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Original Research Article

Ultrasonographic observation of endometrial polyps induced by anti-estrogen endocrine therapy in patients with breast cancer

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Abstract

Purpose: *To investigate the ultrasonic characteristics of endometrial polyps in breast cancer patients after anti-estrogen endocrine therapy.*
Methods: *A total of 91 patients with endometrial polyps who had breast cancer surgery at Yantai Muping District Hospital of Traditional Chinese Medicine, Yantai, China between February 2021 and August 2023 were randomly assigned to study (n = 42) and control groups (n = 49) based on post-surgery anti-estrogen endocrine therapy. The study group received tamoxifen (20 mg orally once daily for 6 months). Control group did not receive any post-surgery anti-estrogen endocrine therapy. Ultrasound characteristics of the study and control groups were assessed and compared.*
Results: *The study group exhibited significantly increased endometrial thickness compared to control group ($p < 0.05$). However, both maximum and mean polyp diameters were significantly larger in the study group ($p < 0.05$). Linear endometrial echoes predominated in treated patients, contrasting with predominantly uniform echoes in the control group. Visualization issues of the uterine cavity line were significantly more common in the study group, while control group experienced more deviation and unclear visualization. Also, the study group mostly presented with strip-shaped polyps, differing from the round or oval shapes prevalent in control group. Furthermore, there were significant variations in internal echo characteristics and blood flow parameters between the two groups ($p < 0.05$).*
Conclusion: *Endometrial polyps caused by postoperative anti-estrogen endocrine therapy in patients with breast cancer have unique ultrasonic characteristics, good ultrasonic diagnostic effect and a high detection rate as long as it is detected early and treated on time. Further analyses are needed with a larger sample size to investigate the underlying mechanism involved in developing endometrial polyps.*

Keywords: *Breast cancer, Anti-estrogen endocrine therapy, Endometrial polyps, Ultrasonic feature*

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INTRODUCTION

Breast cancer is one of the most common malignancies in women, with its incidence increasing annually, making it a significant concern in women's health [1]. The disease is characterized by a tendency for distant metastasis, high recurrence rates, and poor prognosis [1,2]. Therefore, treatment needs to consider multiple factors to develop rational therapeutic strategies. Surgical resection is currently the primary treatment for breast cancer,

particularly in early-stage patients, where timely surgical intervention significantly improves cure rates and reduces risk of recurrence [2,3].

For individuals with hormone-dependent breast cancer, hormonal endocrine therapy is an effective adjuvant treatment [4]. Postoperative administration of anti-estrogenic drugs, such as selective estrogen receptor modulators (tamoxifen, raloxifene, and toremifene), is a common endocrine treatment strategy [5]. These drugs competitively bind to estrogen receptors, effectively reducing systemic estrogen levels, inducing apoptosis in estrogen receptor-positive tumor cells, and inhibiting cancer cell growth [6]. However, these drugs also exert certain effects on the endometrium, with their weak estrogenic effects potentially leading to growth and proliferation of endometrial cells, and resulting in varying degrees of endometrial pathologies. Higher incidence of postoperative endometrial polyps, which are benign growths of the lining of the uterus may cause irregular bleeding which would need to be removed surgically [6].

Endometrial polypoid lesions are benign growths that arise from the endometrial lining and vary in size and shape, potentially leading to symptoms such as irregular menstrual bleeding or postmenopausal bleeding. Traditional diagnostic methods for endometrial polypoid lesions include hysteroscopic examination and diagnostic curettage, which are invasive procedures [6]. However, ultrasound, as a non-invasive, rapid, and cost-effective imaging modality, has found widespread application in the diagnosis of gynecological diseases. Ultrasonography not only allows observation of uterine morphology but also enables detection of intracavitary masses, measurement of endometrial thickness, and assessment of endometrial blood flow parameters, demonstrating high safety and feasibility [6]. Therefore, this study investigated the ultrasonic characteristics of endometrial polyps in patients with breast cancer following anti-estrogenic endocrine therapy. The analysis and summary of these ultrasound features will contribute to enhancing the detection rate and diagnostic accuracy of postoperative endometrial polyps [7].

METHODS

Baseline characteristics

A total of 91 patients who underwent breast cancer surgery at Yantai Muping District Hospital of Traditional Chinese Medicine, Yantai, China from February 2021 to August 2023 and developed endometrial polyps were randomly assigned to study (n = 42) and control groups (n = 49). The study group received 20 mg tamoxifen (AstraZeneca, UK) orally once daily for 6 months. Patients' ages ranged from 32 to 61 years, with a mean age of 48.39 ± 12.94 years. Among them, 59 cases were classified as TNM (tumor, node, metastasis) stage I - II, and 32 cases were classified as stage III. Left-side surgery was performed in 42 cases, right-side surgery in 49 cases, and 36 cases had abnormal uterine bleeding [2].

Ethical matters

This study received approval from the Yantai Muping District Hospital of Traditional Chinese Medicine Ethics Committee (approval no. YTM0020230406) and was conducted in accordance with the guidelines of Declaration of Helsinki [8]. Informed consent was willingly given by the patients and guardians.

Inclusion criteria

Patients who underwent breast cancer surgery with a confirmed pathological diagnosis, received postoperative anti-estrogen endocrine therapy, and had a comprehensive ultrasound examination including two-dimensional, color Doppler, spectral Doppler, and hysteroscopic three-dimensional imaging before hormonal therapy.

Exclusion criteria

Patients allergic to the study drugs, those with unclear ultrasound images, missing data, concurrent hematological disorders, recent use of other hormone-related medications, presence of an intrauterine device, or concurrent uterine diseases.

Ultrasound imaging

The GE LOGIQ E10 color Doppler ultrasound diagnostic instrument was used, employing a 7.5 MHz intracavitary three-dimensional volume probe [5]. Patients emptied their bladders before examination, assumed the lithotomy position, were routinely disinfected, and a disposable sterile contraceptive cover was applied to the probe, which was lubricated with disinfectant gel before slowly inserting it into the patient's vagina for multidimensional, multi-angle continuous scanning. Color Doppler and spectral Doppler were utilized to observe and obtain images of the uterus, endometrium, polyps, and bilateral adnexa. The focus was on evaluating endometrial thickness, polyp diameter, shape, internal echo, and blood flow distribution inside

and around the lesion. Arterial Doppler spectra and resistance indices were recorded, and images were standardized and preserved.

Evaluation of parameters/indices

Uterine bleeding

Abnormal uterine bleeding was documented based on patient reports of irregular bleeding patterns, such as heavy menstrual bleeding, intermenstrual bleeding, or postmenopausal bleeding.

Endometrial echo and thickness

Endometrial echo and thickness were measured using transvaginal ultrasound, with the thickness assessed in the sagittal plane at its thickest point and echo texture noted as homogeneous or heterogeneous.

Hysteroscopy

The uterine cavity lining was evaluated through hysteroscopy, allowing direct visualization of the cavity and assessment for smoothness, irregularities, or the presence of lesions.

Ultrasound measurements

Polyp maximum and mean diameters were determined using ultrasound measurements of three dimensions: maximum diameter (longest dimension), anterior-posterior diameter, and transverse diameter, and the mean value was computed.

Polyp morphology

Polyp morphology was classified based on the ratio of polyp's maximum length to its anterior-posterior diameter, with elongated polyps having a ratio of ≥ 2.5, circular polyps having a ratio of ≤ 1.5, and elliptical polyps having a ratio between > 1.5 and < 2.0.

Polyp internal echo

Polyp internal echo was assessed via ultrasound to determine the internal texture, with homogeneous internal echo indicating uniform tissue structure and heterogeneous internal echo suggesting varied tissue composition.

Color Doppler ultrasound

This was used to evaluate blood flow distribution within the polyp, recording the presence and pattern of blood flow (central or peripheral). Peak flow velocity, indicating the maximum speed of blood flow within vessels supplying the polyp, was measured in cm/s using spectral Doppler ultrasound.

The resistance index (RI)

This was also determined using spectral Doppler ultrasound, providing information on resistance to blood flow within the vessels. Each parameter was systematically investigated using these methods, ensuring a comprehensive assessment of endometrial polyps and their characteristics [7].

Statistical analysis

Statistical analysis was conducted using Statistic Package for Social Science (SPSS) 26.0 software (IBM, Armonk, NY, USA). Count data were expressed as n (%), and group comparisons were made using Chi-square test. Measurement data were presented as mean ± standard deviation (SD) and group comparisons were made using independent sample t-tests. $P < 0.05$ was considered statistically significant.

RESULTS

Baseline characteristics

There were no significant differences in age, TNM stage, surgical site, and abnormal uterine bleeding between the two groups ($p > 0.05$; Table 1).

Two-dimensional imaging findings

The uterine endometrial thickness, maximum and average diameters of polyps in study group were significantly higher in study group ($p < 0.05$) compared to control group. Furthermore, there were significant differences in endometrial echo number, uterine cavity line, polyp morphology and polyp echo between study and control groups ($p < 0.05$; Table 2).

Doppler spectrum

Study group exhibited significantly higher peak flow velocity and resistance index compared to control group ($p < 0.05$; Table 3).

Color doppler blood flow distribution

There was significant difference in color doppler blood flow distribution between both groups ($p < 0.05$; Table 4).

Table 1: Baseline characteristics (mean ± SD; n, %)

Property	Study (n = 42)	Control (n = 49)	χ^2/t	*P*-value
Age	48.26±13.02	48.62±13.07	0.131	0.896
TNM staging			2.024	0.155
Stage I-II	24(57.14)	35(71.43)		
Stage III	18(42.86)	14(28.57)		
Surgical site			1.217	0.270
Left side	22(52.38)	20(40.82)		
Right side	20(47.62)	29(59.18)		
Abnormal uterine bleeding	20(47.62)	16(32.65)	2.119	0.146

Table 2: Two-dimensional imaging (mean ± SD; n, %)

Item	Study (n = 42)	Control (n = 49)	χ^2/t	*P*-value
Endometrial Thickness (mm)	8.63±1.97	4.30±1.08	13.245	0.000
Polyp Max Diameter (mm)	20.19±4.65	13.71±3.94	7.197	0.000
Polyp Avg Diameter (mm)	14.35±4.13	11.06±3.33	4.206	0.000
Endometrial Echo (number)			52.489	0.000
Uniform	4(9.52)	39(79.59)		
Non-Uniform	1(2.38)	4(8.16)		
Honeycomb	1(2.38)	0(0.00)		
Linear	36(85.72)	6(12.25)		
Uterine Cavity Line (number)			26.799	0.000
Offset	3(7.14)	17(34.69)		
Terminal	1(2.38)	9(18.38)		
Central	1(2.38)	6(12.24)		
Unclear Display	37(88.10)	17(34.69)		
Polyp Morphology (number)			36.905	0.000
Oval	2(4.76)	24(48.98)		
Elliptical	15(35.71)	22(44.90)		
Linear	25(59.53)	3(6.12)		
Polyp Echo (number)			75.828	0.000
Uniform	3(7.14)	41(83.67)		
Non-Uniform	0(0.00)	7(14.29)		
Honeycomb	39(92.86)	1(2.04)		

Table 3: Doppler spectrum (mean ± SD)

Group	Peak velocity (cm/s)	Resistance index
Study (n = 42)	15.74±4.00	0.57±0.02
Control (n = 49)	11.49±3.36	0.55±0.03
T-value	5.509	3.675
P-value	0.000	0.000

Table 4: Color doppler blood flow distribution (n, %)

Group	Linear	Punctate	Irregular	No blood flow
Study (n = 42)	35(83.33)	3(7.15)	4(9.52)	0(0.00)
Control (n = 49)	15(30.61)	26(53.07)	5(10.20)	3(6.12)
χ^2		28.986		
P-value		0.000		

DISCUSSION

Estrogen receptor plays a crucial role in treatment of breast cancer, and in postoperative patients with receptor-positive tumors. As a result, application of anti-estrogen drugs is necessary. This treatment effectively prevented recurrence and metastasis of high-risk cancer, improves prognosis, and ultimately enhanced postoperative survival rate of patients with breast cancer [7,9]. However, long-term use of anti-estrogen drugs may lead to endometrial lesions, with development of polyps being a common occurrence. Early-stage lesions often lack obvious symptoms, presenting as a latent onset. However, studies have indicated a certain risk of malignancy in endometrial polyps [10]. Therefore, early detection, diagnosis, and intervention are fundamental in achieving treatment outcomes.

The results of this study showed that study group (treated with anti-estrogen endocrine therapy after surgery), exhibited significantly higher endometrial thickness, maximum and average

diameters of endometrial polyps compared to control group. In study group, endometrial echoes were predominantly linear, while in control group, echoes were mostly uniform. Also, appearance of uterine cavity line in study group was often unclear, while deviations and unclear displays were more common in control group.

The polyps were mostly linear in study group and circular or oval in control group. Internal echoes of polyps were predominantly honeycomb-shaped, and uniform echoes in control group. These findings indicated that ultrasound revealed the characteristics of endometrial lesions, providing high diagnostic value for endometrial polyps in patients undergoing anti-estrogen endocrine therapy [11-13]. Cyclical changes in the endometrium were influenced by changes in estrogen and progesterone levels in the body. Anti-estrogen drugs reduce estrogen levels in the body, leading to atrophy and thinning of the endometrium, resulting in fine linear echoes [11]. In postmenopausal women, anti-estrogen drugs exert a weak estrogenic effect due to low levels of endogenous estrogen. In endometrial cells, these dugs stimulate estrogen receptor β, promoting endometrial proliferation and cell growth. After medication, the resulting polyps, nourished by enlarged blood vessels, grow rapidly. Polyps cause symptoms such as abnormal uterine bleeding and may require surgical removal if they pose serious health risks. They are usually large when discovered, closely resembling the surrounding linear endometrial echoes and often adhering to the endometrium, creating the illusion of increased endometrial thickness. This explains the significantly higher endometrial thickness observed in ultrasound examinations of the study group [14,15].

Abdominal or vaginal ultrasound examinations display unique features of the endometrium in a simple and rapid manner. Vaginal ultrasound examinations place the probe directly into the patient's vaginal fornix, close to the uterus and ovaries, allowing for a clearer and more intuitive observation of the patient's endometrium and polyps. Furthermore, ultrasound examinations are non-invasive, repeatable, and widely used in practice, enabling early detection of endometrial lesions in patients treated with anti-estrogen drugs [16,17]. Results of this study showed that the peak flow velocity and resistance index in the doppler spectrum of blood flow in study group were significantly higher compared to control group. This indicates a certain difference in blood flow characteristics between the two types of endometrial polyps.

Normal endometrial proliferation requires sufficient blood supply, with spiral arteries supplying blood to the endometrium. Diameter of these arteries is closely related to estrogen levels [18]. The tissue of endometrial polyps with endometrial-like lesions thickens the blood vessels under weak estrogenic action of anti-estrogen drugs. Therefore, ultrasound blood flow examination reveals enlarged blood flow signals, higher peak flow velocity, high arterial blood flow resistance, and abundant smooth muscle [18]. Vaginal color doppler ultrasound, with high resolution, high frequency, and insensitive to blood flow direction and low velocity, is highly sensitive in detecting blood flow and may significantly reduce interference from related factors, thereby improving the accuracy of ultrasound examinations [19].

The results of this study also showed that there was significantly difference in blood flow distribution in the polyps between study and control groups. While it was mostly linear in study group, in control group, it was punctate. This indicates a difference in blood flow distribution between the two types of endometrial polyps. Endometrial polyps are mainly characterized by thick-walled blood vessels. Anti-estrogen drugs promote thickening of blood vessels supplying the polyps, resulting in larger volumes of polyps in study group with thicker blood vessels. As a result, blood flow was mostly linear.

Color doppler ultrasound provide information about lesion size, location, and blood flow, helping to evaluate treatment effects and monitor disease progression [19,20]. Studies have shown that vaginal color doppler ultrasound help in early detection and diagnosis of gynecological diseases, providing information about lesion size, location, and blood flow. It is also used to assess treatment effects and monitor disease progression [21]. This study therefore identified unique ultrasound features of endometrial polyps in breast cancer patients after undergoing anti-estrogen endocrine therapy.

Limitations of the study

This study has some limitations. This study did not group patients based on menopausal status, which may introduce some bias.

CONCLUSION

Endometrial polyps caused by anti-estrogen endocrine therapy in breast cancer patients after surgery exhibits unique ultrasound features. Ultrasound diagnosis is effective with a high detection rate, providing a valuable basis for accurate diagnosis and treatment of endometrial polyps. Further analyses are required and a

larger sample size to investigate the underlying mechanism involved in developing endometrial polyps.

DECLARATIONS

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Ethical approval

This study received approval from the Yantai Muping District Hospital of Traditional Chinese Medicine Ethics Committee (approval no. YTM0020230406).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. Haiyun Tao designed the study, and wrote and revised the article. Haiyun Tao and Chunping Qu collected the data. Haiyun Tao and Chentong Zhao collected the data. All the authors read and approved the final manuscript draft for publication.

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