Submitted: 19 May, 2023 Accepted: 18 July, 2023 Published: 15 October, 2023 DOI:10.22514/ejgo.2023.077

ORIGINAL RESEARCH

European Journal of Gynaecological Oncology

# Analysis of risk factors and construction and validation of a predictive model for determining the risk of endometrial cancer in postmenopausal patients with abnormal uterine bleeding

Lili Zhang[1,†], Haiqing Lai[1,†], Qingping Lin[1,*]

[1]Department of Gynecology, Women and Children's Hospital, School of Medicine, Xiamen University, 361000 Xiamen, Fujian, China

***Correspondence**
linqingping3051801@163.com
(Qingping Lin)

[†] These authors contributed equally.

**Abstract**

The data of 174 postmenopausal patients with abnormal uterine bleeding admitted were assessed to determine associated risk factors and develop and validate a prediction model to evaluate the risk of endometrial cancer in these patients. The patients were divided into a study group and a control group, among which 62 patients were diagnosed with endometrial cancer. A binary logistic regression analysis model using multifactorial regression analysis was established, and a column line graph of the prediction model was created using the R software. The model's goodness-of-fit test was performed using the Hosmer-Lemeshow test, and SPSS (version 27, International Business Machines Corporation, Armonk, NY, USA) was used to plot the receiver operating characteristic (ROC) curve to evaluate the model's predictive value. Binary logistic multifactorial regression analysis revealed that elevated body mass index (BMI), human epididymal protein 4 (HE4), cancer antigen 125 (CA125), combined fibroids and thickened endometrial cancer were risk factors for endometrial cancer in patients with abnormal postmenopausal uterine bleeding, based on which a probability model for predicting the risk of developing endometrial cancer in patients with abnormal postmenopausal uterine bleeding was constructed, and represented as $P = 1/[1 + \exp(4.227 - 4.594X_1 - 2.029X_5 - 1.165X_6 - 1.817X_7 - 2.080X_8)]$. In addition, the goodness-of-fit test, assessed using Hosmer and Lemeshow, yielded an $\chi^2$ value of 14.253 and a $p$-value of 0.075. Furthermore, the ROC curve analysis demonstrated an area under the curve (AUC) of 0.993 (95% confidence interval (CI), 0.892–0.974; $p < 0.05$). In conclusion, elevated BMI, HE4 and CA125, along with the presence of combined fibroids and thickened endometrial lining, were identified as significant risk factors for endometrial cancer in postmenopausal patients with abnormal uterine bleeding. The risk prediction model developed in this study provides a scientifically sound approach to assess the risk of endometrial cancer in these patients.

**Keywords**

Abnormal postmenopausal uterine bleeding; Endometrial cancer; Risk factors; Prediction model; Efficacy validation

## 1. Introduction

Clinical investigations [1, 2] have reported that postmenopausal bleeding is prevalent in more than 30% of postmenopausal patients with abnormal uterine bleeding in outpatient clinics. In addition, several studies [3, 4] have identified various causes of irregular uterine bleeding, including benign lesions and cancer. Further, a link between irregular uterine bleeding and the development of endometrial cancer has also been reported. Over the past years, there has been a notable rise in the prevalence of endometrial cancer, and although the 5-year survival rate of affected individuals is generally over 90%, the prognosis substantially deteriorates for those with advanced-stage metastasis, resulting in poor quality of life and elevated mortality rates [5, 6]. Consequently, timely screening of high-risk individuals is important for its early detection to improve treatment outcomes. At present, clinical studies related to the development of early endometrial cancer in postmenopausal patients with abnormal uterine bleeding have primarily focused on identifying and screening risk factors, which include clinical features (*e.g.*, abdominal mass, menstrual volume disorders, *etc.*) and ultrasound findings (*e.g.*, enlarged uterus, substantial inhomogeneous echogenic areas in the uterine cavity, *etc.*). However, there is a lack of


  

scientific methods for predicting the likelihood of endometrial cancer occurrence, and studies aiming to establish prediction models are relatively uncommon [7, 8]. Given this literature gap, we designed this present study to assess the risk factors associated with endometrial cancer, develop a prediction model, and validate its effectiveness in predicting the risk of endometrial cancer in postmenopausal women with abnormal uterine bleeding.

## 2. Information and methods

### 2.1 Clinical data

In this study, the data of patients with abnormal postmenopausal uterine bleeding admitted to the Women and Children's Hospital (School of Medicine, Xiamen University, China) between December 2020 and December 2021 were retrieved and analyzed. Based on their pathological findings, they were divided into a study group and a control group. The study group comprised 62 patients diagnosed with endometrial cancer, while the control group comprised 112 patients with benign lesions.

#### 2.1.1 Sample size estimation

The sample size for the modeling group was determined using the rough formula for logistic regression analysis. An initial estimate indicated that there were five independent variables and that each of these variables required a sample of 10 patients. Considering a malnutrition incidence rate of 35.8% in patients and a projected sample loss of about 10%, the required sample size for the modeling group was calculated as follows: 5 variables $\times$ 10 patients $\times$ (1 + 10% for potential loss) $\div$ 35.8% malnutrition incidence, which yielded an approximate result of 154 patients as the minimum sample size needed to meet the study's requirements adequately.

#### 2.1.2 Inclusion criteria

The study included participants who met the following criteria: natural occurrence of menopause for at least 1 year, presence of vaginal bleeding or bloody discharge, underwent vaginal ultrasound and hysteroscopy, had postoperative histopathological examination, and availability of complete clinical data for study analysis.

#### 2.1.3 Exclusion criteria

Patients with the following conditions were excluded from study analysis: bleeding caused by lesions in the ovaries, fallopian tubes or vagina; presence of coagulation disorders, vaginitis, cervical polyps, congenital uterine malformations or malignant tumors; had intrauterine device(s); were concomitantly affected with immune system diseases; and had received hormone therapy within 1 year.

### 2.2 Methods

A form confidently designed by our hospital was used to collect and record relevant clinical information and case data of the patients, mainly including age, height, weight, pregnancy and delivery history, presence of any comorbidities, endometrial thickness, serum levels of HE4 and CA125 markers, as well as educational level.

#### 2.2.1 Detection methods of serum HE4 and CA125

In the morning, under fasting conditions, a total of 5 mL of peripheral venous blood was drawn from the patients. The HE4 index was determined using an enzyme-linked immunosorbent assay (ELISA), while the CA125 index was determined using electrochemiluminescence immunoassay.

#### 2.2.2 Uterine examination

The patient was placed in a supine position, and their endometrial thickness was measured using trans-guided ultrasonography (PhilipsiU 22 color ultrasonography, Philips, Amsterdam, Netherlands) by an ultrasonographer with 8 years of experience. Briefly, the depth of the patient's uterine cavity and other factors were also measured using a probe, and a comprehensive examination was performed using a hysteroscope, which was inserted after removing the air, and a dilatation fluid was injected with a light source. The patient's uterine cavity was effectively dilated by maintaining an internal pressure between 97 and 120 mmHg. Then, a flexible rotating lens was used to thoroughly examine the uterus, including the condition of the endometrium, and tissue sampling was performed by scraping the endometrium, which was then sent for pathological examination. This study used pathology results as the gold standard for evaluating the patient's endometrial pathology.

### 2.3 Statistical methods

The study data were analyzed using the SPSS v27.0 software (International Business Machines Corporation, Armonk, NY, USA). For measurement data, *t*-test was employed, while the chi-square test ($\chi^2$) was used for count data. The binary logistic regression analysis model was used for multi-factor regression analysis, the R 4.3.0 software (Lucent Technologies Inc., Murray Hill, NJ, USA) was used to plot the column line graph of the prediction model, Hosmer and Lemeshow for performing the goodness-of-fit test of the probability model, and SPSS to plot the ROC curve to evaluate the predictive value of the prediction model. A significance level of $p < 0.05$ was considered to indicate statistically significant differences.

## 3. Results

### 3.1 Incidence of endometrial cancer among postmenopausal patients with abnormal uterine bleeding

Among the 174 patients with abnormal postmenopausal uterine bleeding included in this study, a total of 62 patients were pathologically confirmed to have endometrial cancer, corresponding to an incidence rate of 35.63%. Further analysis revealed that among the 62 patients with endometrial cancer, 42 were classified as type I, while 20 were classified as type II endometrial cancer. The results were detailed in Table 1.

**TABLE 1. Univariate analysis of factors associated with endometrial cancer in patients with abnormal postmenopausal uterine bleeding.**

| Indicators | Benign lesion group (112) | Endometrial cancer group (62) | Statistical values | *p* value |
|---|---|---|---|---|
| Age (yr) | 57.25 ± 5.16 | 57.34 ± 5.09 | 0.109 | 0.913 |
| BMI (kg/m$^2$) | 24.35 ± 2.06 | 28.95 ± 3.01 | 10.908 | <0.001 |
| Years of menopause (yr) | 5.77 ± 1.54 | 6.35 ± 1.69 | 2.323 | 0.021 |
| Number of pregnancy (times) | 2.27 ± 0.68 | 2.19 ± 0.62 | 0.708 | 0.480 |
| Number of childbirths (times) | 2.16 ± 0.56 | 2.11 ± 0.55 | 0.542 | 0.588 |
| Combined hypertension (n, %) | | | | |
| Yes | 6, 5.36 | 9, 14.52 | 4.250 | 0.039 |
| No | 106, 94.64 | 53, 85.48 | | |
| Complicated diabetes mellitus (n, %) | | | | |
| Yes | 8, 7.14 | 11, 17.74 | 4.609 | 0.032 |
| No | 104, 92.86 | 51, 82.26 | | |
| Complicated uterine fibroids (n, %) | | | | |
| Yes | 27, 24.11 | 25, 40.32 | 5.008 | 0.025 |
| No | 85, 75.89 | 37, 59.68 | | |
| Endometrial thickness (mm) | 9.64 ± 2.56 | 10.98 ± 3.26 | 2.972 | 0.003 |
| HE4 (n, %) | | | | |
| >55 pmol/L | 24, 21.43 | 22, 35.48 | 4.054 | 0.044 |
| ≤5 pmol/L | 88, 78.57 | 40, 64.52 | | |
| CA125 (n, %) | | | | |
| >21 U/mL | 15, 13.39 | 17, 27.42 | 5.231 | 0.022 |
| ≤21 U/mL | 97, 86.61 | 45, 72.58 | | |
| Educational level (n, %) | | | | |
| Junior high school and below | 26, 23.21 | 15, 24.19 | 0.118 | 0.943 |
| High School and Junior College | 60, 53.57 | 34, 54.84 | | |
| College and above | 26, 23.21 | 13, 20.97 | | |
| Hormone therapy (n, %) | | | | |
| Yes | 11, 9.82 | 6, 9.68 | 0.001 | 0.976 |
| No | 101, 90.18 | 56, 90.32 | | |

*BMI: body mass index; HE4: human epididymal protein 4; CA125: cancer antigen 125.*

## 3.2 Results of binary logistic multi-factor regression analysis

In the binary logistic regression analysis model, endometrial cancer was used as the dependent variable, while BMI, year of menopause, combined hypertension, combined diabetes mellitus, combined fibroids, endometrial thickness, HE4 and CA125, which were significantly different, were used as independent variables (Table 2). Data analysis indicated that BMI >28 kg/m$^2$, combined uterine fibroids, endometrial thickness, and HE4 and CA125 levels were significantly different ($p < 0.05$), with corresponding odds ratio (OR) values >1, indicating they were among the most common causes of abnormal postmenopausal uterine bleeding and potentially high-risk factors for the development of endometrial cancer in these patients (Table 3).

## 3.3 Probabilistic model of endometrial cancer

Based on the coefficients of the five identified risk factors listed in Table 3, a binary logistic multi-factor regression analysis model was developed as follows:

$$\text{Logit (P)} = \ln[P/(1-P)] = -4.227 + 4.594X_1 + 2.029X_5 + 1.165X_6 + 1.817X_7 + 2.080X_8$$

To obtain the probability model for endometrial cancer, the following equation was used:

$$P = 1/[1 + \exp(4.227 - 4.594X_1 - 2.029X_5 - 1.165X_6 - 1.817X_7 - 2.080X_8)]$$

To visualize the prediction model, a column line diagram, also known as a nomogram, was created using R software, as shown in Fig. 1.

**TABLE 2. Variable assignments for binary logistic multivariate regression analysis of endometrial carcinogenesis in postmenopausal patients with abnormal uterine bleeding.**

| Factors | B | Assignment status |
|---|---|---|
| Endometrial cancer | Y | Yes: Assignment 1; No: Assignment 0 |
| BMI | $X_1$ | >28 kg/m$^2$: Assignment 1; ≤28 kg/m$^2$: Assignment 0 |
| Year of menopause | $X_2$ | >6 years: 1; No: Assignment 0 |
| Combined with hypertension | $X_3$ | Yes: Assignment 1; No: Assignment 0 |
| Combined diabetes mellitus | $X_4$ | Yes: Assignment 1; No: Assignment 0 |
| Combined uterine fibroids | $X_5$ | Yes: Assignment 1; No: Assignment 0 |
| Endometrial thickness | $X_6$ | >10 mm: Assignment 1; ≤10 mm: Assignment 0 |
| HE4 | $X_7$ | >55 pmol/L: Assignment 1; ≤55 pmol/L: Assignment 0 |
| CA125 | $X_8$ | >21 U/mL: Assignment 1; ≤21 U/mL: Assignment 0 |

*BMI: body mass index; HE4: human epididymal protein 4; CA125: cancer antigen 125.*

**TABLE 3. Results of binary logistic multi-factor regression analysis.**

| Factors | $\beta$ | Standard Error | Wald | $p$ | OR value | OR value 95% confidence interval | |
|---|---|---|---|---|---|---|---|
| | | | | | | Lower limit | Upper limit |
| BMI >28 kg/m$^2$ | 4.594 | 0.729 | 39.710 | <0.001 | 98.840 | 23.684 | 412.490 |
| Age of menopause >6 years | 0.545 | 0.559 | 0.952 | 0.329 | 1.725 | 0.577 | 5.161 |
| Combined with hypertension | 0.020 | 1.101 | 0.000 | 0.986 | 1.020 | 0.118 | 8.832 |
| Combined diabetes mellitus | 0.164 | 1.128 | 0.021 | 0.885 | 1.178 | 0.129 | 10.755 |
| Endometrial thickness | 1.165 | 0.549 | 4.511 | 0.034 | 3.207 | 1.094 | 9.402 |
| HE4 | 1.817 | 0.605 | 9.010 | 0.003 | 6.150 | 1.878 | 20.139 |
| CA125 | 2.080 | 0.964 | 4.659 | 0.031 | 8.003 | 1.211 | 52.893 |
| Constants | −4.227 | 0.737 | 32.889 | <0.001 | 0.015 | | |

*OR: odds ratio; BMI: body mass index; HE4: human epididymal protein 4; CA125: cancer antigen 125.*

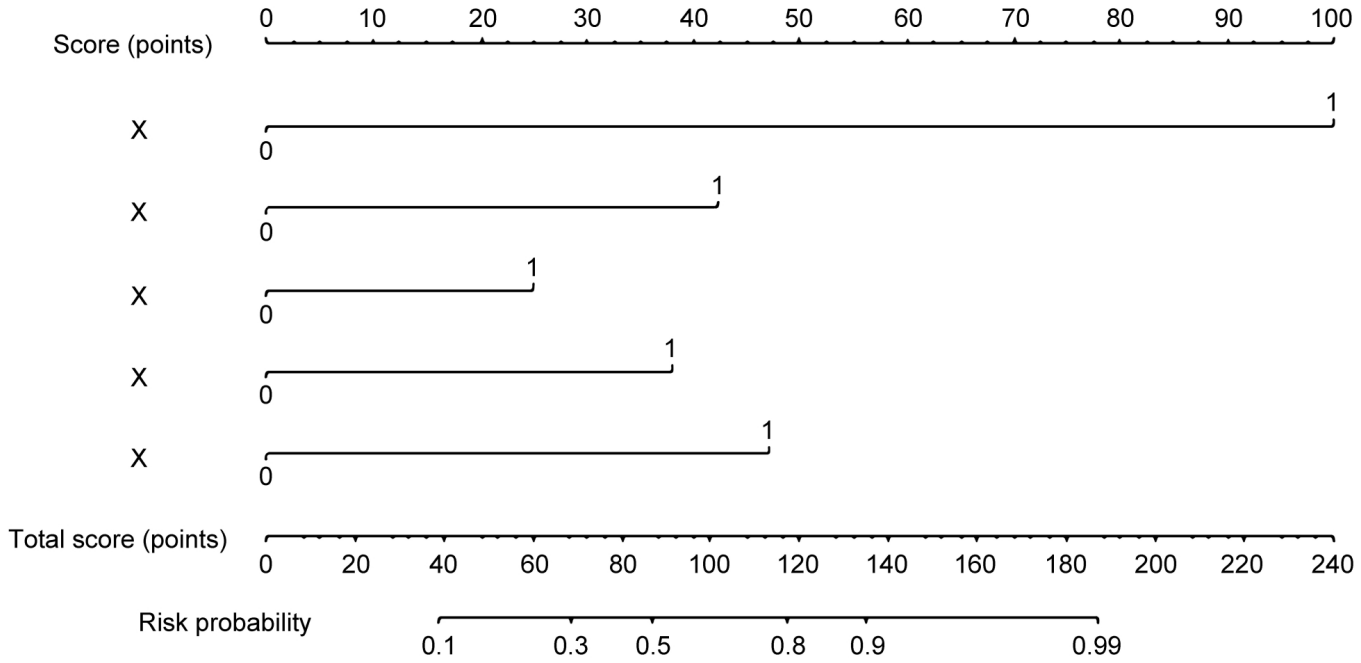


**FIGURE 1. Nomogram illustrating the model for predicting the probability of endometrial cancer in postmenopausal patients with abnormal uterine bleeding.**

### 3.4 Goodness-of-fit tests for probabilistic models

The goodness-of-fit test of the probability model, conducted using the Hosmer and Lemeshow test, yielded a $\chi^2$ value of 14.253 with a corresponding $p$-value of 0.075, indicating that the probability model demonstrated a good fit (Table 4).

**TABLE 4. Hosmer-Lemeshow test of the probability model.**

| $\chi^2$ | Degree of freedom | $p$ |
|---|---|---|
| 14.253 | 8 | 0.075 |

### 3.5 Predictive value analysis of predictive models

ROC curve analysis demonstrated that the predictive model had significant predictive value ($p < 0.05$) with an Area Under the Curve (AUC) of 0.993 and a 95% confidence interval (CI) ranging from 0.892 to 0.974 (Fig. 2).

## 4. Discussion

Abnormal uterine bleeding is a common condition in postmenopausal women in clinical gynecology [9, 10]. Clinical studies [11, 12] have revealed that the causes of abnormal uterine bleeding in postmenopausal women can be classified into benign uterine lesions, non-organic lesions, precancerous lesions and endometrial cancer, with the percentage of patients diagnosed with endometrial cancer after experiencing abnormal uterine bleeding exceeding 40% [13, 14]. The incidence of endometrial cancer in postmenopausal women with abnormal uterine bleeding is significantly higher compared to those without such bleeding, with reports [15, 16] indicating that the rate of endometrial cancer is 2.6 times higher in postmenopausal women with abnormal uterine bleeding compared with healthy women. These findings underscore the association between abnormal uterine bleeding and endometrial cancer in postmenopausal women. Although there is no unanimous consensus regarding the pathogenesis of endometrial cancer, it has been suggested that factors such as prolonged estrogen stimulation and a relative lack of progesterone antagonism may also be important contributors to the occurrence and development of this disease [17, 18]. Neoplastic endometrial lesions exhibit certain physical characteristics in diagnostic endometrial scraping specimens, including sieve-like structures, glandular outgrowth branches, hyperplasia of interstitial fibrous tissue and neoplastic necrosis. In addition, endometrial thickness, microvascular density, ultrasound resistance index and the pulsatility index of patients with endometrial cancer have been reported to be higher than those with simple endometrial hyperplasia on Doppler ultrasonography and may have certain significance in the differential diagnosis of endometrial cancer. Numerous clinical studies have identified [19–21] age, BMI, combined hypertension, diabetes mellitus and menopause as closely related risk factors for endometrial cancer. However, most of these studies have focused on qualitative aspects, and there is a lack of quantitative prediction tools and methods for assessing the risk of cancer in postmenopausal women with abnormal uterine bleeding, with limited research in this field [22, 23]. To this end, we aimed to develop a prediction model for endometrial carcinogenesis in postmenopausal patients with abnormal uterine bleeding and validate its potential clinical efficacy.

The risk factors identified in this study, including BMI, combined uterine fibroids, endometrial thickness, HE4 and CA125, align with those reported in previous literature [24, 25]. Further analysis indicated an association between overweight and the development of endometrial cancer, potentially associated with the increased estrogen levels and decreased progesterone secretion observed in overweight patients. Even though uterine fibroids are still generally considered to be benign lesions, particularly in postmenopausal patients, there is still a sizable percentage of patients whose fibroids have not changed significantly or showed signs of growth, leading to clinical symptoms such as uterine bleeding and abdominal pain. This suggests that hormone levels in these patients have not declined and may even be elevated, significantly increasing the risk of cancer [24]. Endometrial thickness is closely related to endometrial carcinogenesis. Endometrial thickness is closely linked to the development of endometrial cancer. Previous studies examining the clinical use of receiver operating characteristic curves have identified a cut-off value of 10 mm for endometrial thickness, consistent with the findings of this study, thereby highlighting the importance of endometrial thickness in determining the presence of endometrial carcinoma [26, 27]. HE4 is an important tumor marker commonly used clinically in ovarian cancer diagnosis and treatment and belongs to one of the types of small molecule secreted proteins. It has gradually found application in clinical practice for endometrial cancer, with relevant clinical studies confirming its significance in predicting the risk of endometrial cancer [28, 29]. It was also reported that a significant increase in HE4 level may increase the risk of endometrial cancer in patients with abnormal postmenopausal uterine bleeding. CA125, the most widely used tumor marker in gynecological clinics, can be detected in high levels in the blood when the epithelial basement membrane is breached, for instance, when the patient's epithelial basement membrane is damaged. It has been demonstrated to have high diagnostic relevance for early cancer detection [30]. It has also been employed as an important basis for diagnosing, classifying and predicting the prognosis of patients with endometrial cancer.

In this study, a binary logistic multi-factor regression analysis model was constructed based on the five risk factors and their coefficients derived above. The goodness-of-fit of the probabilistic model was assessed using the Hosmer-Lemeshow, and the model's predictive value was analyzed by ROC curves. The results indicated excellent model fit and significant predictive value. Furthermore, when applying this model to the patients in the study, it successfully predicted 43 cases of endometrial cancer and 106 cases of non-disease. The overall prediction accuracy of the model was found to be 85.60%, with a sensitivity of 87.76% and a specificity of 94.59%, further validating its reliability.

The nomogram created using R software based on the prediction model in this study offers a more precise prediction

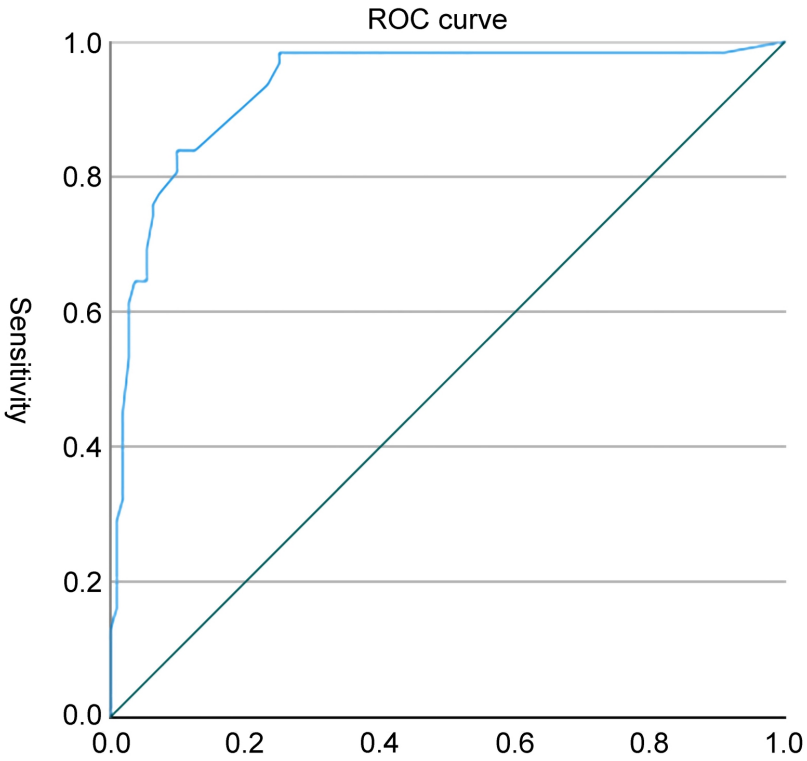


**FIGURE 2. ROC curve depicting the performance of the prediction model.** ROC: receiver operating characteristic.

framework for clinical decision-making. By assigning specific scores to each risk factor, the nomogram enables clinicians to determine patients' risk occurrence probability values, thereby serving as a valuable reference for both clinicians and patients in the diagnosis and treatment process and aiding in clinical decision-making.

The current study has certain limitations stemming from the limited number of cases and data sources, which may impact the generalizability of the findings. Notably, while previous research has indicated that age and the time elapsed since menopause are important factors in the development of endometrial cancer, this study did not reach the same conclusion. Future studies could address these limitations by including a larger and more diverse study population, allowing for more comprehensive and unbiased results regarding the clinical prevention and treatment of endometrial cancer.

## 5. Conclusions

In conclusion, this study found that elevated BMI, HE4, CA125, combined fibroids and endometrial cancer thickening are significant risk factors for the development of endometrial cancer in postmenopausal patients with abnormal uterine bleeding. The risk prediction model developed in this study provides a scientific approach to assess the risk of endometrial cancer in patients. By utilizing this model, clinicians can implement early and proactive clinical interventions and control measures for patients, ultimately improving patient outcomes.

### 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

LLZ, HQL and QPL—designed the study and carried them out; supervised the data collection, analyzed the data, interpreted the data, prepare the manuscript for publication and reviewed the draft of the manuscript. All authors have read and approved the manuscript.

### ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of Women and Children's Hospital, School of Medicine, Xiamen University (Approval no. KY-2020-075). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

### ACKNOWLEDGMENT

Not applicable.

### FUNDING

This research received no external funding.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES


[1] D'Urso S, Arumugam P, Weider T, Hwang LD, Bond TA, Kemp JP, *et al*. Mendelian randomization analysis of factors related to ovulation and reproductive function and endometrial cancer risk. BMC Medicine. 2022; 20: 419.

[2] Dou Y, Song K, Fu Y, Shen Y, Zhang C, Yao S, *et al*. Risk factors and prognosis of early recurrence in stage I–II endometrial cancer: a large-scale, multi-center, and retrospective study. Frontiers in Medicine. 2022; 9: 808037.

[3] Rebegea LF, Stoleriu G, Manolache N, Serban C, Craescu M, Lupu MN, *et al*. Associated risk factors of lower limb lymphedema after treatment of cervical and endometrial cancer. Experimental and Therapeutic Medicine. 2020; 20: 181.

[4] Wedin M, Stalberg K, Marcickiewicz J, Ahlner E, Ottander U, Åkesson Å, *et al*. Risk factors for lymphedema and method of assessment in endometrial cancer: a prospective longitudinal multicenter study. International Journal of Gynecologic Cancer. 2021; 31: 1416–1427.

[5] Otani S, Himoto Y, Nishio M, Fujimoto K, Moribata Y, Yakami M, *et al*. Radiomic machine learning for pretreatment assessment of prognostic risk factors for endometrial cancer and its effects on radiologists' decisions of deep myometrial invasion. Magnetic Resonance Imaging. 2022; 85: 161–167.

[6] Pigott A, Obermair A, Janda M, Vagenas D, Ward LC, Reul-Hirche H, *et al*. Incidence and risk factors for lower limb lymphedema associated with endometrial cancer: results from a prospective, longitudinal cohort study. Gynecologic Oncology. 2020; 158: 375–381.

[7] Faber MT, Sperling CD, Bennetsen AKK, Aalborg GL, Kjaer SK. A Danish nationwide study of risk factors associated with type I and type II endometrial cancer. Gynecologic Oncology. 2021; 161: 553–558.

[8] Jin X, Yan R, Li Z, Zhang G, Liu W, Wang H, *et al*. Evaluation of amide proton transfer-weighted imaging for risk factors in stage I endometrial cancer: a comparison with diffusion-weighted imaging and diffusion kurtosis imaging. Frontiers in Oncology. 2022; 12: 876120.

[9] Gaudet Chardonnet A, Azaïs H, Ballester M, Raimond E, Bendifallah S, Ouldamer L, *et al*. Prognostic value and risk factors of peritoneal carcinomatosis recurrence for patients with endometrial cancer: a multicenter study from the FRANCOGYN group. Annals of Surgical Oncology. 2021; 28: 212–221.

[10] Lei M, Adambekov S, Edwards RP, Wang R, Yuan J, Kalix E, *et al*. Endometrial cancer risk factors in Singapore Chinese: a prospective cohort study. Annals of Epidemiology. 2022; 71: 9–14.

[11] Lin Q, Lu Y, Lu R, Chen Y, Wang L, Lu J, *et al*. Assessing metabolic risk factors for LVSI in endometrial cancer: a cross-sectional study. Therapeutics and Clinical Risk Management. 2022; 18: 789–798.

[12] Sarink D, Wilkens LR, White KK, Le Marchand L, Wu AH, Setiawan VW, *et al*. Racial/ethnic differences in anthropometric and hormone-related factors and endometrial cancer risk: the multiethnic cohort study. British Journal of Cancer. 2021; 124: 1724–1733.

[13] Bogani G, Papadia A, Buda A, Casarin J, Di Donato V, Plotti F, *et al*. Factors predicting morbidity in surgically-staged high-risk endometrial cancer patients. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2021; 266: 169–174.

[14] Pin S, Mateshaytis J, Ghosh S, Batuyong E, Easaw JC. Risk factors for venous thromboembolism in endometrial cancer. Current Oncology. 2020; 27: 198–203.

[15] Angeles MA, Migliorelli F, León Ramírez LF, Ros C, Perissinotti A, Tapias A, *et al*. Predictive factors of preoperative sentinel lymph node detection in intermediate and high-risk endometrial cancer. The Quarterly Journal of Nuclear Medicine and Molecular Imaging. 2023; 67: 37–45.

[16] Zhang Y, Liu H, Han X, Tang Y. Analysis of risk factors for sentinel lymph node metastasis in patients with endometrial cancer. American Journal of Translational Research. 2022; 14: 8650–8658.

[17] Washington CR, Haggerty A, Ronner W, Neff PM, Ko EM. Knowledge of endometrial cancer risk factors in a general gynecologic population. Gynecologic Oncology. 2020; 158: 137–142.

[18] Zhao J, Hu Y, Zhao Y, Chen D, Fang T, Ding M. Risk factors of endometrial cancer in patients with endometrial hyperplasia: implication for clinical treatments. BMC Women's Health. 2021; 21: 312.

[19] Sponholtz TR, Palmer JR, Rosenberg L, Chen C, Chen Y, Clarke MA, *et al*. Risk factors for endometrial cancer in Black women. Cancer Causes & Control. 2023; 34: 421–430.

[20] Togami S, Kubo R, Kawamura T, Yanazume S, Kamio M, Kobayashi H. Risk factors for lymphatic complications following lymphadenectomy in patients with endometrial cancer. Taiwanese Journal of Obstetrics and Gynecology. 2020; 59: 420–424.

[21] Toprak S, Sahin EA, Sahin H, Tohma YA, Yilmaz E, Meydanli MM. Risk factors for cervical stromal involvement in endometrioid-type endometrial cancer. International Journal of Gynecology & Obstetrics. 2021; 153: 51–55.

[22] Anderson EM, Luu M, Lu DJ, Chung EM, Kamrava M. Pathologic primary tumor factors associated with risk of lymph node involvement in patients with non-endometrioid endometrial cancer. Gynecologic Oncology. 2022; 165: 281–286.

[23] Shin W, Yang SJ, Park SY, Kang S, Lee DO, Lim MC, *et al*. A predictive model based on site-specific risk factors of recurrence regions in endometrial cancer patients. BMC Cancer. 2022; 22: 1111.

[24] Anic K, Flohr F, Schmidt MW, Krajnak S, Schwab R, Schmidt M, *et al*. Frailty assessment tools predict perioperative outcome in elderly patients with endometrial cancer better than age or BMI alone: a retrospective observational cohort study. Journal of Cancer Research and Clinical Oncology. 2023; 149: 1551–1560.

[25] Kurosu H, Todo Y, Yamada R, Minowa K, Tsuruta T, Minobe S, *et al*. A BMI-category distribution pattern of intrinsic and treatment-related prognostic factors in endometrial cancer. Japanese Journal of Clinical Oncology. 2021; 51: 722–727.

[26] Shang W, Zhang J, Song H, Zhu S, Zhang A, Hua Y, *et al*. Mechanism of tetrandrine against endometrial cancer based on network pharmacology. Drug Design, Development and Therapy. 2021; 15: 2907–919.

[27] Zhong Z, Guo X, Zheng Y. Network pharmacology-based and molecular docking analysis of resveratrol's pharmacological effects on type I endometrial cancer. Anti-Cancer Agents in Medicinal Chemistry. 2022; 22: 1933–1944.

[28] Feng W, Jia N, Jiao H, Chen J, Chen Y, Zhang Y, *et al*. Circulating tumor DNA as a prognostic marker in high-risk endometrial cancer. Journal of Translational Medicine. 2021; 19: 51.

[29] Romera AE, Guardiola TC, Vielba MB, Torralba CD, Martin PCJ, Mainar LB. HE4 tumor marker as a predictive factor for lymphatic metastasis in endometrial cancer. International Journal of Gynecology & Obstetrics. 2020; 149: 265–268.

[30] LyBarger KS, Miller HA, Frieboes HB. CA125 as a predictor of endometrial cancer lymphovascular space invasion and lymph node metastasis for risk stratification in the preoperative setting. Scientific Reports. 2022; 12: 19783.


**How to cite this article:** Lili Zhang, Haiqing Lai, Qingping Lin. Analysis of risk factors and construction and validation of a predictive model for determining the risk of endometrial cancer in postmenopausal patients with abnormal uterine bleeding. European Journal of Gynaecological Oncology. 2023; 44(5): 39-45. doi: 10.22514/ejgo.2023.077.