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Combining demographic data and transvaginal ultrasonography: a predictive model for endometrial carcinoma in postmenopausal patients

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Abstract

Background Although clinical guidelines exist for diagnosing abnormal uterine bleeding, there is a significant lack of agreement on the best management strategies for women presenting with symptom, particularly in diagnosing endometrial cancer. This study aimed to develop a preoperative risk model that utilizes demographic factors and transvaginal ultrasonography of the endometrium to assess and predict the risk of malignancy in females with endometrial cancer.

Methods In this retrospective study, a logistic regression model was developed to predict endometrial carcinoma using data from 356 postmenopausal women with endometrial lesions and an endometrial thickness (ET) of 5 mm or more. These patients had undergone transvaginal ultrasonography prior to surgery, with findings including 247 benign and 109 malignant cases. The model's predictive performance was evaluated using receiver operating characteristic (ROC) curve analysis and compared with post-surgical pathological diagnoses.

Results Our model incorporates several predictors for endometrial carcinoma, including age, history of hypertension, history of diabetes, body mass index (BMI), duration of vaginal bleeding, endometrial thickness, completeness of the endometrial line, and endometrial vascularization. It demonstrated a strong prediction with an area under the curve (AUC) of 0.905 (95% CI, 0.865–0.945). At the optimal risk threshold of 0.33, the model achieved a sensitivity of 82.18% and a specificity of 92.80%.

Conclusions The established model, which integrates ultrasound evaluations with demographic data, provides a specific and sensitive method for assessing and predicting endometrial carcinoma.

Keywords Endometrial cancer, Demography, Transvaginal ultrasonography, Sensitivity and specificity

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Background

Endometrial cancer (EC) is the sixth most common gynecologic malignancy worldwide, with 400,000 new cases and over 80,000 deaths in 2023 [1, 2]. Over the past three decades, the incidence of EC has consistently increased, particularly among women aged 50 to 60 and those with risk factors such as obesity, menopause, hypertension, polycystic ovary syndrome, or a family history of cancer [3]. EC develops when cells from the endometrial epithelial tissue lining the uterus undergo abnormal and uncontrolled growth [4, 5]. Depending on the tumor cell morphology, EC can be categorized into various subtypes, such as endometrioid carcinoma (the most common), mucinous adenocarcinoma, serous adenocarcinoma, and clear cell carcinoma [4, 5]. Typical treatments for EC include radiation therapy and surgical removal of the uterus, fallopian tubes, and ovaries [6]. However, the administration of treatment requires careful consideration of tumor staging and malignancy, due to the aggressive and invasive nature of EC [7]. Consequently, there is a pressing need for precise diagnosis and the evaluation of the tumor staging and malignancy risk.

Traditionally, the diagnosis of EC is based on the histopathological assessment of an endometrial sample obtained via endometrial biopsy or hysteroscopic biopsy [8]. However, these methods are invasive, associated with potential morbidity, and are not always effective in detecting early-stage cancer [9–11], posing challenges for early diagnosis and differentiation between malignant and benign tumors. Recently, the integration of transvaginal ultrasonography into clinical assessments has significantly enhanced diagnostic accuracy [12]. This imaging modality provides a cost-effective, well-tolerated, and efficient way to assess tumor size, potential myometrial invasion, and cervical stromal invasion, which are all closely linked to malignancy risk and advanced stages of cancer [13]. Recent studies highlight the high sensitivity and specificity of malignancy assessments through transvaginal ultrasound, providing valuable insights into staging and malignancy evaluations of EC [14, 15]. However, these studies often focus primarily on ultrasound parameters, with limited consideration given to other potential clinical indicators from demographic data that could also contribute to EC diagnosis.

In this study, our goal is to develop a logistic regression model that combines both transvaginal ultrasonography and demographic data. This model is designed to predict the individual risk of EC malignancy with increased sensitivity and specificity.

Materials and methods

Patients and design

This is a retrospective analysis of postmenopausal (PM) women with endometrial thickness greater than 5 mm and postmenopausal bleeding (PMB). The study included 356 female patients aged 43–78 who presented with postmenopausal endometrial disorders or underwent routine examination at the Hospital of Cardiovascular and Cerebrovascular Diseases, General Hospital of Ningxia Medical University, from January 1, 2019, to December 31, 2021. All patients underwent transvaginal ultrasonography. Diagnostic curettage, hysteroscopy, and surgical treatment were also performed if necessary. Detailed demographic information, including age, years since menopause, menstrual and reproductive history, histories of hypertension, diabetes, polycystic ovary syndrome, BMI, and vaginal bleeding, was collected under an approved protocol. Each postmenopausal patient was identified following routine examinations by a gynecologist. ET and BMI values were transformed into dichotomous variables based on threshold values of 8 mm for ET and >25 kg/m^2 for BMI. The research protocol received approval from the Hospital of Cardiovascular and Cerebrovascular Diseases, General Hospital of Ningxia Medical University. Written informed consent was obtained from patients for the collection of demographic information.

Inclusion and exclusion criteria were rigorously applied to define the study population. Inclusion Criteria: Menopause for more than 1 year; Ultrasound measurement of endometrial thickness$\geq$5 mm; Not receiving estrogen treatment. Exclusion Criteria: Pathological diagnosis obtained only by segmental curettage, hysteroscopic biopsy, or endometrial biopsy; Poor image quality in ultrasonography; Presence of an intrauterine device; Undergoing hormone replacement therapy.

Transvaginal ultrasonography

Patients were positioned in the dorsal lithotomy position with an empty bladder for transvaginal 2D ultrasound examinations conducted before any surgical treatment. These ultrasounds were performed using Samsung ws80A, GE Voluson E8, or GE Voluson E10 ultrasound diagnostic systems, equipped with transvaginal ultrasound probes operating at a frequency of 3 to 12 MHz. Two experienced sonographers, each with over five years of experience, independently scanned the uterus and bilateral appendages. The examinations adhered to the criteria for endometrial morphology established by the International Endometrial Tumor Analysis (IETA) group [16]. Parameters assessed included uterine effusion, interruption of endometrial continuity, and blood flow signals around the endometrium. Tumor characteristics such as endometrial thickness, echogenicity, presence of cystic structures, smoothness of the endometrial line, integrity of the endometrial junction, and vascular features were meticulously evaluated (Fig. 1). In cases of

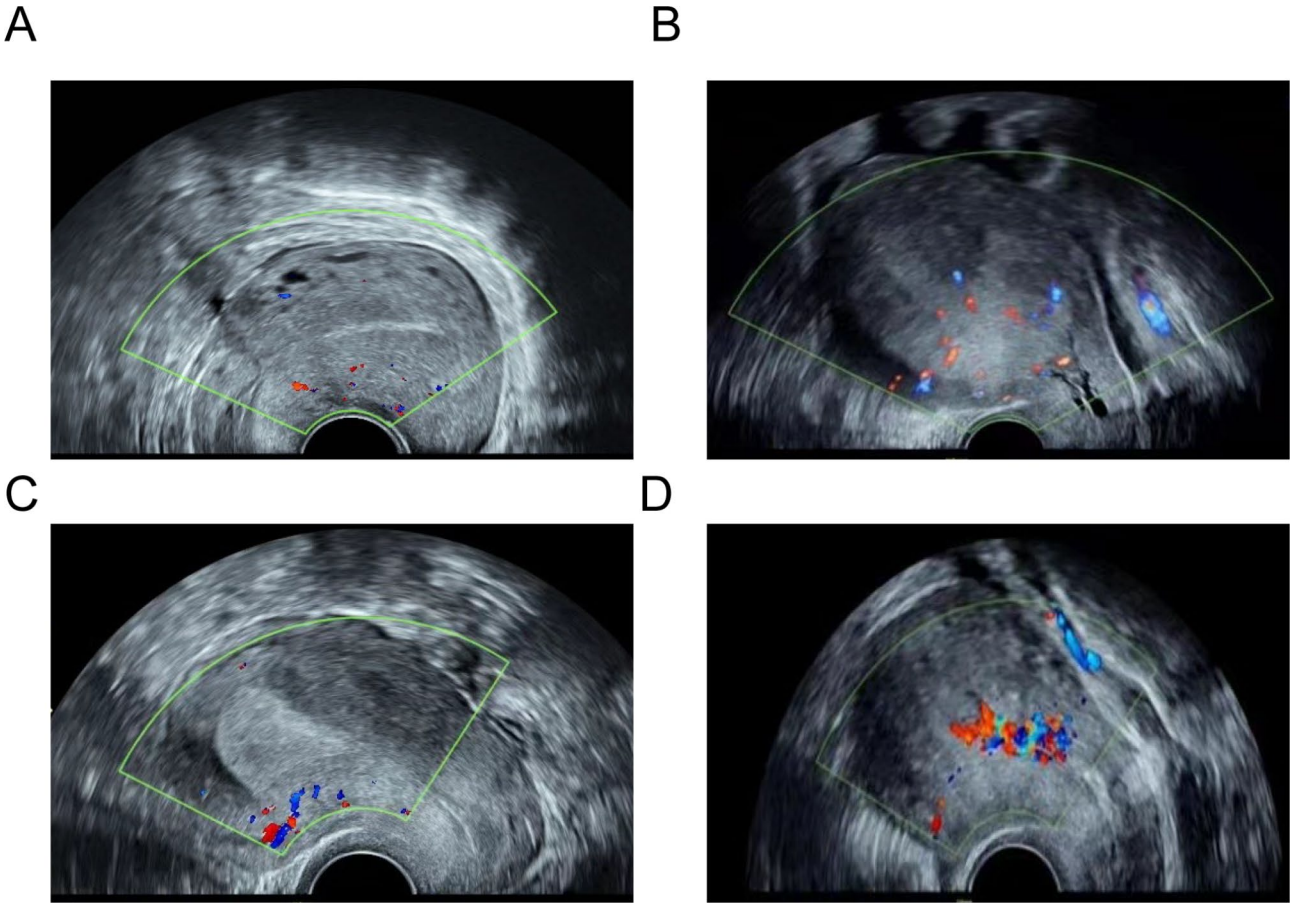

Fig. 1 Representative images of endometrial disease. (**A**) A 65-year-old healthy volunteer with normal endometrium. (**B**) A 69-year-old patient with endometrial hyperplasia, thickened endometrium, multiple cystic cavities of varying sizes, unclear intimal line, and smoothen intima-muscle junction. (**C**) A 66-year-old patient with endometrial polyps. The patient has an intrauterine inhomogeneous echo mass with small cysts and uterine effusion. (**D**) A 52-year-old patient with endometrial cancer. The patient has multi-origin and multi-vessel blood flow signals at the endometrial-myometrial junction

disagreement between the sonographers, the subjective assessment of the investigator was taken into account.

Statistical analysis

Data were analyzed using SPSS statistical software (version 20.0, SPSS, Inc., Chicago, IL, USA). Graphical analysis was performed with Graph Pad Prism 7. Categorical data were expressed as frequency and percentage and were evaluated using the χ^2 test to assess the significance of differences between groups. Normally distributed and equal variance data were presented as mean ± standard deviation (SD) and analyzed with the Student's t-test to determine group differences.

Logistic regression analysis was conducted using data from the modeling subgroup, which included 105 benign cases and 69 malignant cases. To develop a diagnostic model, positive observation indices were coded as 1, while negative indices were coded as 0. The model's performance was evaluated using the area under the curve (AUC) from receiver operating characteristic (ROC) curve analysis. The calibration ability of the model was assessed with the Hosmer-Lemeshow goodness-of-fit test. The validation subgroup, consisting of 52 benign cases and 35 malignant cases, was used to validate the model. A p-value of <0.05 was considered statistically significant.

Logistic regression model

We employed a logistic regression model to estimate the risk of Endometrial Carcinoma based on several clinical and demographic factors. Predictor variables included history of hypertension (X_1; coded as 1 for presence, 0 for absence), history of diabetes (X_2), age over 60 years (X_3), BMI greater than 25 kg/m^2 (X_4), abnormal vaginal bleeding (X_5), endometrial thickness greater than 8 mm (X_6), incomplete endometrial line (X_7), and presence of endometrial vascularization (X_8).

Table 1 Summary of the demographic data of patients involved in the study

Index	Benign group	Malignant group	t	*P* value
Age(year)	52.42 ± 4.81	62.30 ± 3.62	4.627	0.000
Age at menarche (years)	14.20 ± 1.34	14.41 ± 2.47	0.721	0.641
Menopause age (years)	53.21 ± 1.67	54.18 ± 1.01	1.354	0.314
pregnancy history	3.48 ± 1.62	2.93 ± 1.47	1.862	0.081
Production times	3.32 ± 1.41	2.91 ± 1.58	0.061	0.627
BMI	21.38 ± 1.23	26.17 ± 2.53	8.124	0.000
endometrial thickness	0.51 ± 0.32	1.22 ± 0.86	6.324	0.001

Data are shown as means ± SD. BMI, Body mass index; *t*, results of student *t* test; *P* value, $P<0.05$ is considered to be significant

Table 2 Summary of the identified dichotomous risk factors in distinguishing benign versus malignant tumors

index		Benign group	Malignant group	χ^2	*P* value
History of hypertension	yes	31	84	1.50	0.000
	no	226	25		
Diabetes	yes	17	32	34.14	0.000
	no	240	77		
Polycystic ovary syndrome	yes	26	56	66.02	0.000
	no	229	53		
Post-menopausal Bleeding	yes	49	93	1.41	0.000
	no	208	16		
ET>8 mm	yes	51	76	82.65	0.000
	no	206	33		
BMI>25	yes	67	86	86.28	0.000
	no	190	23		
Age>60	yes	46	61	75.12	0.000
	no	211	48		
Non-uniform echogenicity	yes	546	107	0.490	0.483
	no	9	2		
Irregular endometrial line	yes	244	108	3.160	0.075
	no	13	1		
Endometrial cavity fluid	yes	51	32	3.720	0.054
	no	206	77		
Interruption of endometrial line continuity	yes	63	47	34.760	0.000
	no	194	62		
Endometrial vascularization	yes	103	52	12.120	0.001
	no	154	57		

Data are shown as means ± SD. ET, endometrial thickness; BMI, Body mass index; results of χ^2 test; *P*-value. $P<0.05$ is considered to be significant

Results

Univariate analysis of demographic data to identify risk factors of malignancy

Based on the results of pathological examinations from either diagnostic curettage or hysteroscopy specimens, cases were classified into benign and malignant groups. The benign group comprised 247 cases, including 156 cases of endometrial polyps, 7 cases of endometritis, 34 cases of submucosal fibroids, and 46 cases of simple hyperplasia. The malignant/premalignant group included 109 cases, with 83 cases of endometrial cancer and 26 cases of atypical hyperplasia, which are classified as premalignant due to their possible coexistence with cancer [17–19]. The cases were then randomly divided into modeling and validation subgroups, following a 2:1 ratio, with 237 cases in the modeling subgroup and 119 cases in the validation subgroup.

We then summarized the demographic data of patients in the benign and malignant groups (Table 1). Compared between the two groups, there are significant differences in patients' age, BMI, and ET, suggesting they may potentially be factors of malignancy (Table 1). Next, we performed a univariate analysis of the demographic data in Table 1 as well as patients' clinical history to further identify risk factors. Both the χ^2 test and the t-test were used to examine differences between the benign and malignant groups. Dichotomous risk factors showing significant differences between the groups were identified. These risk factors included a history of hypertension and diabetes, a BMI exceeding 25 kg/m^2, postmenopausal bleeding, age over 60, endometrial thickness greater than 8 mm, non-uniform echogenicity, an irregular endometrial line, an incomplete endometrial line, and endometrial vascularization (Table 2).

Generating a logistic regression model to predict and distinguish malignancy

Subsequently, we constructed a Logistic regression model based on the identified risk factors to distinguish malignant from benign cases. The risk regression formula is represented as follows:

Risk score (RS) $=-5.214+0.856X_1+0.961X_2+0.641X_3+0.912X_4+2.636X_5+1.378X_6+0.721X_7+0.813X_8$, where X_1 through X_8 represent the predictors as defined in the Methods section.

Evaluating the model's performance by ROC analysis

To evaluate the model's ability to distinguish between malignant and benign endometrial tumors, we conducted ROC curve analyses (Fig. 2; Table 3). Our risk model exhibited a strong discriminatory capacity, with an AUC of 0.905 (95% CI, 0.865–0.975), a sensitivity of 82.18% (95% CI, 75.40–88.96), and a specificity of 92.80% (95% CI, 87.44–98.16). These results suggest our model's strong ability to predict malignancy.

Evaluating the model's performance by the Hosmer-Lemeshow test

To further evaluate the performance of our logistic regression model, we conducted the Hosmer-Lemeshow test to assess the model's goodness of fit. The test yielded a p-value of 0.46, which exceeds the threshold of 0.05, indicating that the model demonstrates

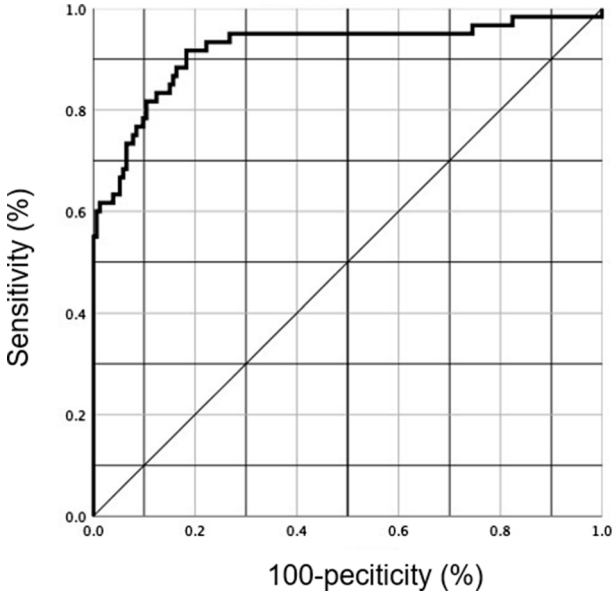

Fig. 2 Receiver operating characteristic (ROC) curve analysis assessing the performance of our model. $P < 0.05$ was considered statistically significant

satisfactory fitness and good calibration ability (Table 4). These results confirm the model's reliability in predicting malignancy.

Evaluating the model's performance in the validation group

We subsequently applied our logistic regression model to a validation group consisting of 119 patients (72 benign cases and 47 malignant cases) to evaluate its performance in distinguishing between benign and malignant cases. Using an optimal threshold value of 0.28, where RS equal to or greater than 0.28 indicates malignancy, the model identified 45 malignant cases and 68 benign cases. Upon comparison with clinical diagnosis results, it was found that out of the 119 cases, 45 were accurately predicted as malignant, and 68 were correctly identified as benign. The model demonstrated high diagnostic efficiency with an accuracy of 89.41%, a sensitivity of 92.31%, a specificity of 84.20%, a positive predictive value of 86.21%, and a negative predictive value of 91.32%. These results affirm the model's robustness and reliability in clinical settings.

Discussion

In this study, we developed and validated a logistic regression model to identify and malignancy of endometrial tumors and evaluated its performance. This model integrates patients' demographic data and transvaginal ultrasonography results. Our findings suggested that the combination of ultrasound evaluation and demographic data provides specific and sensitive predictions of malignancy.

Table 4 Analysis results of binary logistic regression model

independent variable	Regression coefficients	OR value	*P*
History of hypertension	0.856	2.147	0.000
diabetes	0.961	2.738	0.000
Age>60	0.641	1.542	0.000
BMI>25	0.912	3.002	0.007
Vaginal bleeding	2.636	17.317	0.009
ET>8 mm	1.378	8.234	0.013
Interruption of endometrial line continuity	0.721	0.854	0.002
Endometrial vascularization	0.813	1.927	0.003
Constant	-5.241	0.007	0.003

Data are shown as means ± SD. ET, endometrial thickness; BMI, Body mass index; results of χ^2 test; *P*-value, $P < 0.05$ is considered to be significant

Transvaginal ultrasonography has become a crucial component of preoperative assessments for endometrial cancer, offering valuable insights into staging and malignancy risk [20]. While numerous risk models have been developed based on transvaginal ultrasonography data, many focus solely on ultrasound findings, neglecting other potential clinical indicators [21]. Our risk model, instead, includes a range of clinical indicators from demographic data such as age, age at menarche, menopause, pregnancy history, parity, body mass index, hypertension, diabetes, polycystic ovary syndrome, and symptoms like vaginal bleeding. These indicators are readily obtainable from routine clinical exams, which minimizes the financial and emotional strain on patients. The ultrasonographic data utilized in our model includes uterine effusion, disruption of endometrial continuity, and multiple blood flow signals around the endometrium, which are also parameters commonly assessed during exams. Hence, our model, which offers the trustable evaluation of malignancy without requiring additional clinical exams, is very practical in clinical settings.

Our model demonstrated excellent distinguishing and predicting capabilities for malignancy, showing an accuracy rate of 89.41%, with a sensitivity of 92.31%, a specificity of 84.20%, a positive predictive value of 86.21%, and a negative predictive value of 91.32%. These results were confirmed when applying our model to a validation group of 119 cases, confirming the prediction power of our model. While prior studies often focus on patients with postmenopausal vaginal bleeding [22], our approach

Table 3 Analysis results of receiver operating characteristic (ROC) curve

	AUC	95% CI	Sensitivity (95% CI)	Specificity (95% CI)	BCV	*P*
Logistic regression model	0.905	0.865 to 0.975	82.18 (75.40 to 88.96)	92.80 (87.44 to 98.16)	0.33	< 0.0001

AUC: area under the ROC curve; BCV: Best Critical Value; $P < 0.05$ was considered statistically significant

broadens the applicability of the model. In our study, only 142 out of 356 patients reported vaginal bleeding symptoms, and the presence of such symptoms was considered one of the clinical indicators for model generation. This divergence from a singular focus on postmenopausal vaginal bleeding expands the utility of our model to a more diverse range of endometrial cancer patients, regardless of bleeding symptoms [23, 24].

Although our model is promising, there are limitations to acknowledge. Firstly, the involved samples are limited to the Ningxia region in northwest China, which may affect the generalizability of the findings. Future research with a more diverse population is needed to validate the model's effectiveness more broadly. Additionally, the exclusion of individuals undergoing estrogen replacement therapy, which is common in China, might limit the model's applicability. Lastly, the reliance on static images for evaluating intima morphology and blood flow may introduce assessment inaccuracies, particularly in evaluating the integrity of the intima-muscle junction and blood flow characteristics. Future studies could address these limitations to enhance the model's reliability and applicability.

Conclusion

Our logistic regression model, which integrates both demographic and transvaginal ultrasonography data, has shown high specificity and sensitivity in predicting the malignancy of endometrial tumors. This method provides a valuable tool for healthcare providers, enhancing decision-making processes and potentially improving treatment outcomes.

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None.

Author contributions
All authors (XL, HC, FW and WW) contributed to the study of conception and design. XL, HW, TW, LW, and LW coordinated and managed all parts of the study. FW and WW carried out the literature search. XL, HC conducted data collection and performed preliminary data preparations. FW conducted data analyses and all the authors contributed to the interpretation of data. XL, HC, FW, and WW wrote the draft of the paper and all authors provided substantive feedback on the paper and contributed to the final manuscript. All authors read and approved the final manuscript.

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Data availability
The datasets used during the current study are available from the corresponding author on request.

Declarations

Ethics approval and consent to participate
The Local Ethics Commission for Scientific Research of General Hospital of Ningxia Medical University (record number 187/19.072019) approved the study. We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during the course of this research. All procedures were performed by the relevant guidelines in the manuscript. Written informed consent was obtained from patients for the collection of demographic information.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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