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ORIGINAL RESEARCH

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# Endometrial cancer risk factors in patients with endometrial echogenicity: a logistic regression analysis

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## Abstract

This study aimed to investigate the factors associated with the risk of detecting endometrial cancer in women with endometrial echogenicity suggested by ultrasound diagnosis, using the results of hysteroscopic pathology and histology as the "gold standard". The study enrolled 160 hospitalized patients from January 2020 to January 2023, all exhibiting uneven endometrial echogenicity based on ultrasound findings. Following this, hysteroscopy was conducted on all patients, and the hysteroscopy pathological examination results were considered as the reference standard. Data on clinical and ultrasound examinations of the patients were gathered, and logistic regression analysis was employed to investigate the factors impacting the identification of endometrial cancer. Of the 160 patients whose ultrasound indicated uneven endometrial echogenicity, 119 (74.38%) were diagnosed with benign lesions, while 41 (25.63%) were found to have malignant lesions according to the hysteroscopy pathological examination. Results showed that compared to patients with benign lesions, patients with malignant endometrial lesions had higher ages, were more likely to be menopausal, had irregular vaginal bleeding, had endometrial thickening, and had real-time blood flow grading of the endometrium and adjacent myometrium graded II–III. These differences were statistically significant ($p < 0.05$). The endometrium and surrounding myometrium's real-time blood flow grading, which are ranked II–III (Odds Ratio (OR) = 3.473, 95% Confidence Interval (CI) 1.540–7.833), are independent variables. In conclusion, doctors should be aware that endometrial cancer may be present in postmenopausal women who have irregular vaginal bleeding, watch for strong real-time blood flow signals between the endometrium and surrounding muscle layers, and use transvaginal ultrasound (TVUS) to detect endometrial thickening.

## Keywords

Endometrial cancer; Ultrasound; Uneven endometrial echogenicity; Hysteroscopy; Pathological histology examination results; Logistic regression model

## 1. Introduction

Endometrial lesions are common gynecological diseases, with patients mainly presenting symptoms such as increased menstrual flow, abnormal vaginal bleeding, and lower abdominal pain. Currently, two-dimensional grayscale transvaginal ultrasound (TVUS) is the most widely used method for diagnosing gynecological diseases clinically [1–4]. In 2010, the International Endometrial Tumor Analysis (IETA) group suggested that when ultrasound reveals a consistent and balanced echogenicity in the endometrium, it signifies a uniform echogenicity. Conversely, an irregular, imbalanced, or cystic echogenicity in the endometrium indicates an uneven echogenicity, which frequently signals the presence of endometrial lesions [5–9]. Previous research has indicated that TVUS findings of irregular endometrial echogenicity may be an unfavorable prognostic indicator for patients. However, there is a lack of extensive studies on this subject, leading to uncertainty regarding the clinical significance of uneven endometrial echogenicity [10–13]. Clinically, endometrial localization biopsy under hysteroscopy is the "gold standard" for the diagnosis of endometrial lesions. However, hysteroscopy is an invasive procedure that carries a high risk of bleeding, infection, uterine perforation, and other complications. Therefore, it is crucial to enhance the capacity to differentiate between benign and malignant endometrial lesions in patients exhibiting uneven endometrial echogenicity as indicated by TVUS, reduce unnecessary invasiveness and extensive diagnostic procedures, and alleviate the distress experienced by patients during therapy. Improving the identification of benign and malignant endometrial lesions in patients with heterogeneous endometrial echogenicity by TVUS is of great significance in reducing unnecessary trauma and excessive diagnostic tests, and alleviating the pain of patient diagnosis


  

and treatment.

## 2. Data and methods

### 2.1 Study population

A total of 160 patients admitted to the hospital between January 2020 and January 2023, with ultrasound findings suggesting uneven endometrial echogenicity, were included as the study population.

(1) Inclusion criteria: All patients with ultrasound findings suggesting uneven endometrial echogenicity underwent hysteroscopy examination; full ultrasound examination data, hysteroscopy pathological data, and clinical data were available. A normal endometrium was identified by its homogeneous and symmetrical appearance. Conversely, an abnormal endometrium was characterized by heterogeneity, localized enhancement, cystic changes, irregular or nonlinear endometrial midline, and indistinct borders with the myometrium.

(2) Exclusion criteria: Ultrasound evidence of space-occupying endometrial lesions, a history of previous uterine removal, and a combination of psychiatric disorders.

### 2.2 Methods

#### 2.2.1 Transvaginal ultrasound examination

(1) Equipment: GE Voluson E8 ultrasound diagnostic instrument (General Electric Company, Boston, MA, USA).

(2) Pre-examination Preparation: Patients were instructed to empty their bladder before the examination, lie supine on the examination table, and assume the lithotomy position.

(3) Examination Procedure: Following the application of coupling gel on the ultrasound probe and covering it with a condom, the probe was initially placed in the superficial area of the vagina for cervix observation. Subsequently, a deeper insertion was made to examine the uterine body, with adjustments made to guarantee the uterus was properly positioned in the mid-sagittal plane, allowing for clear display of the uterine cavity and cervix. In this plane, the length, anterior-posterior diameter of the uterus, and endometrial thickness were measured, and the echogenicity of the endometrium was observed. Based on the patient's age and menstrual cycle, it was determined whether the endometrial thickness and echogenicity were abnormal, as well as the relationship between the endometrium and the surrounding muscle layers. Additionally, information on the dimensions of the uterus, the thickness of the endometrium, the location, number, size, morphology and Doppler ultrasound results of the lesions were also documented.

#### 2.2.2 Definitions

(1) Uterine Size: Classified as normal/shrinkage/enlargement based on the patient's age and menopausal status.

(2) Endometrial Thickness: Endometrial thickness $\geq$1.5 cm in premenopausal patients and $\geq$0.5 cm in postmenopausal patients is defined as endometrial thickening.

(3) Relationship Between Lesion Boundary and Surrounding Muscle Layers: Classified as a clear or unclear boundary.

(4) Real-time Blood Flow in the Endometrium and Adjacent Muscle Layers: According to the Adler semi-quantitative grading method [14], graded as 0, I, II, III, where 0 indicates no blood flow signal, I indicate scattered dot-like signals, II indicates rod-like or strip-like signals, and III indicates mesh-like signals.

#### 2.2.3 Pathological examination

Data collected included the age of patients, menopausal status, years since menopause, pregnancy and childbirth history, presence of hypertension, diabetes mellitus, polycystic ovarian syndrome, clinical manifestations of abnormal vaginal bleeding, serum cancer antigen 19-9 (CA199) levels, family history of endometrial cancer, and past use of hormone replacement therapy.

#### 2.2.4 Sample size calculation

Logistic regression model was established to analyze the influence of multiple factors on the outcome of categorical variables, the sample size is generally 5–10 times the number of independent variables, a total of 16 independent variables were included in this study, and the required sample size was: 80–160 cases, taking into account the actual number of cases received in the hospital, a total of 160 cases of research subjects were included in this paper.

### 2.3 Statistical methods

Statistical software SPSS 19.0 (IBM Corporation, Armonk, NY, USA) was used for the analysis, and the measurement data were tested for normal distribution and chi-square test, and data conforming to normal distribution were expressed as ($\bar{x} \pm s$). The counting data were expressed as the number of cases (n) and the percentage (%), and were tested by the $\chi^2$ test. The multifactorial logistic regression analysis was used to analyze the relevant factors affecting the detection of endometrial cancer. The results were analyzed by multivariate logistic regression, and the statistical significance was indicated by $p < 0.05$.

## 3. Results

### 3.1 Analysis of pathological diagnosis results of study subjects

Among the 160 patients with irregular endometrial echogenicity detected by ultrasound, benign lesions were identified in 119 individuals (74.38%), whereas malignant lesions were detected in 41 individuals (25.63%) based on the hysteroscopy pathological examination data presented in Table 1.

### 3.2 Comparison of clinical characteristics and ultra-sonographic diagnostic results between patients with benign and malignant lesions

The analysis showed that patients with malignant endometrial lesions were more likely to be older, postmenopausal, and present with irregular vaginal bleeding, endometrial thickening, and high-grade real-time blood flow signals between the endometrium and adjacent muscle layers (grade II–III), compared to those with benign lesions. These differences were

**TABLE 1. Analysis of pathological diagnosis results of patients with ultrasound findings suggesting uneven endometrial echogenicity.**

| Pathological diagnosis results | Classification | Number of cases (percentage) |
|---|---|---|
| Benign lesion | | |
| | Endometrial polyp | 74 (46.25%) |
| | Submucosal fibroid | 28 (17.50%) |
| | Endometrial hyperplasia | 17 (10.63%) |
| | Total | 119 (74.38%) |
| Malignant lesion | | |
| | Endometrial cancer | 41 (25.63%) |

statistically significant ($p < 0.05$), as shown in Table 2.

### 3.3 Single-factor logistic regression analysis of factors affecting the incidence of endometrial cancer

The analysis of a single factor indicated that the occurrence of endometrial cancer was closely associated with factors such as age, menopausal status, irregular vaginal bleeding, endometrial thickening, and real-time blood flow in the endometrium and adjacent muscle layer, as detailed in Table 3.

### 3.4 Multifactorial logistic regression analysis of factors affecting the incidence of endometrial cancer

According to the results of multifactorial logistic regression analysis presented in Table 4, independent factors influencing the occurrence of endometrial cancer include menopausal status, irregular vaginal bleeding, thickening of the endometrium, as well as real-time blood flow in the endometrial and adjacent muscle layer.

## 4. Discussion

The typical ultrasonic image of the endometrium usually displays a mostly uniform and evenly distributed pattern [15–18]. When transvaginal ultrasound (TVUS) indicates uneven endometrial echogenicity, different types of endometrial lesions show little difference in ultrasound imaging, and in such cases, malignant endometrial lesions are easily missed. It was discovered in this study, which used the final pathological diagnosis as the "gold standard", that out of 160 cases with TVUS showing uneven endometrial echogenicity, 41 cases had endometrial cancer (25.63% malignant detection rate), and the remaining 119 patients (74.38%) had benign lesions. It is suggested that the risk of endometrial cancer remains elevated in situations where TVUS indicates irregular endometrial echogenicity without the presence of intracavitary masses. To further improve the differentiation between benign and malignant endometrial lesions, this study combined ultrasound imaging features with clinical parameters and analyzed the factors affecting endometrial cancer through logistic regression models. The findings indicate that menopause, unpredictable vaginal bleeding, thickening of the endometrium, and real-time blood flow between the endometrium and neighboring muscle layers were identified as autonomous factors influencing endometrial disorders.

Malignant tumors lack perimetrium, so there is no clear boundary between them and the surrounding tissues, which manifests as unclear demarcation with the surrounding tissues in the ultrasound. The main characteristic of endometrial cancer is its invasive growth pattern, where malignant cells proliferate rapidly within the uterine cavity before infiltrating and expanding into the adjacent muscle layer, parietal tissues, blood vessels, and lymphatic system [19, 20]. However, in this study, the unclear boundary of the lesion and the surrounding muscle layer did not enter into the regression equation, which may be related to the error caused by the small sample size of the study and the factors such as the early stage of endometrial cancer and the low degree of tumor invasion. In early-stage endometrial cancer, the lesions were limited and only showed uneven endometrial echogenicity, while in progressive endometrial cancer, endometrial thickening was observed. Furthermore, the endometrial cancer lesions exhibited increased vascularity, with a reduced presence of smooth muscle and nerves within the vessel walls. Consequently, they displayed more pronounced blood flow signals on color Doppler ultrasonography [21–24]. In this study, endometrial thickening and real-time blood flow signal grading between the endometrium and adjacent myometrium were found to be independent risk factors for the development of endometrial cancer. Regarding clinical data, postmenopausal women and individuals experiencing clinical irregular vaginal bleeding were identified as autonomous risk factors for endometrial cancer, aligning with the discoveries of Clarke MA *et al.* [25].

Endometrial echogenicity is proposed as a clinical marker that may indicate the presence of endometrial cancer in postmenopausal individuals experiencing irregular vaginal bleeding, along with endometrial thickening observed on transvaginal ultrasound (TVUS) and high real-time blood flow grading in the interface between the endometrium and the adjacent myometrium.

Furthermore, there is a clear link between Body mass index (BMI) and endometrial cancer, with obese women being more likely to develop the disease, which is connected with chronic inflammation, elevated estrogen metabolites, DNA damage, and lower genetic stability as a result of obesity. However, the research failed to establish a direct correlation between BMI and the onset of endometrial cancer, diverging from the results reported by Hazelwood E *et al.* [26]. This discrepancy

**TABLE 2. Comparison of clinical characteristics and ultra-sonographic diagnostic results between patients with benign and malignant lesions.**

| Indicator | Group | Benign lesions (n = 119) | Malignant lesions (n = 41) | $\chi^2$ | $p$ |
|---|---|---|---|---|---|
| Age (yr) | | | | | |
| | <50 yr | 74 | 17 | 5.338 | 0.021 |
| | ≥50 yr | 45 | 24 | | |
| BMI (kg/m$^2$) | | | | | |
| | <18.5 | 25 | 7 | | |
| | 18.5–23.9 | 64 | 25 | 0.653 | 0.722 |
| | >23.9 | 30 | 9 | | |
| Menopause | | | | | |
| | Yes | 67 | 31 | 4.789 | 0.029 |
| | No | 52 | 10 | | |
| Irregular vaginal bleeding | | | | | |
| | Yes | 37 | 20 | 4.160 | 0.041 |
| | No | 82 | 21 | | |
| Hypertension (High blood pressure) | | | | | |
| | Yes | 24 | 6 | 0.613 | 0.434 |
| | No | 95 | 35 | | |
| Diabetes | | | | | |
| | Yes | 13 | 5 | 0.049 | 0.824 |
| | No | 106 | 36 | | |
| Polycystic Ovary Syndrome (PCOS) | | | | | |
| | Yes | 18 | 5 | 0.213 | 0.645 |
| | No | 101 | 36 | | |
| Parity (number of pregnancies) | | | | | |
| | <3 times | 96 | 32 | 0.131 | 0.717 |
| | ≥3 times | 23 | 9 | | |
| Gravidity (number of pregnancies carried to viable gestational age, regardless of the outcome) | | | | | |
| | <2 times | 102 | 35 | 0.003 | 0.956 |
| | ≥2 times | 17 | 6 | | |
| Serum CA199 (a tumor marker) | | | | | |
| | ≤37 U/mL | 52 | 25 | 3.647 | 0.056 |
| | >37 U/mL | 67 | 16 | | |
| Uterine size | | | | | |
| | Normal | 40 | 15 | | |
| | Reduction/Shrinkage | 52 | 20 | 1.213 | 0.545 |
| | Enlargement | 27 | 6 | | |
| Thickening of the endometrium (lining of the uterus) | | | | | |
| | Yes | 35 | 21 | 6.375 | 0.012 |
| | No | 84 | 20 | | |
| Relationship between lesion borders and surrounding muscle layers | | | | | |
| | Unclear boundary | 6 | 9 | 1.157 | 0.282 |
| | Clear boundary | 113 | 32 | | |
| Real-time blood flow between the endometrium and adjacent muscle layers | | | | | |
| | Grade 0–I | 65 | 10 | 11.192 | <0.001 |
| | Grade II–III | 54 | 31 | | |
| Family history of endometrial cancer | | | | | |
| | Yes | 3 | 2 | 0.560 | 0.454 |
| | No | 116 | 39 | | |
| History of treatment with hormone replacement therapy | | | | | |
| | Yes | 5 | 2 | 0.033 | 0.855 |
| | No | 114 | 39 | | |

*BMI: Body Mass Index; CA: Cancer Antigen.*

**TABLE 3. Single-factor logistic regression analysis of factors affecting the incidence of endometrial cancer.**

| Factors | $\beta$ | SE | Wald $\chi^2$ | OR | 95% CI | $p$ |
|---|---|---|---|---|---|---|
| Age | 1.465 | 0.451 | 10.552 | 4.328 | 1.788–10.475 | 0.001 |
| BMI | 0.785 | 0.439 | 3.197 | 2.192 | 0.927–5.183 | 0.074 |
| Menopause | 0.845 | 0.268 | 9.941 | 2.328 | 1.377–3.936 | 0.002 |
| Irregular vaginal bleeding | 0.915 | 0.348 | 6.913 | 2.497 | 1.262–4.939 | 0.009 |
| Hypertension | 0.265 | 0.174 | 2.319 | 1.303 | 0.927–1.833 | 0.129 |
| Diabetes | 0.343 | 0.211 | 2.643 | 1.409 | 0.932–2.131 | 0.105 |
| Polycystic ovary syndrome | 0.441 | 0.279 | 2.498 | 1.554 | 0.900–2.685 | 0.115 |
| Parity | 1.254 | 0.678 | 3.421 | 3.504 | 0.928–13.235 | 0.065 |
| Gravidity | 1.744 | 1.024 | 2.901 | 5.720 | 0.769–42.565 | 0.089 |
| Serum CA199 | 0.844 | 0.431 | 3.835 | 2.326 | 0.999–5.413 | 0.051 |
| Uterine size | 0.741 | 0.413 | 3.219 | 2.098 | 0.934–4.714 | 0.073 |
| Endometrial thickening | 0.844 | 0.244 | 11.965 | 2.326 | 1.442–3.752 | $<$0.001 |
| Relationship between lesion boundary and surrounding muscle layer | 1.121 | 0.652 | 2.956 | 3.068 | 0.855–11.011 | 0.086 |
| Real-time blood flow in the endometrium and adjacent muscle layer | 1.179 | 0.468 | 6.347 | 3.251 | 1.299–8.136 | 0.012 |

*SE: Standard Error; OR: Odds Ratio; CI: Confidence Interval; BMI: Body Mass Index; CA: Cancer Antigen.*

**TABLE 4. Multifactorial logistic regression analysis of factors affecting the incidence of endometrial cancer.**

| Factors | $\beta$ | SE | Wald $\chi^2$ | OR | 95% CI | $p$ |
|---|---|---|---|---|---|---|
| Age | 1.645 | 0.846 | 3.781 | 5.181 | 0.987–27.198 | 0.053 |
| Menopause | 0.746 | 0.215 | 12.039 | 2.109 | 1.383–3.214 | $<$0.001 |
| Irregular vaginal bleeding | 0.979 | 0.311 | 9.909 | 2.661 | 1.447–4.897 | 0.002 |
| Endometrial thickening | 0.785 | 0.274 | 8.208 | 2.192 | 1.281–3.751 | 0.004 |
| Real-time blood flow in the endometrium and adjacent muscle layer, grade II–III | 1.245 | 0.415 | 9.000 | 3.473 | 1.540–7.833 | 0.003 |

*SE: Standard Error; OR: Odds Ratio; CI: Confidence Interval.*

could possibly be attributed to the oversight stemming from the homogeneity in the BMI measurements among the participants in this study.

As a study conducted at a single center, the research comprises a small sample size and a restricted collection of clinical indicators, potentially leading to biased conclusions. To enhance the reliability of the study findings, future research could expand the sample size by incorporating data from multiple centers, allowing for a more comprehensive and detailed analysis during follow-up.

## 5. Conclusions

In summary, postmenopausal patients with symptoms of irregular vaginal bleeding, endometrial thickening on TVUS, and high real-time blood flow grading between the endometrium and the adjacent myometrium should be screened for endometrial malignant lesions based on endometrial echogenicity.

### AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper and any raw data can be obtained from the corresponding author upon request.

### AUTHOR CONTRIBUTIONS

XJD, YH—designed the study and carried them out; supervised the data collection; analyzed the data; prepared the manuscript for publication and reviewed the draft of the manuscript. XJD—interpreted the data. Both of authors have read and approved the manuscript.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of General Hospital of Northern Theater Command (Approval

no. 20200112). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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