patients increased the risk of developing malignant endometrial pathology 1.17 times, and each 1 mm increase in ultrasonographic endometrial thickness increased the risk of developing malignant endometrial pathology 1.16 times. The cut-off point for ultrasonographic endometrial thickness was found to be >12 mm. According to this cut-off point. the sensitivity and specificity of ultrasonographic endometrial thickness in predicting endometrial pathology were found to be 70% and 62.9%. respectively.

Iatrogenic causes and polyps were found to be the most common etiological causes in women presenting with AUB.[12] Apart from this, leiomyomas were found to be the other common etiology of AUB.[13] A history of leiomyoma was present in 22 (22%) of the women included in this study.

In the studies in the literature. PCOS is one of the causes of AUB in women in the reproductive period and is among the etiological causes included in the PALM-COIN classification. In different studies. it has been reported to be detected in 1.3%-19% patients.[12,14] In a meta-analysis study published by Amiri et al.[15] it was found that the risk of endometrial cancer was higher in women with PCOS compared to those without PCOS in all age groups. In this study, only 1 of the women had a history of PCOS. Therefore. it was not identified as a risk factor. In our study, the etiological factors of AUB were not grouped according to the PALM-COIN classification. unlike many studies presented above. In this study. the etiological causes were presented from the

perspective of benign and malignant causes and the risk factors associated with both benign causes and especially malignant etiologies were investigated. When the studies in the literature are analysed. it is seen that benign endometrial pathologies such as polyps. leiomyomas and endometrial hyperplasia are between 24% and 70% of the etiology of AUB.[16,17] In this study, benign pathology was observed in 45% of the patients by the literature.

When malignant pathologies are analysed in the etiology of AUB. It is seen that age is an important factor. Under the age of 50 years. malignant pathology was found in less than 1% of patients. whereas it was found in 10% to 15% of women over the age of 50 years.[18] As expected in this study. age was not found to be a risk factor for benign pathologies by univariate analysis. whereas it was found to be a risk factor for malignant pathologies. Each year increase in the age of the patients was found to increase the risk of malignant pathology development statistically significantly by 1.16 times. In multivariate logistic regression analysis. age was found to be an independent risk factor for the risk of developing malignant endometrial pathology. According to the results of our analysis. each 1-year increase in the age of women statistically significantly increased the risk of developing malignant endometrial pathology by 1.17 times.

Studies have reported that endometrial cancers are more common in postmenopausal women. In a recent study by Clarke et al.[19] the prevalence of endometrial cancer in postmenopausal women was found to be 7.9%. which is approximately 6.5 times (1.2%) higher than premenopausal and perimenopausal women. In this study. in accordance with the literature. the risk of developing malignant pathology in postmenopausal women was found to be statistically significantly 4.33 times higher than in premenopausal women.

In other studies in which endometrial hyperplasia and endometrial cancer risk factors were evaluated. obesity. PCOS. nulliparity and diabetes mellitus were reported as risk factors.[8] Harvey et al.[20] reported that high BMI increased the risk of endometrial cancer in a study. In this study. BMI was not found to be a risk factor for benign and malignant pathologies. When compared with the literature data. we think that the small number of patients in this study was effective in these results. In a metanalysis published by McVicker et al.[21] a significant association between diabetes and endometrial cancer was shown. In this study. it was determined by univariate analysis that the presence of DM increased the risk of malignant pathology statistically significantly by 7.07 times (p=0.026). DM was not found to be a risk factor in multivariate analysis.

In a study conducted by Main et al.[22] it was reported that having at least one or more children significantly decreased the risk of endometrial cancer compared with nulliparity. In the same study. they reported that endometrial cancer RR decreased with the number of pregnancies. In this study. pregnancy and parity were not found to be risk factors for endometrial malignant pathologies. This result is thought to be due to the small number of patients. It has been reported that IUD use may be a factor among iatrogenic causes of AUB and that women give up IUD use because of AUB associated with IUD use.[23] In our study. IUD use was present in 9% of the patients. In our study. benign and malignant diseases risk factors of IUD use in women presenting with AUB were evaluated. IUD use was not found to be a risk factor for both benign and malignant conditions.

Measurement of endometrial thickness by ultrasonography is important in the evaluation of endometrial pathologies in both premenopausal and postmenopausal periods.[13] Studies have reported that endometrial thickness determined by ultrasonography in women of childbearing age is between nearly 4-8 mm in the proliferative phase and 8-14 mm in the secretory phase.[24] The American College of Obstetricians and Gynecologists (ACOG) and the Society of Radiologist in Ultrasound (SRU) consider an endometrial thickness of <4 mm and <5 mm respectively as normal for postmenopausal women. It is stated that the risk of malignancy is quite low under these limit values.[25] In this study. ultrasonographic endometrial thickness was found to be below 8 mm in 23 patients (23.0%). between 8-11 mm in 27 patients (27.0%) and 12 mm or more in 50 patients (50.0%). The mean endometrium thickness was found to be 12.9±6.1 mm.

Ultrasonography is the first examination performed in women presenting with AUB and is performed under emergency conditions. As explained in the previous sections. the phase of the menstrual cycle cannot be evaluated clearly in emergency conditions and this situation negatively affects the standardisation of USG evaluation.[26] Further analyses showed that endometrial thickness had no statistically significant effect on the risk of benign pathology development in our study. However. with univariate risk factor analysis. each 1 mm increase in endometrial thickness statistically significantly increased the risk of developing malignant endometrial pathology by 1.13 times. With multivariate risk factor analysis. each 1 mm increase in ultrasonographic endometrial thickness increases the risk of developing malignant endometrial pathology by 1.16 times in a statistically significant way and independent of age. DM presence and menopausal status.

Different studies in the literature have investigated the sensitivity and specificity of ultrasonography in detecting different clinical pathologies. Kılınç et al.[27] reported the sensitivity and specificity of USG in the diagnosis of endometrial polyp as 78.26% and 51.35%. respectively. In a study conducted by Saccardi et al.[28] patients with endometrial thickness ≥11 mm were compared with patients with endometrial thickness between 5-10 mm by transvainal USG. In the same study it was reported that the risk of endometrial cancer or endometrial hyperplasia with atypia was 2.6 times higher in women with endometrial thickness ≥11 mm than in women with endometrial thickness 5-10 mm. In another meta-analysis endometrial cancer risk was analysed according to the cut-off value of ultrasonographic endometrial thickness 5 mm in asymptomatic postmenopausal women. The sensitivity and specificity of transvaginal USG with a cut-off value of 5 mm were found to be 83% and 72%. respectively.[29] In this study, the cut-off point for ultrasonographic endometrial thickness was determined as >12 mm by ROC curve analysis. According to this cut-off point, the sensitivity and specificity of ultrasonographic endometrial thickness in predicting endometrial pathology were found to be 70% and 62.9%, respectively. It is seen that these values we found are similar to the studies in the literature in which various endometrial pathologies were evaluated ultrasonographically. In addition, in various studies investigating the role of USG in predicting endometrial pathologies, the factors affecting different sensitivity and specificity values were listed as the experience of the practitioner. menstrual periods of the patients. being in menopause and hormonal treatments.[29,30]

It has been reported that ultrasonography or hysteroscopy may not be sufficient to identify endometrial pathologies in women presenting with AUB.[30] In this context. evaluation with endometrial biopsy should be considered in patients aged 40 years and older presenting with AUB in whom the etiology cannot be determined or who do not respond to treatment. In this study. endometrial biopsy was performed in all women presenting with AUB along with ultrasonographic evaluation.

In conclusion. identification of malignant disease risk factors is an important step in women presenting with AUB. In women with risk factors, early application of invasive methods such as endometrial biopsy would be the appropriate approach. It is thought that this study contributed to the literature by investigating and revealing the risk factors of malignant disease.

Limitations

The small number of patients in the study can be considered as a limitation. In addition, the fact that the patients included in the study were not homogenous is one of the limitations of the study.

CONCLUSION

In conclusion, based on the correlation between age and ultrasonographic endometrial thickness and the development of malignant endometrial pathology, it is important to evaluate the patients in terms of possible malignant pathologies, especially in elderly women when the endometrial thickness measurement by USG is above 12 mm. In addition. it is predicted that determination of malignant disease risk factors in women presenting with AUB and early application of invasive methods such as endometrial biopsy in women with risk factors will directly affect the success of treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethics approval was obtained from Adıyaman University Non-interventional Clinical Researches Ethics Committee (Date: 22.09.2020, Decision No: 2020/08-21).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design. execution. and analysis of the paper. and that they have approved the final version.

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