

Risk Factors and Preoperative Prediction Model for Endometrial Lesions in Postmenopausal Patients with Benign Ovarian Tumors: A Retrospective Single-Center Study

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Background: Benign ovarian tumor is a common clinical gynecological disease. Bilateral salpingo-oophorectomy is currently recommended for postmenopausal benign ovarian tumor, and whether the uterus needs to be removed simultaneously is controversial. In this study, we proposed to evaluate the risk factors for combined endometrial lesions, aiming to provide reference for the surgical scope selection of postmenopausal benign ovarian tumor patients by constructing a preoperative prediction model.

Methods: This was a single-center retrospective study of 471 postmenopausal patients with benign ovarian tumors who were hospitalized between January 2018 and December 2024. A multivariate analysis was carried out to find out independent risk factors for coexisting endometrial lesions. A preoperative prediction model was established and its performance was evaluated by receiver operating characteristic curves, calibration curves, and decision curves.

Results: Among 471 postmenopausal benign ovarian tumor patients, 36 (7.6%) had concurrent endometrial lesions. Menarche age, endometrial thickness under ultrasound, solid tumor under ultrasound and $E_2 \geq 10\text{pg/mL}$ were independent risk factors for endometrial lesions in postmenopausal benign ovarian tumor patients ($P < 0.001$, $P < 0.001$, $P = 0.049$, $P = 0.022$). The preoperative prediction model was developed based on independent risk factors and demonstrated good predictive performance (AUC = 0.821). The final model showed moderate discrimination (optimism-corrected C-index = 0.809). The nomogram exhibited excellent calibration (mean absolute error = 0.017). The decision curve analysis confirmed its potential to offer substantial clinical net benefit. The model may help identify postmenopausal patients at higher risk of coexisting endometrial lesions and inform individualized surgical decision-making pending further validation.

Conclusion: This study identified independent risk factors for coexisting endometrial lesions and developed a preoperative prediction model that shows promise for risk stratification. The nomogram offers a non-invasive, supportive triage tool to guide individualized management for postmenopausal patients with benign ovarian tumors.

Keywords: ovarian tumor, endometrial lesion, postmenopausal period, prediction model, estrogen

Introduction

Benign ovarian tumor is common clinical gynecologic disease. Although postmenopausal women exhibit a higher incidence of ovarian cancer compared to younger women, the majority of ovarian masses remain benign. The incidence of postmenopausal benign ovarian tumor has progressively increased in recent years with the development of imaging techniques and the extension of mean lifespan. Studies have shown that its worldwide incidence is approximately 5% ~17%¹⁻³ and benign ovarian tumor account for approximately 7% of gynecologic inpatients.⁴ According to the 2020 World Health Organization (WHO) classification criteria, endometrial hyperplasia can be categorized into endometrial hyperplasia without atypia (EH) and endometrial atypical hyperplasia (EAH) or Endometrial intraepithelial neoplasia



(EIN).^{5,6} The primary mechanism of endometrial hyperplasia is unopposed estrogen exposure, leading to abnormal glandular proliferation and an elevated gland-to-stroma ratio. Infertility, obesity, early menarche, late menopause, family history of tumor, etc. are high-risk factors for endometrial hyperplasia.^{7–9} Endometrial hyperplasia can further develop into endometrial cancer (EC) if not diagnosed and treated promptly.

Postmenopausal benign ovarian tumor patients are at risk of concurrent endometrial lesions. Studies have shown that 50% of endometrial hyperplasia cases occur during the menopausal transition and postmenopausal period.¹⁰ Bilateral salpingo-oophorectomy is currently recommended for postmenopausal benign ovarian tumor, while the necessity of concurrent hysterectomy remains controversial.¹¹ Clinically, some postmenopausal benign ovarian tumor patients were unexpectedly found to have combined endometrial lesions after hysterectomy and bilateral salpingo-oophorectomy. Current domestic and international research has explored cases of incidentally detected gynecological tumor in benign ovarian tumor patients undergoing hysterectomy. Reinholdt et al followed 149,807 benign ovarian tumor patients, among whom 656 women were diagnosed with EC during follow-up.¹² Desai et al analyzed 229,536 women who underwent hysterectomy for benign gynecological diseases, finding an unexpected postoperative finding of EC in 0.75% of patients, and in 1.43% of the 78,255 patients who underwent hysterectomy for benign ovarian tumor.¹³

Therefore, performing total hysterectomy with bilateral salpingo-oophorectomy in postmenopausal benign ovarian tumor patients may prevent missed diagnosis of some asymptomatic endometrial diseases. However, studies indicate that compared to salpingo-oophorectomy alone, hysterectomy prolongs operative time, elevates surgical complexity, and increases the probability of postoperative complications.¹⁴ Whether postmenopausal benign ovarian tumor patients should undergo hysterectomy remains controversial. In recent years, several recent studies have attempted to develop predictive models for endometrial lesions and cancer.^{15,16} Despite this growing body of work, most existing models focus primarily on endometrial cancer risk or specific subgroups, and few address prediction of all endometrial lesions in postmenopausal women with benign ovarian tumors. Moreover, many models lack integration of diverse clinical, ultrasonographic, and serological markers. There is currently very limited research on the prediction of concurrent endometrial lesions in postmenopausal patients with benign ovarian tumors. Although diagnostic dilatation and curettage (D&C) or hysteroscopy is routinely used for preoperative evaluation of endometrial pathology, these invasive procedures may not be necessary for all postmenopausal patients with benign ovarian tumors. There remains a need for a non-invasive approach to preoperatively stratify the risk of concomitant endometrial lesions in this population. This study aims to analyze the risk factors for endometrial lesions in postmenopausal benign ovarian tumor patients and develop a preoperative predictive model, thereby providing reference for standardized management of postmenopausal patients with benign ovarian tumor.

Materials and Methods

Design and Participants

This retrospective study was conducted using data from patients with postmenopausal benign ovarian tumor admitted to the Department of Obstetrics and Gynecology at Tianjin Medical University General Hospital between January 2018 and December 2024.

The inclusion criteria were: (1) naturally postmenopausal women with ≥ 1 year of amenorrhea; (2) surgically treated for ovarian masses with postoperative pathological confirmation of benign ovarian tumor. The exclusion criteria were: (1) Premenopausal patients or patients with a menopausal duration of less than one year; (2) concurrent gynecological conditions requiring surgical intervention; (3) prior hysterectomy or adnexectomy due to other diseases; (4) Patients with missing clinical data. Consecutive patients were screened for eligibility. Patients with missing data for any of the variables were excluded from the univariate analysis, and a complete-case analysis was performed. Details regarding variables with missing values and their proportions are summarized in [Table S1](#). Based on preoperative diagnostic curettage and postoperative endometrial histopathology, patients were categorized into two groups: postmenopausal benign ovarian tumor with endometrial lesion (BOT-E group) and without endometrial lesion (BOT group).

A total of 471 consecutive postmenopausal patients with benign ovarian tumors were enrolled ([Figure 1](#)). Based on preoperative diagnostic D&C or hysteroscopy and postoperative endometrial histopathology, patients were categorized

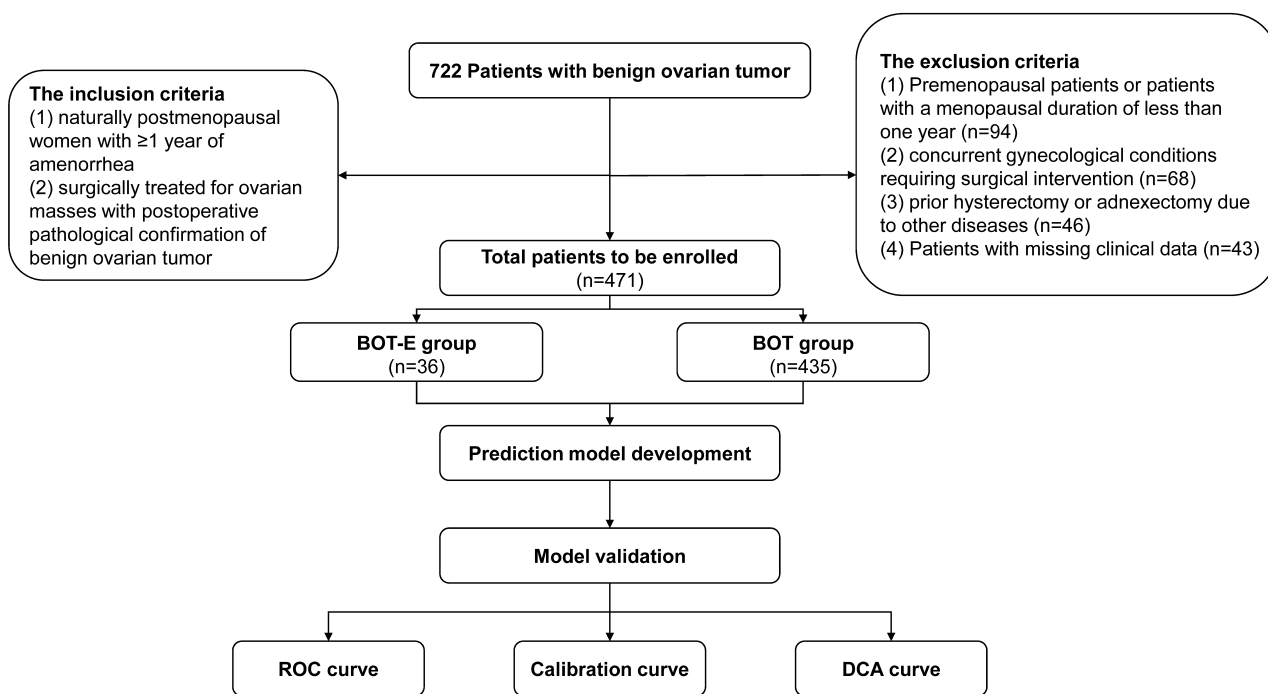


Figure 1 The flow chart of the selection process for patients and prediction model development.
Abbreviations: ROC, receiver operating characteristic curve; DCA, decision curve analysis.

into two groups: postmenopausal benign ovarian tumor with endometrial lesion (BOT-E group, n=36) and without endometrial lesion (BOT group, n=435). The risk factors for postmenopausal benign ovarian tumor patients with endometrial lesions were analyzed, and a preoperative prediction model was constructed to provide reference for the management of postmenopausal benign ovarian tumor patients. This study was conducted in compliance with the principles of the Declaration of Helsinki and received approval from the institutional review boards (Tianjin Medical University General Hospital IRB, protocol number IRB2025-YX-501-01). Informed consent was obtained from patients prior to investigations, treatment, and participation.

Definitions

Post-menopause was defined as the absence of menstruation for at least 12 consecutive months. The age at menopause among the included patients ranged from 32 to 58 years.

According to the consensus opinion from the International Endometrial Tumor Analysis (IETA) group,¹⁷ endometrial thickness was measured in the sagittal plane including both endometrial layers. In the presence of intracavitary fluid, both single layers were measured, and the sum was recorded. All measurements were performed by experienced sonographers according to routine clinical practice. To ensure consistency, measurements were performed according to a standardized protocol, and the maximal thickness recorded during the examination was used for analysis. As this is a retrospective study based on real-world clinical practice, the ultrasound operators had access to the patients' preliminary clinical diagnoses (eg, adnexal masses) as part of routine clinical workflow, they were blinded to the final endometrial pathological findings, which were only confirmed postoperatively.

Solid means exhibiting high echogenicity.¹⁸ A solid tumor is defined as a tumor in which the solid component occupies the entire lesion. Tumors containing cystic components were defined as non-solid. These areas typically appeared anechoic on ultrasound. Ovarian masses were classified as solid or non-solid based on a retrospective review of ultrasound report descriptions. Masses composed of solid components were defined as solid, whereas masses that were purely cystic or contained cystic components without definite solid areas were defined as non-solid. Due to the retrospective design of the study, no formal inter-observer agreement assessment was conducted.

Serum estradiol (E_2) was measured as part of routine preoperative laboratory testing, performed 3–5 days before surgery. All measurements were performed in the central laboratory of Tianjin Medical University General Hospital using a standardized automated chemiluminescent immunoassay system. The assay had a lower limit of quantification (LOQ) of 10 pg/mL. Based on the assay characteristics, established clinical laboratory reference data,¹⁹ and previously published studies,²⁰ serum E_2 was analyzed as a categorical variable, with 10 pg/mL used as the cutoff value. In the study, E_2 was treated as a categorical variable, with patients having E_2 levels below 10 pg/mL categorized into the $E_2 < 10$ pg/mL group.

Endometrial Specimens and Histopathological Interpretation

Endometrial sampling was performed by diagnostic D&C or hysteroscopy according to routine clinical practice. Diagnostic D&C was conducted using a standard sharp curette to perform a systematic, circumferential sampling of the uterine cavity. For hysteroscopy, a hysteroscope was utilized under saline distention to systematically inspect the uterine walls; when focal lesions were identified, targeted biopsies or fragmented curettage were performed under direct visualization. All procedures were carried out by experienced gynecologists. Among the 471 included patients, 88 underwent preoperative diagnostic D&C or hysteroscopy, of whom 13 were diagnosed with concomitant endometrial lesions. For patients who did not undergo preoperative curettage or hysterectomy, endometrial status was assessed through postoperative clinical follow-up and structured telephone interviews. All specimens were submitted for histopathological examination by two experienced gynecologic pathologists who were blinded to clinical outcomes.

Endometrial lesions were classified in order of increasing severity as follows: irregular endometrial hyperplasia, simple endometrial hyperplasia, complex endometrial hyperplasia, EAH, and EC. When both preoperative endometrial samples and postoperative hysterectomy specimens were available and yielded discordant pathological results, the more advanced lesion according to this hierarchical classification was defined as the final endometrial pathological diagnosis.

Statistical Analysis

Clinical data of all eligible postmenopausal patients with benign ovarian tumors were collected. Statistical analyses were performed using SPSS version 27.0 (IBM Corp., Armonk, NY) and R software (version 4.5.1), with a two-sided P value < 0.05 considered statistically significant.

Continuous variables were compared using the independent *t*-test for normally distributed data or the Mann–Whitney *U*-test for non-normally distributed data and are presented as the mean \pm standard deviation or median (interquartile range), as appropriate. Categorical variables were analyzed using the χ^2 -test or Fisher's exact test, and expressed as frequencies and percentages.

Variables with $P < 0.05$ in univariate analysis were simultaneously entered into a multivariable logistic regression model. Predictors that remained statistically significant ($P < 0.05$) were retained for final model construction and nomogram development. Multivariable logistic regression was conducted using the `lrm()` function from the `rms` package in R. Continuous variables were entered as continuous terms. Multicollinearity was assessed using the variance inflation factor (VIF), and no significant collinearity was detected (all VIFs < 5). Interaction terms were not included.

Model performance was evaluated regarding discrimination, calibration, and clinical utility using the receiver operating characteristic (ROC) curve, calibration plots, and decision curve analysis (DCA), respectively. Internal validation with 1000 bootstrap repetitions was performed to correct for overfitting. The optimism-corrected concordance index (C-index) was used to quantify discrimination, while calibration was assessed via bootstrap-corrected calibration plots, intercept, and slope. Given the limited number of events, 95% confidence intervals for the area under the receiver operating characteristic curve (AUC), sensitivity, and specificity were estimated using stratified bootstrap resampling with 1000 iterations.

This study was developed and reported in accordance with the TRIPOD guidelines for prediction model development and internal validation.²¹

Results

Endometrial Pathology and Ovarian Tumor Histological Subtypes in Postmenopausal Benign Ovarian Tumor Patients

Histological types of endometrial pathology in postmenopausal benign ovarian tumor patients were summarized (Table 1). Among 36 cases with concurrent endometrial lesion, irregular endometrial hyperplasia was the most prevalent subtype (n=18, 50.0%).

Patients were divided by the presence of endometrial lesion into two groups: postmenopausal benign ovarian tumor with endometrial lesion (BOT-E group, n=36, 7.6%) and postmenopausal benign ovarian tumor without endometrial lesion (BOT group, n=435, 92.4%). Histological types of ovarian tumor in postmenopausal benign ovarian tumor patients were analyzed (Table 2), with serous cystadenoma being the most common overall (146 cases, 30.9%). Ovarian fibroma

Table 1 Histological Types of Endometrial Pathology in Postmenopausal Benign Ovarian Tumor Patients

Histological Type	Cases	%
Irregular endometrial hyperplasia	18	50.0
Simple endometrial hyperplasia	9	25.0
Complex endometrial hyperplasia	5	13.9
EAH	3	8.3
EC	1	2.8
Total	36	100.0

Abbreviations: EAH, endometrial atypical hyperplasia; EC, endometrial cancer.

Table 2 Histological Types of Ovarian Tumor in Postmenopausal Benign Ovarian Tumor Patients

Histological Type	Total, n (%)	BOTE Group, n (%)	BOT Group, n (%)
Cases, n (%)	471 (100.0)	36 (7.6)	435 (92.4)
Epithelial tumor			
Serous cystadenoma	146 (31.0)	5 (13.9)	141 (32.5)
Mucinous cystadenoma	43 (9.1)	5 (13.9)	38 (8.7)
Seromucinous cystadenoma	3 (0.6)	2 (5.6)	1 (0.2)
Benign Brenner tumor	14 (3.0)	1 (2.8)	13 (3.0)
Adenofibroma	18 (3.8)	0 (0.0)	18 (4.1)
Germ cell tumor			
Mature cystic teratoma	83 (17.6)	4 (11.1)	79 (18.2)
Struma ovarii	6 (1.3)	1 (2.7)	5 (1.1)
Sex cord-stromal tumor			
Fibroma	110 (23.4)	12 (33.3)	98 (22.6)
Thecoma	7 (1.5)	1 (2.7)	6 (1.4)
Sclerosing stromal tumor	2 (0.4)	1 (2.7)	1 (0.2)
Steroid cell tumor	4 (0.8)	2 (5.6)	2 (0.5)
Leydig cell tumor	1 (0.2)	0 (0.0)	1 (0.2)
Sertoli cell tumor	1 (0.2)	0 (0.0)	1 (0.2)
Tumor-like lesions			
Simple cyst	21 (4.5)	0 (0.0)	21 (4.9)
Inclusion cyst	5 (1.1)	0 (0.0)	5 (1.1)
Endometriosis cyst	7 (1.5)	2 (5.6)	5 (1.1)

Note: Percentages may not total 100% due to rounding.

was most common in the BOT-E group (12 cases, 33.4%). Serous cystadenoma was most common in the BOT group (141 cases, 32.5%).

Analysis of Risk Factors and Construction of a Prediction Model for Endometrial Lesions in Postmenopausal Benign Ovarian Tumor Patients

An analysis was performed on the general clinical data, transvaginal ultrasound data, serological marker data, and ovarian tumor pathological data of patients in the BOT-E group and the BOT group. The differences between the two groups in menarche age, endometrial thickness under ultrasound, ovarian tumor nature under ultrasound, E_2 , follicle stimulating hormone (FSH), luteinizing hormone (LH), and platelet (PLT) were statistically significant (Table 3). Variables that did not show statistical significance in univariate analysis were not included in Table 3 but are presented in Table S2.

Variables showing statistically significant differences in univariate analysis were included in a binary logistic regression model. The results revealed statistically significant differences between the two groups in the age at menarche ($P < 0.001$), endometrial thickness on ultrasound ($P < 0.001$), presence of pure solid tumor on ultrasound ($P = 0.049$), E_2 levels ($P = 0.022$) (Table 4). The results suggest that menarche age, endometrial thickness, pure solid tumor on ultrasound, and $E_2 \geq 10$ pg/mL are independent risk factors for endometrial lesions in postmenopausal benign ovarian tumor patients.

Evaluation of Prediction Model for Endometrial Lesions in Postmenopausal Benign Ovarian Tumor Patients

A nomogram was created to forecast the risk of coexisting endometrial lesions (Figure 2). This nomogram was produced using the independent risk factors. The Hosmer-Lemeshow test showed $P = 0.076$, indicating good model fit. Logistic regression analysis was performed according to the above variables and ROC curves were plotted (Figure 3A). The ROC analysis found that the highest AUC was achieved by combining the four factors (AUC=0.821 (95% CI: 0.744–0.8979)), the sensitivity was 66.7%, and the specificity was 87.6%. The 95% confidence intervals for the AUC, sensitivity, and specificity were estimated using stratified bootstrap resampling with 1000 iterations. The 95% CI for sensitivity and specificity was calculated using bootstrap resampling (Table S3). The results suggest that the model has good discriminatory ability. The optimism-corrected C-index was 0.809 (95% CI: 0.730–0.896), indicating good discriminatory ability of the model. Calibration assessment based on bootstrap correction showed the calibration intercept was -0.115 , and the calibration slope was 0.933. The calibration curve further confirmed that the predicted and observed probabilities were well aligned. The bootstrap-corrected calibration curve showed good agreement between predicted and observed risks,

Table 3 Univariate Analysis of Risk Factors for Endometrial Lesions in Postmenopausal Benign Ovarian Tumor Patients

	Total, n (%)	BOTE Group, n (%)	BOT Group, n (%)	OR (95% CI)	P
Cases, n (%)	471 (100.0)	36 (7.6)	435 (92.4)		
Menarche age, years, M (P25–P75)	14.0 (13.0–15.0)	13.0 (12.0–15.0)	14.0 (13.0–15.0)	0.594 (0.459–0.769)	<0.001
Endometrial thickness under ultrasound, mm, M (P25–P75)	3.0 (2.0–4.0)	6.0 (3.0–7.0)	3.0 (2.0–4.0)	1.377 (1.209–1.568)	<0.001
Ultrasound characteristics of ovarian tumor, n (%)					
Non-solid	320 (67.9)	18 (50.0)	302 (69.4)	2.271 (1.145–4.502)	0.019
Solid	151 (32.1)	18 (50.0)	133 (30.6)		
E_2 , pg/mL, n (%)					
<10	282 (59.9)	9 (25.0)	273 (62.8)	5.056 (2.320–11.018)	<0.001
≥ 10	189 (40.1)	27 (75.0)	162 (37.1)		
FSH, IU/L, M (P25–P75)	49.9 (38.9–65.8)	39.8 (22.0–49.0)	51.8 (39.9–66.1)	0.964 (0.946–0.983)	<0.001
LH, IU/L, M (P25–P75)	20.5 (15.3–26.3)	16.3 (11.1–23.4)	20.8 (15.8–26.6)	0.957 (0.919–0.996)	0.031
PLT, $\times 10^9/L$, M (P25–P75)	224.0 (185.0–262.0)	248.5 (205.3–290.5)	223.0 (183.0–260.0)	1.004 (1.000–1.008)	0.043

Abbreviations: OR, odds ratio; CI, confidence interval; E_2 , estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; PLT, platelet.

Table 4 Multivariate Analysis of Risk Factors for Endometrial Lesions in Postmenopausal Benign Ovarian Tumor Patient

Variable	β	SE	OR (95% CI)	P
Menarche age, years	-0.468	0.136	0.626 (0.479–0.818)	<0.001
Endometrial thickness under ultrasound, mm	0.232	0.069	1.261 (1.102–1.444)	<0.001
Nature of ovarian mass under ultrasound				
Non-solid (ref)				
Solid	0.804	0.408	2.235 (1.005–4.969)	0.049
E ₂				
<10, pg/mL (ref)			–	
≥10, pg/mL	1.023	0.446	2.782 (1.161–6.664)	0.022
FSH, IU/L	-0.017	0.014	0.983 (0.956–1.010)	0.212
LH, IU/L	-0.011	0.028	0.990 (0.936–1.046)	0.710
PLT, *10 ⁹ /L	0.004	0.002	1.004 (0.999–1.008)	0.131

Note: Reference categories are indicated as ref.

Abbreviations: SE, standard error; OR, odds ratio; CI, confidence interval; E₂, estradiol; FSH, follicle stimulating hormone; LH, luteinizing hormone; PLT, platelet.

with an average absolute error of 0.017 (Figure 3B). Regarding clinical utility, the DCA curve demonstrated favorable performance of the nomogram (Figure 3C). The model offered a positive net benefit compared with “treat-all” or “treat-none” strategies across a threshold probability range of approximately 0.1 to 0.5. Within this range, using the nomogram to guide clinical decisions provided superior net benefit. However, given the limited number of events, this effective range should be interpreted as a preliminary observation requiring validation in larger cohorts.

Discussion

Current Situation of Benign Ovarian Tumor Patients with Endometrial Lesions

Benign ovarian tumor is one of the common gynecological diseases in postmenopausal women. Current guidelines and consensus uniformly recommend bilateral salpingo-oophorectomy as the standard surgical approach for postmenopausal benign ovarian tumor patients.¹¹ Some guidelines or studies recommend that hysterectomy can be performed

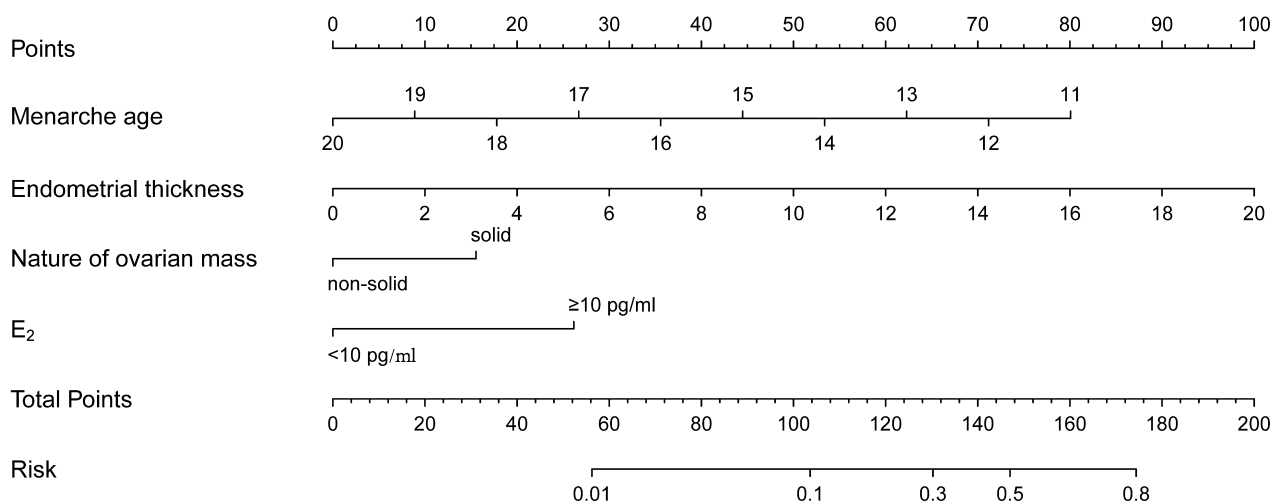


Figure 2 The Nomogram for predicting the risk of coexisting endometrial lesions in postmenopausal benign ovarian tumor patients.

Abbreviation: E₂, Estradiol.

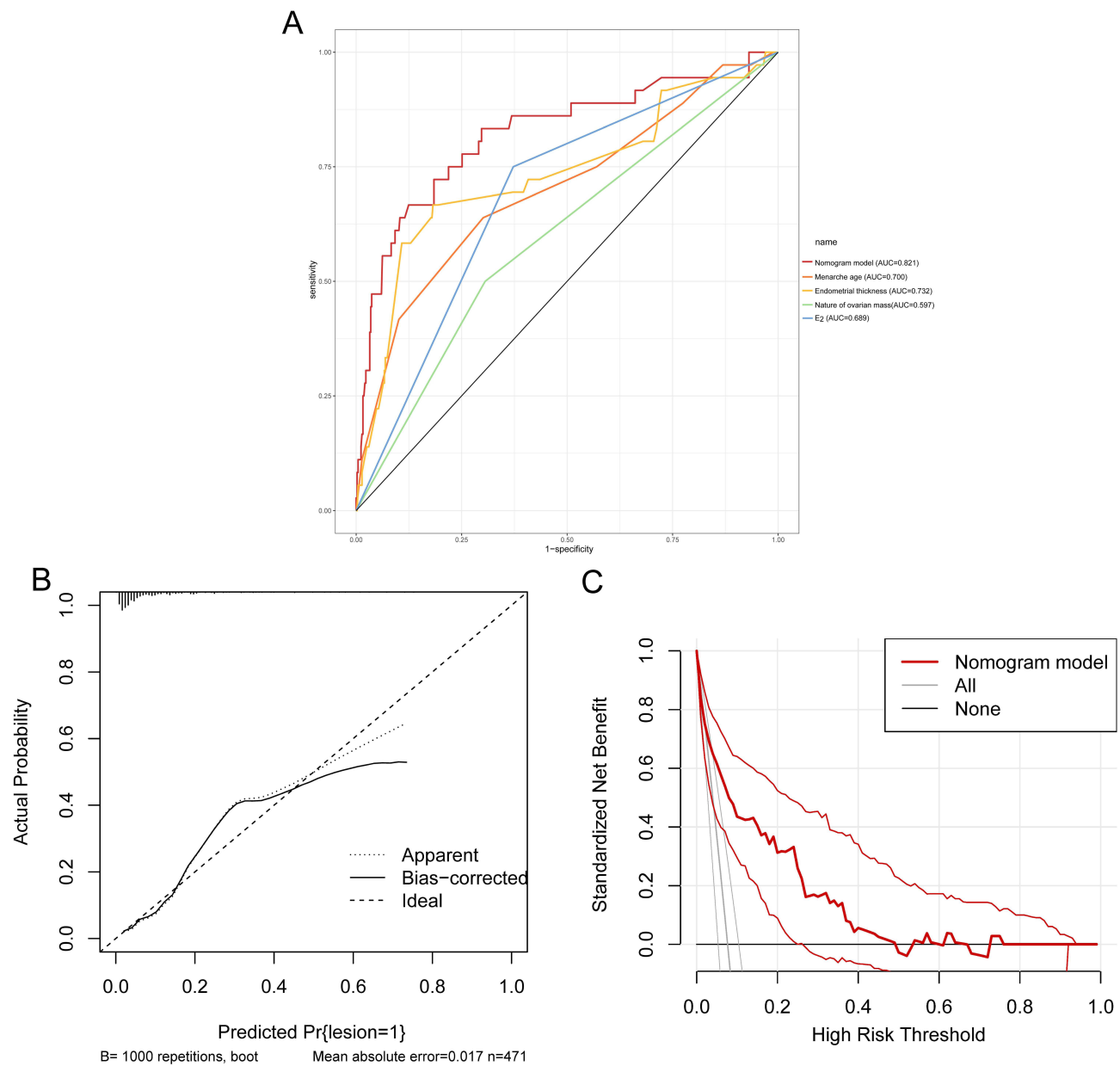


Figure 3 Model Performance and Validation. **(A)** ROC curves of nomogram model (AUC=0.821), menarche age (AUC=0.700), endometrial thickness (AUC=0.732), nature of ovarian mass (AUC=0.597), E₂ (AUC=0.689). **(B)** The calibration curve of the nomogram model. **(C)** The decision curve of the nomogram model.

Abbreviation: E₂, Estradiol.

simultaneously in patients who need hysterectomy. However, most patients in clinical practice do not present with other indications for hysterectomy, leading to controversy over whether hysterectomy should be performed simultaneously.²² Postmenopausal women face a higher risk of endometrial lesions compared to premenopausal women and study showed that postmenopausal women with atypical endometrial hyperplasia have a higher risk of progressing to EC compared to premenopausal women.^{10,23} The 2020 WHO Classification of Tumor of the Female Genital Tract indicates that endometrial hyperplasia carries a risk of progression to EC, with a progression risk of 1% for endometrial hyperplasia and 33% for atypical endometrial hyperplasia.⁶ The global incidence rate of EC is increasing year by year, with an approximate annual growth of 1% in lifetime risk.²⁴ Therefore, timely diagnosis and treatment of endometrial hyperplasia is of great significance.

Additionally, reports have shown that endometrial lesions are unexpectedly discovered after hysterectomy in some patients.^{12,13,25,26} In conclusion, when determining the surgical scope for postmenopausal benign ovarian tumor patients, it is essential to evaluate their concurrent risk of endometrial lesions. This study provides a predictive model to offer guidance for clinical treatment decisions.

The gold standard for diagnosing endometrial lesions remains histopathological evidence, primarily obtained through D&C or surgical resection specimens. D&C provides reference for the diagnosis of endometrial lesions before surgery, avoid surgical trauma and overtreatment, and serves as a critical method for determining surgical scope. Suh-Burgmann et al involving 824 patients with EAH found that D&C reduced the risk of unexpected cancer detection after hysterectomy. However, 18% of women were still unexpectedly diagnosed with EC after surgery,²⁷ which was associated with the limitations in comprehensive endometrial sampling via D&C and diagnostic challenges posed by fragmented specimens. Therefore, during diagnostic D&C, multi-point biopsies and thorough curettage should be prioritized, integrated with a comprehensive assessment of preoperative factors including the patient's clinical profile, transvaginal ultrasound data, and serological biomarkers to determine concurrent endometrial lesions. The predictive model for endometrial lesions constructed in this study offers references for whether endometrial lesions are present.

Risk Factors of Benign Ovarian Tumor Patients with Endometrial Lesions

This study identified menarche age, endometrial thickness, pure solid tumor under ultrasound, and $E_2 \geq 10\text{pg/mL}$ as independent risk factors for endometrial lesions in postmenopausal benign ovarian tumor patients and included them in preoperative predictive model. A prospective cohort study by Katagiri et al involving 332,625 Asian women demonstrated that late menarche was significantly associated with a reduced risk of EC.²⁸ O'Mara et al found that a later age at menarche had a protective effect against EC.²⁹ The study by Lv et al revealed that age at menarche is also causally associated with various gynecological diseases, including EC, ovarian cancer, endometriosis, preeclampsia, and uterine fibroids.³⁰ This study highlights the importance of paying increased attention to menarche age, which may serve as an early screening indicator for multiple gynecological conditions.

Endometrial thickening under ultrasound is associated with increased risk of postmenopausal endometrial hyperplasia and EC.^{31,32} The American College of Obstetricians and Gynecologists (ACOG) suggests that endometrial thickness in postmenopausal women should be ≤ 4 mm, presenting as a linear and uniformly consistent echo.³³ This study used 4 mm as the threshold for analysis and incorporated endometrial thickness >4 mm into the clinical prediction model. For postmenopausal women with endometrial thickening, close attention should be paid to whether they present high-risk factors for EC.

Ovarian fibroma is a type of ovarian sex cord-stromal tumor, a solid and firm tumor, which is common in perimenopausal and menopausal women and accounts for 4% of all ovarian tumor.³⁴ Chechia et al retrospectively analyzed 24 ovarian fibroma cases, all exhibiting hormone-secreting activity.³⁵ Haroon et al retrospectively analyzed the clinicopathological data of 480 ovarian sex cord-stromal tumor, in which 1 patient with EC and 1 patient with endometrial hyperplasia in 98 patients with ovarian fibroma, indicating that ovarian fibroma has a certain hormonal secretory function.³⁶ Wang et al also reported cases of postmenopausal bleeding and endometrial hyperplasia caused by ovarian fibromas.³⁷ This study revealed that among postmenopausal patients with benign ovarian tumor complicated by endometrial lesions, ovarian fibroma was the most common pathological type. Moreover, purely solid ovarian masses under ultrasound were identified as an independent risk factor. This may be attributed to the fact that ovarian fibromas can secrete estrogen, which induces endometrial changes under estrogen influence.

Patients with simple endometrial hyperplasia face a 3- to 4-fold elevated EC risk under prolonged unopposed estrogen exposure, this risk exceeds 10-fold after >10 years of exposure. For atypical endometrial hyperplasia, the EC risk increases 14 to 45 fold under sustained estrogen stimulation.⁶ $E_2 \geq 10$ pg/mL was identified as an independent risk factor and was incorporated into the clinical prediction model.

Clinical Application

To bridge the gap between our predictive model and clinical practice, we propose a preliminary tiered management framework. Notably, previous studies have reported discrepancies between preoperative predictive models and final

clinicopathological findings,³⁸ underscoring the need for cautious interpretation of model-based risk estimates. To use the nomogram for individualized risk assessment, first locate the value of each clinical variable on its respective axis. Draw a straight line vertically upward to the Points axis to determine the score for each predictor. Sum these individual scores to calculate the Total Points. Finally, locate the Total Points on the corresponding axis and draw a vertical line downward to the Risk axis. This provides the specific predicted probability of endometrial lesions for the patient. A predicted risk threshold of 13.2%, derived from the optimal Youden Index, could serve as a clinical trigger for transitioning from observation to targeted diagnostics such as hysteroscopy or D&C. This threshold balances lesion detection with an 87.6% specificity, sparing low-risk individuals from unnecessary invasive trauma. For patients in the highest-risk category, we propose a more stringent threshold of 42.1%, achieving a high specificity of 98.6%. At this level, the substantial likelihood of pathology may warrant an intensive discussion regarding total hysterectomy.

However, we emphasize that this model is exploratory and requires external validation before broad clinical implementation. Given the irreversible nature of hysterectomy and its associated morbidity, these benchmarks should not directly dictate major surgery but rather function as a triage tool. Any final surgical intervention must be based on confirmed pathology and an individualized risk-benefit assessment within a shared decision-making framework.

Limitation

Several limitations of this study should be acknowledged. First, the retrospective design may harbor inherent selection bias. Second, the relatively small number of observed events ($n=36$) and the limited sample size of the BOT-E group may restrict the precision of our estimates. This limited statistical power likely explains why certain well-established risk factors evaluated in our study, such as BMI and diabetes, did not reach statistical significance and were therefore not retained in the final model. Consequently, the generalizability of the results to broader populations warrants caution. Notably, with only one case of endometrial cancer, the model is better suited for predicting general endometrial lesions rather than specific malignancy risk. Third, potential measurement variability exists, as ultrasound is operator-dependent and hormone assays may vary across laboratory techniques. Furthermore, formal inter-rater reliability metrics such as Cohen's kappa were not assessed, though standardized protocols were followed. Finally, while internal validation via bootstrapping was performed, the lack of external validation limits the generalizability of our nomogram. Future large-scale, multicenter studies are essential to re-evaluate these metabolic factors and validate these findings in broader clinical settings.

Conclusion

This study developed a preoperative prediction model that shows promise in assessing the risk of endometrial lesions in postmenopausal patients with benign ovarian tumors. By integrating clinical, ultrasound, and serological biomarkers, the model provides a non-invasive approach to supplement preoperative evaluation. However, given the limited number of malignancy cases in our cohort, this model should be distinguished as a triage tool for general endometrial pathology, primarily hyperplasia, rather than a specific predictor of cancer. While internal validation demonstrated favorable performance, prospective and external validation are essential prior to clinical adoption. Furthermore, future large-scale studies are warranted to re-evaluate the predictive value of metabolic risk factors including BMI, diabetes, and hormone replacement therapy in broader populations. Ultimately, this nomogram serves as a supportive instrument to aid in individualized management and contribute to the standardization of diagnostic strategies.

Data Sharing Statement

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Ethics Approval and Consent to Participate

All experimental protocols were approved by the Ethics Committee of Tianjin Medical University General Hospital (Tianjin Medical University General Hospital IRB, protocol number IRB2025-YX-501-01). Informed consent was obtained from all the participants. All methods were carried out in accordance with Declaration of Helsinki.

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Disclosure

The authors report no conflicts of interest in this work.

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