

Diagnostic Value of FAR, CAR, and PNI in Differentiating Benign From Malignant Endometrial Lesions and Assessing High-Risk Pathological Features

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AIM: Benign endometrial lesions and endometrial cancer often overlap in clinical and ultrasonographic features. This study evaluated the ability of the fibrinogen-to-albumin ratio (FAR), C-reactive protein-to-albumin ratio (CAR), and prognostic nutritional index (PNI) to differentiate benign endometrial lesions from endometrial cancer and examined their associations with high-risk pathological features. **METHODS:** This retrospective case-control study included 374 patients with histopathologically confirmed endometrial lesions, comprising 250 benign lesions and 124 endometrial cancers. Receiver operating characteristic (ROC) curves were used to assess discrimination, and a clinical ultrasound model was constructed. PNI, CAR, and FAR were separately added to the model, followed by bootstrap internal validation. Associations with high-risk pathological features were evaluated using Firth logistic regression adjusted for age, body mass index (BMI), and histologic type.

RESULTS: Patients with endometrial cancer had lower PNI and higher CAR and FAR levels. The areas under the curve (AUCs) for FAR, PNI, and CAR were 0.820, 0.793, and 0.781, respectively. The clinical ultrasound model had an AUC of 0.863, which increased to 0.918 after adding FAR and remained 0.903 after bootstrap correction. After correction for multiple comparisons, lower PNI and higher FAR were associated with deep myometrial invasion, lymphovascular space invasion, International Federation of Gynecology and Obstetrics stage III–IV, and grade 3 tumors, whereas CAR showed no statistically significant associations.

CONCLUSIONS: FAR showed the highest observed discriminatory performance among PNI and CAR and provided incremental information beyond the clinical ultrasound model. Prospective multicenter validation is warranted.

Keywords: endometrial cancer; endometrial lesion; fibrinogen-to-albumin ratio; C-reactive protein-to-albumin ratio; prognostic nutritional index; diagnostic model; risk stratification

Introduction

Endometrial abnormalities are common in gynecological practice and may represent either benign lesions or endometrial cancer [1,2]. Although histopathological examination remains the reference standard, benign lesions and early-stage endometrial cancer often overlap in their clinical manifestations and ultrasonographic features, making reliable preoperative differentiation challenging [3]. Accurate preoperative risk assessment is therefore important for identifying patients who require prompt invasive evaluation or surgical management [4].

Current preoperative assessment mainly combines clinical risk factors, such as age, body mass index (BMI), menopausal status, and diabetes mellitus, with transvaginal ultrasonographic features, including endometrial thickness

and endometrial–myometrial junction integrity [5]. However, models based solely on clinical and ultrasonographic variables still have limited discriminatory performance [6]. Additional objective markers reflecting tumor-related systemic changes may therefore improve risk assessment.

Tumor development is accompanied by alterations in inflammation, nutritional status, immune function, and coagulation [7]. The prognostic nutritional index (PNI), C-reactive protein-to-albumin ratio (CAR), and fibrinogen-to-albumin ratio (FAR) are readily available composite biomarkers derived from routine blood tests and have been investigated primarily for prognostic assessment in gynecological malignancies [8,9,10]. However, their value in distinguishing benign from malignant endometrial lesions and their incremental contribution beyond conventional clinical and ultrasonographic factors remain unclear. It is also uncertain whether these markers are associated with high-risk pathological features of endometrial cancer [11].

Therefore, this study compared the diagnostic performance of PNI, CAR, and FAR for differentiating benign endometrial lesions from endometrial cancer and evaluated their incremental value when added to a clinical ultrasound model. We also examined their associations with high-

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risk pathological features in patients with endometrial cancer. By integrating systemic inflammatory, nutritional, and coagulation-related information with local ultrasonographic features, this study aimed to improve preoperative risk stratification in patients with suspected endometrial lesions undergoing invasive diagnostic evaluation or surgical management.

Methods

Study Design and Study Population

This retrospective case-control study reviewed patient records from the electronic medical record, laboratory, ultrasound, and pathology information systems at Jinhua Municipal Central Hospital for all consecutive female patients who underwent hysteroscopy, diagnostic curettage, endometrial biopsy, or surgical treatment for suspected endometrial lesions between September 2022 and September 2025. The screening process involved identifying potentially eligible records during the study period, applying the predefined inclusion and exclusion criteria, and confirming the final histopathological diagnosis. Laboratory measurements and transvaginal ultrasonography performed within 14 days before the index diagnostic procedure or surgery were collected, and the results closest to the procedure were used when repeated measurements were available. All patients were classified into the benign endometrial lesion group and the endometrial cancer group according to the final histopathological diagnosis. The primary outcome was the diagnosis of endometrial cancer. Patients with endometrial cancer were further included in the analysis of high-risk pathological features. The study was approved by the Ethics Committee of Jinhua Municipal Central Hospital (Approval No. 2026-264). Because this was a retrospective study and all patient information was anonymized before analysis, the requirement for informed consent was waived by the Ethics Committee of Jinhua Municipal Central Hospital.

The inclusion criteria were as follows: (1) female aged 18 years or older; (2) patients who underwent diagnostic evaluation or treatment for endometrial lesions or suspected endometrial lesions; (3) patients with a definitive histopathological diagnosis; (4) patients with complete laboratory data, including routine blood tests, C-reactive protein (CRP), fibrinogen, and albumin, within 2 weeks before treatment or surgery; and (5) patients with complete clinical, laboratory, ultrasonographic, and pathological findings required for the relevant analyses. The exclusion criteria were pregnancy; previous endometrial cancer or other concurrent malignancies; preoperative radiotherapy, chemotherapy, immunotherapy, targeted therapy, or hormone-related therapy; preoperative acute infection, overt inflammatory conditions, autoimmune diseases, hematological diseases, or long-term immunosuppressive status; and missing key clinical, laboratory, ultra-

sonographic, or pathological findings. The flowchart of patient inclusion and exclusion is shown in Fig. 1.

Variable Collection and Definitions

General characteristics, reproductive and endocrine-related data, comorbidities, preoperative laboratory parameters, and transvaginal ultrasonographic findings were collected. General characteristics included age, BMI, age at menarche, menopausal status, parity, and family history of gynecological malignancy. Comorbidities included hypertension, diabetes mellitus, and polycystic ovary syndrome (PCOS). Ultrasonographic data included endometrial thickness, endometrial–myometrial junction integrity, intrauterine mass, intrauterine fluid, and blood flow distribution. Endometrial thickness was measured at the maximal double-layer thickness in the midsagittal uterine plane. The endometrial–myometrial junction was classified as complete when the interface was continuous, regular, and clearly visible, and as incomplete when focal or diffuse interruption, irregularity, or indistinct visualization was present. Blood flow was graded as no obvious flow, mild flow, or rich flow according to the absence of detectable vascular signals, sparse punctate or short linear signals, or multiple branching or penetrating signals, respectively. Blood flow grading was treated as an ordinal variable in model construction. Ultrasonographic variables were extracted from the original reports completed by the examining sonographers.

Preoperative laboratory parameters were obtained from test results performed within 2 weeks before surgery, hysteroscopy, diagnostic curettage, or endometrial biopsy, with the measurement closest to the time of pathological diagnosis or surgery selected for analysis. Preoperative peripheral venous blood samples were collected from all patients. Complete blood count parameters were measured in dipotassium ethylenediaminetetraacetic acid (K2-EDTA)-anticoagulated whole blood using a Genegeo DX-120 (Genegeo) automated hematology analyzer. Leukocyte differential counts were determined using fluorescence flow cytometry, red blood cell and platelet counts using the impedance method, and hemoglobin using a colorimetric method. CRP was measured by immunoturbidimetry using the Genegeo DX-120 (Genegeo) automated hematology analyzer. Serum albumin was measured using a dry chemistry colorimetric method on a VITROS XT 3400 automated chemistry analyzer (Ortho-Clinical Diagnostics, Inc.). Plasma fibrinogen was measured in sodium citrate-anticoagulated plasma using a transmission turbidimetric method on an ACL TOP 750 automated coagulation analyzer (Instrumentation Laboratory, Werfen). All measurements were performed according to the manufacturers' instructions and routine laboratory quality-control procedures.

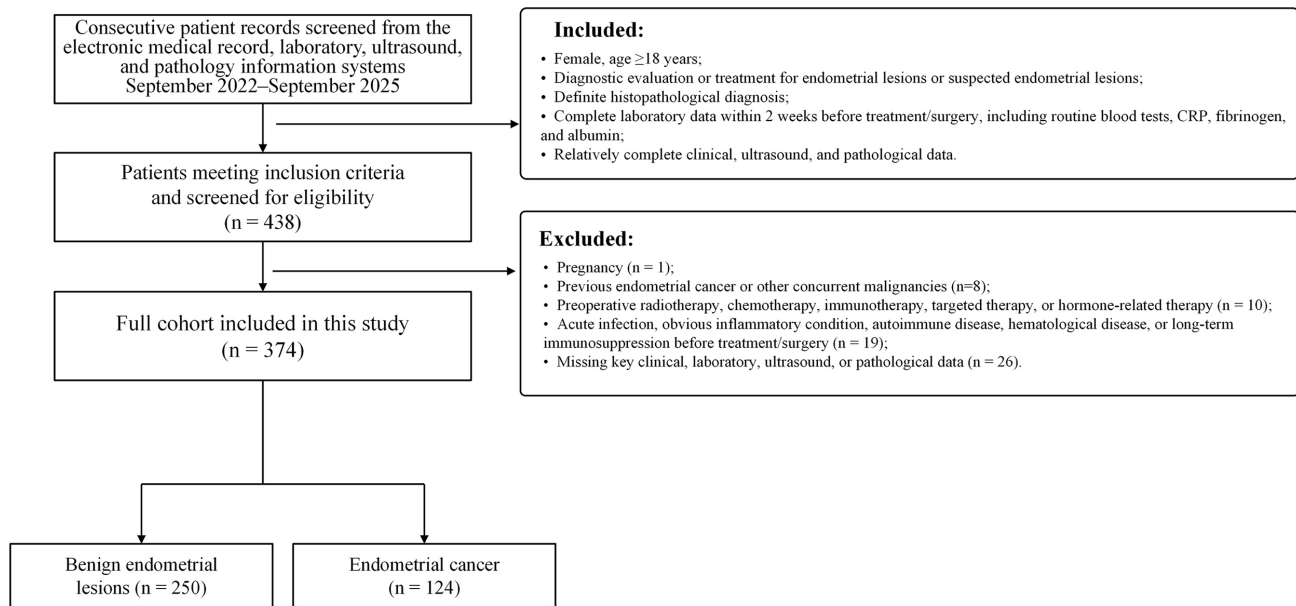


Fig. 1. Study flowchart of patient inclusion and exclusion. CRP, C-reactive protein.

Definitions of FAR, CAR, and PNI

PNI, CAR, and FAR were the key markers evaluated in this study. PNI was calculated as follows: $\text{PNI} = \text{albumin (g/L)} + 5 \times \text{lymphocyte count} (\times 10^9/\text{L})$ [8]. A lower PNI indicates poorer nutritional and immune status. CAR was calculated as follows: $\text{CAR} = \text{CRP (mg/L)} / \text{albumin (g/L)}$ [12], reflecting the combined changes in systemic inflammation and nutritional status. FAR was calculated as follows: $\text{FAR} = \text{fibrinogen (g/L)} / \text{albumin (g/L)}$ [13], reflecting combined features of coagulation activation, inflammatory response, and nutritional status. To avoid information overlap and overadjustment, the clinical ultrasound model did not include the component variables of PNI, CAR, or FAR, such as albumin, lymphocyte count, CRP, or fibrinogen, when evaluating the incremental predictive value of these markers.

Definition of High-Risk Pathological Features

Histopathological diagnosis served as the reference standard. Specimens were obtained by hysteroscopy-guided biopsy, diagnostic curettage, endometrial biopsy, or surgical resection. Pathological findings were assessed by 2 pathologists experienced in gynecologic pathology. Diagnostic discrepancies were resolved through joint review and consensus, with referral to a senior pathologist when necessary.

Pathological variables used in the present analyses included histologic type, tumor grade, depth of myometrial invasion, lymphovascular space invasion (LVSI), cervical stromal invasion, and International Federation of Gynecology and Obstetrics (FIGO) stage. Five high-risk pathological endpoints were selected based on clinical relevance and completeness of ascertainment. Adnexal involvement was not

analyzed as a separate endpoint because it contributes to FIGO staging. Immunohistochemical and molecular findings were not included as analytic variables because testing was incomplete and nonuniform across the cohort, precluding complete molecular classification. FIGO stage was determined based on postoperative pathological findings according to the 2023 FIGO staging system.

The main high-risk pathological features in this study were defined according to the final postoperative pathological results. Deep myometrial invasion was defined as myometrial invasion involving 50% or greater of the myometrial thickness. LVSI positivity was defined as the presence of lymphovascular space invasion reported in the pathological report. Cervical stromal invasion was defined as cervical stromal involvement reported in the pathological report. Advanced FIGO stage was defined as FIGO stage III to IV. Grade 3 disease was defined as endometrial cancer with a pathological grade of G3.

Statistical Analysis

Statistical analyses were performed using R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria). Missing data were defined as absent or indeterminate records for variables required for the corresponding analysis. Complete-case analysis was performed without imputation, and no missing values remained among the included participants. Normality was assessed using the Shapiro–Wilk test and quantile–quantile (Q–Q) plots. Continuous variables were presented as mean $\pm$ standard deviation or median (interquartile range) and compared using the independent-samples *t*-test or Mann–Whitney U test, as appropriate. Categorical variables were presented as n (%) and compared using Pearson’s chi-square test when its as-

assumptions were satisfied; Fisher's exact test was used when expected cell counts were insufficient.

Endometrial cancer diagnosis was used as the dependent variable. Clinically relevant variables were evaluated using univariable logistic regression, and variables with $p < 0.05$ were entered into multivariable logistic regression. Variables remaining statistically significant were included in the clinical ultrasound model. Continuous predictors were entered as continuous terms without categorization, whereas blood flow score was treated as an ordinal variable. Linearity between continuous predictors and the logit was assessed using the Box-Tidwell test, and potential nonlinearity was further examined using restricted cubic splines. Multicollinearity was assessed using the variance inflation factor (VIF), with $VIF < 5$ indicating no substantial multicollinearity. Receiver operating characteristic (ROC) curves and the area under the curve (AUC) were used to assess discrimination. Optimal cut-off values were determined using the Youden index. PNI, CAR, and FAR were separately added to the clinical ultrasound model. Regression coefficients and the intercept of the best-performing extended model were reported to enable calculation of individual predicted probabilities and facilitate model reproducibility. Internal validation was performed using 1000 nested bootstrap resamples. Within each resample, univariable screening, multivariable variable selection, and model refitting were repeated; mean optimism was then subtracted from the apparent AUC to derive the optimism-corrected AUC. Calibration curves, decision curve analysis, and clinical impact curves were used to assess calibration and clinical utility. Changes in apparent AUC were reported descriptively. Nested models were compared using likelihood ratio tests, and the added markers were evaluated using Wald tests. For high-risk pathological features, separate Firth-penalized logistic regression models were fitted for each marker-endpoint association, with adjustment for age, BMI, and histologic type. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were reported. ORs were calculated per 1-point increase in PNI and per 0.01 increase in CAR or FAR. Bonferroni correction was applied to the 15 marker-endpoint comparisons. All tests were two-sided, with $p < 0.05$ considered statistically significant unless otherwise specified.

Results

Baseline Characteristics of the Patients

A total of 374 patients were included in this study, comprising 250 patients with benign endometrial lesions and 124 patients with endometrial cancer. Compared with the benign group, patients in the malignant group were older, had a higher BMI, and had an earlier age at menarche. The proportions of postmenopausal status, diabetes mellitus, and family history of gynecological malignancy were also higher in the malignant group. Regarding ultrasono-

graphic features, patients in the malignant group had greater endometrial thickness and higher proportions of incomplete endometrial-myometrial junction integrity, intrauterine fluid, and rich blood flow. In terms of laboratory parameters, the malignant group showed higher levels of neutrophil count, platelet count, CRP, fibrinogen, CAR, and FAR, whereas lymphocyte count, hemoglobin, albumin, and PNI levels were lower. Detailed baseline characteristics are shown in Table 1.

The pathological composition of benign endometrial lesions is shown in **Supplementary Table 1**. Among these lesions, endometrial polyps were observed in 105 patients (42.0%), endometrial hyperplasia without atypia in 55 patients (22.0%), proliferative or secretory endometrium in 40 patients (16.0%), atrophic endometrium in 25 patients (10.0%), chronic endometritis in 15 patients (6.0%), and submucosal leiomyoma with benign endometrial pathology in 10 patients (4.0%).

Among the 124 patients with endometrial cancer, endometrioid carcinoma was the predominant histological type, accounting for 106 cases (85.5%). Serous carcinoma was observed in 10 cases (8.1%), and other non-endometrioid carcinomas were observed in 8 cases (6.5%). Grade 1 (G1), grade 2 (G2), and grade 3 (G3) tumors were identified in 44 cases (35.5%), 44 cases (35.5%), and 36 cases (29.0%), respectively. Deep myometrial invasion of 50% or greater was observed in 51 cases (41.1%), LVSI positivity in 38 cases (30.6%), and cervical stromal invasion in 19 cases (15.3%). FIGO stages I, II, III, and IV were identified in 86 cases (69.4%), 8 cases (6.5%), 28 cases (22.6%), and 2 cases (1.6%), respectively, with 30 patients (24.2%) classified as FIGO stage III to IV. Detailed clinicopathological characteristics of patients with endometrial cancer are presented in **Supplementary Table 2**.

Logistic Regression Analyses of Factors Associated With Endometrial Cancer

Univariate logistic regression analysis showed that age, BMI, postmenopausal status, family history of gynecological malignancy, diabetes mellitus, endometrial thickness, incomplete endometrial-myometrial junction integrity, intrauterine fluid, and blood flow score were associated with endometrial cancer. Multivariable logistic regression analysis showed that age, BMI, diabetes mellitus, endometrial thickness, incomplete endometrial-myometrial junction integrity, and intrauterine fluid remained independently associated with endometrial cancer, whereas family history of gynecological malignancy showed a borderline association. All variables included in the multivariable model had VIF values below 5, indicating no substantial multicollinearity. Menopausal status was no longer statistically significant after multivariable adjustment, possibly because age accounted for much of the malignancy-related information represented by menopausal status in the univariate analysis; therefore, the adjusted OR should not be interpreted as

Table 1. Baseline characteristics of patients with benign and malignant endometrial lesions.

Characteristic	Benign (N = 250)	Malignant (N = 124)	p value
Demographic and reproductive characteristics			
Age, years	52.20 ± 9.88	60.25 ± 10.38	<0.001
BMI, kg/m ²	23.20 (21.30–25.58)	25.25 (23.05–27.80)	<0.001
Age at menarche, years	14.00 (13.00–14.00)	13.00 (12.00–14.00)	0.010
Menopausal status, n (%)			<0.001
Premenopausal	151 (60.40%)	47 (37.90%)	
Postmenopausal	99 (39.60%)	77 (62.10%)	
Parity, n (%)			0.830
0	25 (10.00%)	14 (11.29%)	
1	92 (36.80%)	42 (33.87%)	
≥2	133 (53.20%)	68 (54.84%)	
Family history of gynecologic malignancy, n (%)			0.042
No	243 (97.20%)	114 (91.94%)	
Yes	7 (2.80%)	10 (8.06%)	
Comorbidities			
Hypertension, n (%)			0.137
No	200 (80.00%)	90 (72.58%)	
Yes	50 (20.00%)	34 (27.42%)	
Diabetes mellitus, n (%)			<0.001
No	230 (92.00%)	87 (70.16%)	
Yes	20 (8.00%)	37 (29.84%)	
PCOS, n (%)			0.781
No	239 (95.60%)	120 (96.77%)	
Yes	11 (4.40%)	4 (3.23%)	
Laboratory parameters and inflammatory-nutritional indices			
Neutrophil count, ×10 ⁹ /L	3.48 (3.04–4.39)	4.14 (3.41–5.06)	<0.001
Lymphocyte count, ×10 ⁹ /L	1.81 (1.18–2.44)	1.46 (0.99–2.19)	0.008
Platelet count, ×10 ⁹ /L	235.42 ± 51.66	267.21 ± 63.76	<0.001
Hemoglobin, g/L	121.51 ± 15.32	114.10 ± 14.38	<0.001
Albumin, g/L	43.70 (41.12–45.98)	42.05 (39.00–43.92)	<0.001
Fibrinogen, g/L	3.40 (2.94–3.83)	4.13 (3.72–4.74)	<0.001
C-reactive protein, mg/L	3.16 ± 1.22	4.50 ± 1.31	<0.001
PNI	52.66 ± 2.48	49.79 ± 2.57	<0.001
CAR	0.07 ± 0.03	0.11 ± 0.03	<0.001
FAR	0.08 ± 0.02	0.10 ± 0.02	<0.001
Ultrasonographic characteristics			
Endometrial thickness, mm	8.05 (5.85–11.88)	13.50 (9.15–19.42)	<0.001
Endometrial-myometrial junction integrity, n (%)			<0.001
Complete	236 (94.40%)	84 (67.74%)	
Incomplete	14 (5.60%)	40 (32.26%)	
Intrauterine mass, n (%)			0.769
No	125 (50.00%)	64 (51.61%)	
Yes	125 (50.00%)	60 (48.39%)	
Intrauterine fluid, n (%)			<0.001
No	221 (88.40%)	88 (70.97%)	
Yes	29 (11.60%)	36 (29.03%)	
Blood flow, n (%)			<0.001
No obvious flow	104 (41.60%)	20 (16.13%)	
Mild flow	114 (45.60%)	53 (42.74%)	
Rich flow	32 (12.80%)	51 (41.13%)	

Note: Data are presented as mean ± standard deviation, median (interquartile range), or n (%), as appropriate. p values were calculated using the independent-samples *t*-test, Mann–Whitney U test, Pearson's chi-square test, or Fisher's exact test, as appropriate.

Abbreviations: BMI, body mass index; PCOS, polycystic ovary syndrome; PNI, prognostic nutritional index; CAR, C-reactive protein-to-albumin ratio; FAR, fibrinogen-to-albumin ratio.

Table 2. Univariate and multivariate logistic regression analyses for endometrial cancer.

Variables	Univariate logistic analysis			Multivariate logistic analysis			
	OR	95% CI	p value	β	OR	95% CI	p value
Age, years	1.082	1.057–1.109	<0.001	0.088	1.092	1.055–1.131	<0.001
BMI, kg/m ²	1.185	1.108–1.271	<0.001	0.159	1.172	1.077–1.276	<0.001
Postmenopausal, n (%)	2.499	1.611–3.909	<0.001	−0.367	0.693	0.352–1.364	0.288
Family history of gynecologic malignancy, n (%)	3.045	1.140–8.580	0.028	1.149	3.156	0.917–10.858	0.068
Diabetes mellitus, n (%)	4.891	2.720–9.029	<0.001	1.278	3.588	1.664–7.738	0.001
Endometrial thickness, mm	1.129	1.090–1.172	<0.001	0.067	1.070	1.008–1.136	0.027
Incomplete endometrial-myometrial junction integrity, n (%)	8.027	4.252–15.978	<0.001	1.386	3.997	1.741–9.178	0.001
Intrauterine fluid, n (%)	3.118	1.807–5.425	<0.001	0.983	2.672	1.351–5.285	0.005
Blood flow score	2.904	2.105–4.074	<0.001	0.451	1.571	0.904–2.729	0.109

Note: For categorical variables, the reference categories were premenopausal status, no family history of gynecological malignancy, no diabetes mellitus, complete endometrial-myometrial junction integrity, and no intrauterine fluid. Blood flow score was treated as an ordinal variable. The variance inflation factor (VIF) values for age, BMI, menopausal status, family history of gynecological malignancy, diabetes mellitus, endometrial thickness, endometrial-myometrial junction integrity, intrauterine fluid, and blood flow score were 1.669, 1.046, 1.617, 1.023, 1.108, 2.229, 1.300, 1.089, and 2.113, respectively; all values were below 5, indicating no substantial multicollinearity.

Abbreviation: OR, odds ratio.

Table 3. Diagnostic performance of PNI, CAR, FAR and their component indicators for malignant endometrial lesions.

Variables	AUC (95% CI)	Cut-off value	Sensitivity (95% CI)	Specificity (95% CI)
FAR	0.820 (0.775–0.866)	0.089	0.774 (0.690–0.844)	0.760 (0.702–0.812)
PNI	0.793 (0.744–0.841)	51.425	0.774 (0.690–0.844)	0.708 (0.647–0.764)
CAR	0.781 (0.731–0.831)	0.102	0.589 (0.497–0.676)	0.836 (0.784–0.880)
CRP	0.773 (0.722–0.824)	4.135	0.613 (0.521–0.699)	0.808 (0.754–0.855)
Fibrinogen	0.767 (0.715–0.819)	3.755	0.742 (0.656–0.816)	0.716 (0.656–0.771)
Albumin	0.629 (0.569–0.690)	43.45	0.702 (0.613–0.780)	0.536 (0.472–0.599)
Lymphocyte	0.584 (0.523–0.646)	1.515	0.524 (0.433–0.615)	0.624 (0.561–0.684)

Abbreviations: AUC, area under the curve; CRP, C-reactive protein. For PNI, albumin, and lymphocyte count, values below the cut-off values were considered indicative of endometrial cancer, whereas for FAR, CAR, CRP, and fibrinogen, values above the cut-off values were considered indicative of endometrial cancer.

indicating a protective effect of postmenopausal status. Detailed results are shown in Table 2.

Diagnostic Performance of FAR, PNI, CAR, and Their Component Indicators

ROC curve analysis showed that FAR, PNI, and CAR all had auxiliary value in distinguishing benign endometrial lesions from endometrial cancer. FAR showed the highest observed AUC of 0.820 (95% CI: 0.775–0.866), although formal pairwise comparisons between biomarkers were not performed. The AUC was 0.793 (95% CI: 0.744–0.841) for PNI and 0.781 (95% CI: 0.731–0.831) for CAR. Among the individual component indicators, CRP and fibrinogen also showed certain discriminatory ability, whereas albumin and lymphocyte count had relatively lower AUC values. The cut-off values determined by the Youden index reflected only the optimal discriminatory thresholds in the present cohort and require further validation in external cohorts. Detailed results are presented in Table 3 and Fig. 2.

Incremental Performance, Internal Validation, and Clinical Utility of the Extended Models

The clinical ultrasound model showed good discriminatory ability for malignant endometrial lesions, with an apparent AUC of 0.863 (95% CI: 0.823–0.903). After adding PNI, CAR, and FAR separately to the clinical ultrasound model, the AUC values increased to varying degrees. Among these models, the Clinical + FAR model showed the best performance, with an apparent AUC of 0.918 (95% CI: 0.887–0.948). Following 1000 bootstrap resamples using Harrell's optimism-correction procedure, the optimism-corrected AUCs of the clinical ultrasound model, Clinical + PNI, Clinical + CAR, and Clinical + FAR models were 0.841, 0.866, 0.859, and 0.903, respectively. The corresponding mean optimism values for AUC were 0.022, 0.017, 0.018, and 0.015, respectively, and the optimism-corrected calibration slopes were 0.873, 0.889, 0.889, and 0.891, respectively. The Clinical + FAR model retained the highest discriminatory ability after optimism correction. Detailed results are shown in Table 4.

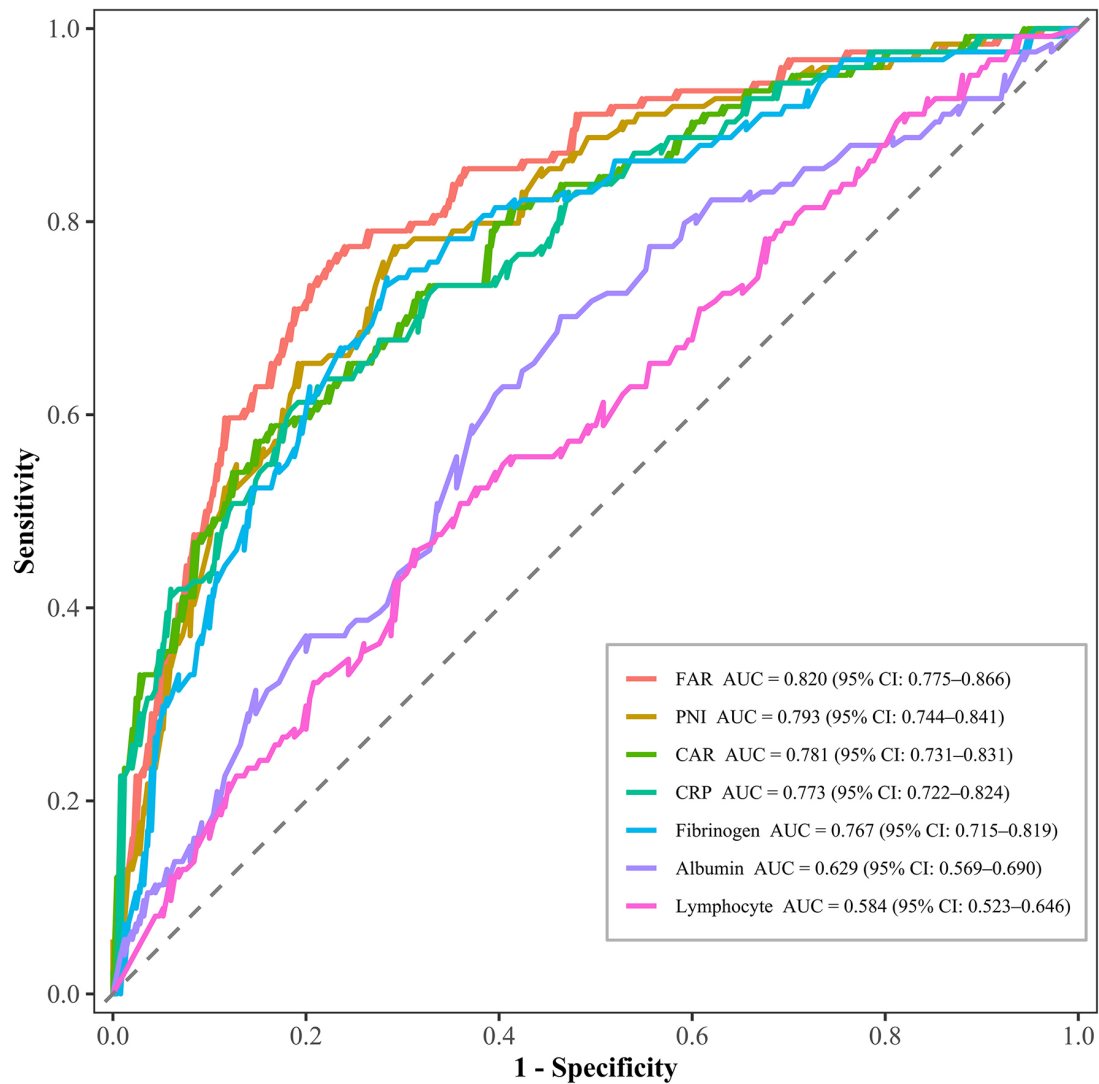


Fig. 2. Receiver operating characteristic curves comparing PNI, CAR, FAR and their component indicators for malignant endometrial lesion discrimination. Note: The curves compare FAR, PNI, CAR, CRP, fibrinogen, albumin and lymphocyte count. Abbreviations: AUC, area under the curve; PNI, prognostic nutritional index; CAR, C-reactive protein-to-albumin ratio; FAR, fibrinogen-to-albumin ratio.

Table 4. Diagnostic performance and bootstrap internal validation of the clinical ultrasound model and extended models for malignant endometrial lesions.

Model	Apparent AUC (95% CI)	Optimism-corrected AUC	Optimism-corrected calibration slope	Cut-off	Sensitivity (95% CI)	Specificity (95% CI)
Clinical ultrasound model	0.863 (0.823–0.903)	0.841	0.873	0.304	0.806 (0.726–0.872)	0.800 (0.745–0.848)
Clinical + PNI	0.883 (0.846–0.920)	0.866	0.889	0.338	0.782 (0.699–0.851)	0.844 (0.793–0.887)
Clinical + CAR	0.877 (0.836–0.917)	0.859	0.889	0.441	0.750 (0.664–0.823)	0.904 (0.861–0.938)
Clinical + FAR	0.918 (0.887–0.948)	0.903	0.891	0.371	0.855 (0.780–0.912)	0.880 (0.833–0.918)

Note: The optimism-corrected AUC and calibration slope were obtained using 1000 bootstrap resamples following Harrell's procedure. A predicted probability above the cut-off value was considered indicative of endometrial cancer.

Table 5. Incremental value of PNI, CAR, and FAR beyond the clinical ultrasound model.

Comparison	Δ AUC	Likelihood ratio test p	Wald test p for added marker
Clinical ultrasound model vs Clinical + PNI	0.020	2.64×10^{-6}	7.92×10^{-6}
Clinical ultrasound model vs Clinical + CAR	0.013	5.45×10^{-6}	1.97×10^{-5}
Clinical ultrasound model vs Clinical + FAR	0.054	1.31×10^{-16}	4.30×10^{-12}

For reproducibility, the final Clinical + FAR model was expressed as: $\text{logit}(P) = -16.5654 + 0.0724 \times \text{Age} + 0.1168 \times \text{BMI} + 1.5664 \times \text{Diabetes} + 0.1045 \times \text{Endometrial thickness} + 1.4464 \times \text{Incomplete endometrial-myometrial junction} + 0.7704 \times \text{Intrauterine fluid} + 79.2106 \times \text{FAR}$. Diabetes mellitus, incomplete endometrial-myometrial junction integrity, and intrauterine fluid were coded as 1 for presence and 0 for absence. The predicted probability was calculated as $P = 1 / [1 + \exp(-\text{logit}(P))]$.

Comparisons of the nested models showed that the addition of PNI, CAR, or FAR significantly improved model fit compared with the clinical ultrasound model, with all likelihood ratio test p values < 0.001 . The corresponding Wald tests for the added markers were also statistically significant (all $p < 0.001$). Among the three extended models, the Clinical + FAR model showed the largest descriptive increase in apparent AUC (Δ AUC = 0.054) (Table 5). Calibration curves, decision curve analysis, and clinical impact curves further supported the favorable overall performance and potential clinical net benefit of the Clinical + FAR model (Fig. 3).

Associations of PNI, CAR, and FAR With High-Risk Pathological Features

Among the 124 patients with malignant endometrial lesions, separate Firth-penalized logistic regression models were fitted to assess each marker–endpoint association, with adjustment for age, BMI, and histologic type. Bonferroni correction was applied to account for multiple comparisons. After correction, PNI was inversely associated with deep myometrial invasion, LVSI, FIGO stage III–IV, and grade 3 tumors, with adjusted ORs of 0.640 (95% CI: 0.495–0.796), 0.683 (95% CI: 0.518–0.867), 0.621 (95% CI: 0.430–0.839), and 0.609 (95% CI: 0.439–0.798), respectively. All four associations remained statistically significant after Bonferroni correction.

FAR was positively associated with the same four high-risk pathological features. The adjusted ORs for deep myometrial invasion, LVSI, FIGO stage III–IV, and grade 3 tumors were 3.476 (95% CI: 2.114–6.472), 4.058 (95% CI: 2.206–8.963), 2.746 (95% CI: 1.528–5.660), and 2.316 (95% CI: 1.441–4.099), respectively, and all remained statistically significant after correction. The association between FAR and cervical stromal invasion was statistically significant before correction but did not remain significant after Bonferroni adjustment. None of the associations between CAR and the high-risk pathological features survived correction for multiple comparisons. Detailed results are presented in Table 6.

Discussion

This study systematically compared the diagnostic performance of three preoperative composite markers related to inflammation, nutrition, and coagulation, namely PNI, CAR, and FAR, in the preoperative differentiation of benign and malignant endometrial lesions. We further analyzed the incremental value of these markers beyond the clinical ultrasound model and their associations with high-risk pathological features in endometrial cancer. The results showed that, compared with patients with benign endometrial lesions, patients with endometrial cancer had significantly lower preoperative PNI levels and significantly higher CAR and FAR levels. Among the three markers, FAR showed not only the strongest discriminatory ability as an individual marker, but also provided more evident incremental diagnostic information beyond the clinical ultrasound model composed of age, BMI, diabetes mellitus, and ultrasonographic features. The Clinical + FAR model retained favorable discrimination after bootstrap internal validation and showed improved model fit and potential clinical net benefit. In the adjusted pathological analyses, lower PNI and higher FAR were associated with deep myometrial invasion, LVSI, FIGO stage III–IV, and grade 3 tumors, whereas none of the associations involving CAR remained significant after correction for multiple comparisons. These findings suggest that FAR, which reflects the preoperative systemic inflammatory, coagulation, and nutritional status, may further refine malignant risk stratification in patients with suspected endometrial lesions by providing information distinct from clinical risk factors and local morphological findings.

The higher observed performance of FAR in this study may be explained by the relationship between its biological components and systemic responses to malignancy. Fibrinogen is an important acute phase protein synthesized by the liver and a key component of the coagulation system. It plays a role in tumor-associated hypercoagulability, inflammatory responses, and interactions between tumor cells and the host microenvironment [14]. A mechanistic study showed that fibrinogen can promote adhesion between tumor cells and platelets and may help tumor cells evade natural killer cell-mediated cytotoxicity [15]. Meanwhile, tumor-related inflammation and acute phase responses can alter hepatic protein synthesis patterns, leading to increased levels of positive acute phase proteins such as fibrinogen. In contrast, albumin is a negative acute phase protein, and decreased albumin levels are often associated with malnutrition and systemic inflammatory status [16,17]. Therefore,

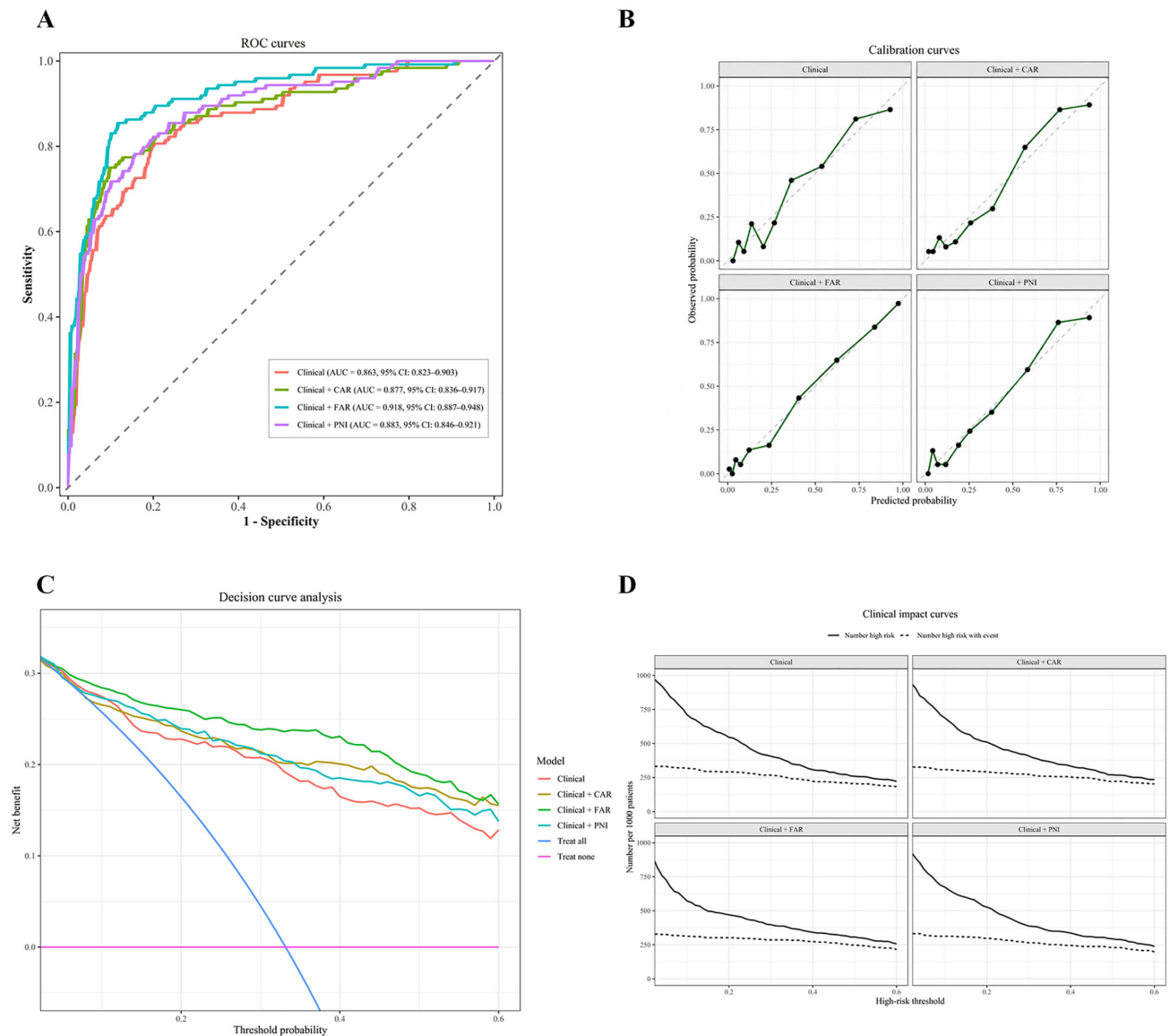


Fig. 3. Model performance of the clinical ultrasound model and extended models for malignant endometrial lesion discrimination. Note: (A) Receiver operating characteristic (ROC) curves of the clinical ultrasound model and extended models. (B) Calibration curves. (C) Decision curve analysis. (D) Clinical impact curves.

FAR, as a ratio-based marker, simultaneously captures two changes in opposite directions, namely increased fibrinogen and decreased albumin, both of which are related to tumor-associated systemic status. Its informational value may therefore be greater than that of either individual component alone [18]. A meta-analysis of gynecological malignancies has also suggested that higher FAR is associated with poorer overall survival and progression-free survival [10], indicating that the procoagulant, inflammatory, and nutritional depletion status reflected by FAR has clinical relevance in gynecological malignancies.

The incremental value of FAR beyond the clinical ultrasound model may be related to the complementarity of these two information sources. In the clinical ultrasound model, age, BMI, and diabetes mellitus primarily reflect the

epidemiological and metabolic risk profile associated with endometrial cancer, whereas ultrasonographic features, including endometrial thickness, endometrial-myometrial junction integrity, and intrauterine fluid, mainly reflect the morphological and hemodynamic changes of local endometrial lesions [5,19]. These variables are important for pre-operative risk assessment. However, benign and malignant endometrial lesions often overlap in clinical manifestations and imaging features, and some cases of endometrial hyperplasia, polyps, atrophic endometrium, or submucosal leiomyomas may also present with endometrial thickening, intrauterine masses, or abnormal blood flow [3,20]. Therefore, once the clinical ultrasound model has incorporated baseline metabolic risk and local morphological information, further gains in model performance

Table 6. Adjusted associations of PNI, CAR, and FAR with high-risk pathological features among patients with malignant endometrial lesions.

Pathological endpoint	Marker	Adjusted OR (95% CI)	Raw <i>p</i> value	Bonferroni adjusted <i>p</i> value
Deep myometrial invasion: <50% (n = 73) vs ≥50% (n = 51)	PNI	0.640 (0.495–0.796)	<0.001	<0.001*
	CAR	1.086 (0.953–1.245)	0.217	1.000
	FAR	3.476 (2.114–6.472)	<0.001	<0.001*
LVSI: negative (n = 86) vs positive (n = 38)	PNI	0.683 (0.518–0.867)	0.001	0.018*
	CAR	1.082 (0.924–1.271)	0.327	1.000
	FAR	4.058 (2.206–8.963)	<0.001	<0.001*
Cervical stromal invasion: negative (n = 105) vs positive (n = 19)	PNI	0.775 (0.506–1.079)	0.140	1.000
	CAR	0.869 (0.626–1.155)	0.344	1.000
	FAR	2.925 (1.339–7.660)	0.005	0.081
FIGO stage: I–II (n = 94) vs III–IV (n = 30)	PNI	0.621 (0.430–0.839)	0.001	0.018*
	CAR	1.159 (0.943–1.446)	0.163	1.000
	FAR	2.746 (1.528–5.660)	<0.001	0.004*
Histologic grade G3: G1–G2 (n = 88) vs G3 (n = 36)	PNI	0.609 (0.439–0.798)	<0.001	0.002*
	CAR	1.217 (1.025–1.470)	0.024	0.364
	FAR	2.316 (1.441–4.099)	<0.001	0.003*

Note: *Statistically significant after Bonferroni correction, corresponding to an unadjusted significance threshold of $p < 0.0033$. For each pathological endpoint, the high-risk category was modeled as the outcome, with the corresponding low-risk category as the reference. ORs were calculated per 1-point increase in PNI and per 0.01 increase in CAR or FAR. Abbreviations: LVSI, lymphovascular space invasion; FIGO, International Federation of Gynecology and Obstetrics; ORs, odds ratios.

may be limited if additional variables are derived from the same information layer. In contrast, FAR reflects the combined changes in preoperative peripheral blood inflammation, coagulation, and nutritional status, representing systemic biological information that differs from morphological and epidemiological factors. Previous evidence also supports this complementarity. The combination of mean platelet volume (MPV), platelet distribution width (PDW), and neutrophil-to-lymphocyte ratio (NLR) may help distinguish benign from malignant endometrial lesions [21]. The combined use of NLR, platelet-to-lymphocyte ratio (PLR), and monocyte-to-lymphocyte ratio (MLR) has shown better discriminatory performance for benign uterine diseases and endometrial malignancies than some individual markers [22]. D-dimer, fibrinogen, and their combinations with tumor markers have shown diagnostic value and have been associated with some clinicopathological features [23,24]. D-dimer combined with transvaginal ultrasonography has also been reported to improve the diagnostic performance for endometrial cancer in postmenopausal women [4]. Therefore, the superior performance of the Clinical + FAR model over the Clinical model in this study does not imply that FAR can replace age, metabolic factors, or ultrasonographic assessment. Rather, it suggests that FAR can provide additional information on systemic inflammation, coagulation, and nutritional status beyond existing baseline risk and local morphological assessment.

In the present cohort, FAR showed a greater numerical increase in model performance than PNI and CAR, which may partly reflect its incorporation of coagulation-related

information in addition to inflammatory and nutritional information. PNI mainly reflects immune nutritional status, and CAR mainly reflects inflammatory nutritional status. FAR further integrates fibrinogen with albumin, thereby capturing nutritional depletion, inflammatory response, and coagulation activation simultaneously. Tumor-associated coagulation activation is not merely a late accompanying phenomenon. The tissue factor pathway and its downstream signaling may contribute to tumor cell proliferation, angiogenesis, and metastasis [25]. This mechanistic background may help explain why FAR provided more complementary information than PNI and CAR in differentiating benign from malignant endometrial lesions. In the present study, FAR showed consistent performance in individual-marker discrimination, provided incremental value beyond the clinical ultrasound model, and was associated with high-risk pathological features, further supporting this interpretation.

Among patients with endometrial cancer, lower PNI and higher FAR were independently associated with deep myometrial invasion, LVSI, FIGO stage III–IV, and grade 3 tumors after adjustment for age, BMI, and histologic type and correction for multiple comparisons. These findings suggest that impaired immune-nutritional status and coagulation-related systemic responses may accompany more aggressive pathological characteristics. However, the association between FAR and cervical stromal invasion did not remain significant after Bonferroni correction, and CAR was not independently associated with any of the evaluated pathological features. A previous study re-

ported associations of coagulation markers, including D-dimer and fibrinogen, with FIGO stage, myometrial invasion, and cervical involvement [24]. Low PNI has also been associated with FIGO stage III–IV, grade 3 tumors, LVSI, and deep myometrial invasion in endometrial cancer [26]. These findings support the biological plausibility of the observed associations, although the present results remain exploratory and should not be interpreted causally.

From the perspective of clinical translation, the findings of this study have practical implications. Current risk stratification systems for endometrial cancer mainly rely on post-operative pathological and molecular features, including depth of myometrial invasion, cervical stromal invasion, LVSI, histological type and grade, and molecular classification information such as polymerase epsilon (POLE) mutation, mismatch repair (MMR) deficiency, p53 abnormality, and no specific molecular profile (NSMP) [27,28]. However, in the preoperative setting, objective indicators that can be used for refined risk quantification remain relatively limited. In clinical practice, preliminary assessment still largely depends on ultrasonographic findings, hysteroscopy, or endometrial sampling results. For patients in whom the distinction between benign and malignant lesions remains uncertain after transvaginal ultrasonography and histological sampling, the integration of preoperative inflammation-, coagulation-, and nutrition-related markers such as FAR may provide supplementary information. This may be particularly relevant for patients with ultrasonographic features intermediate between benign and malignant lesions, inconclusive initial sampling results, or findings suggesting low-risk lesions combined with advanced age and multiple metabolic risk factors. Such markers may provide information on tumor-related systemic responses beyond morphological assessment and histological sampling. This may assist clinicians in risk stratification and treatment decision-making. It should be emphasized that PNI, CAR, and FAR are all nonspecific systemic markers. Their clinical value is better suited to serving as auxiliary tools for risk stratification rather than as alternative diagnostic indicators, and they cannot replace histopathological confirmation. Future studies should validate FAR in prospective multicenter cohorts and directly compare its diagnostic performance with established serum markers such as cancer antigen 125 (CA125) and human epididymis protein 4 (HE4).

This study has several strengths. First, this study simultaneously compared the diagnostic performance of PNI, CAR, FAR, and their component indicators, which helps clarify the potential advantages of composite markers over individual blood-based indicators. Second, the three markers were not evaluated as isolated diagnostic tools. Instead, their incremental value was assessed within the framework of a clinical ultrasound model composed of age, BMI, diabetes mellitus, and ultrasonographic features, which is more consistent with the actual process of comprehensive pre-

operative clinical assessment. Third, model performance was evaluated using ROC analysis, bootstrap internal validation, likelihood ratio and Wald tests for nested models, calibration curves, decision curve analysis, and clinical impact curves, covering discrimination, optimism, model fit, calibration, and clinical utility. This approach improves the completeness of result interpretation. Finally, PNI, CAR, and FAR are all derived from routine preoperative blood tests, are easy to calculate, have low cost, and do not require additional equipment or specialized reagents, supporting their feasibility for further investigation and validation as auxiliary markers for risk stratification.

This study also has several limitations. First, the single-center retrospective design and modest sample size may limit the generalizability of the findings. Although internal validation was performed using 1000 nested bootstrap resamples, independent external validation was not available. The modest optimism estimates may partly reflect the relatively parsimonious final Clinical + FAR model, which included seven predictors for 124 malignant events and did not incorporate interaction terms or machine-learning-based tuning. Nevertheless, bootstrap validation assesses internal reproducibility rather than transportability; therefore, the model should be evaluated in prospective multicenter cohorts and independent populations before broader clinical application. Second, PNI, CAR, and FAR are nonspecific markers and may still be affected by inflammatory status, organ function, and nutritional condition. Although patients with acute infection and overt inflammatory diseases were excluded, this strict selection may also have restricted the variability of C-reactive protein (CRP), thereby attenuating the discriminatory performance of CAR and partly influencing the observed comparison between FAR and CAR. Therefore, the relative advantage of FAR observed in this study requires further validation in populations with a broader distribution of inflammatory markers. In addition, complete data on CA125 and HE4 were unavailable, precluding direct comparisons of FAR, CAR, and PNI with these serum tumor markers. This limited a comprehensive assessment of the relative diagnostic value of FAR, and direct head-to-head comparisons should be performed in future studies. Third, the optimal cut-off values obtained in this study were based on the Youden index in the current cohort and are therefore sample-dependent. They should not be directly generalized as universally applicable clinical diagnostic thresholds for other institutions or populations. External validation and recalibration of these cut-off values are needed before clinical application. Fourth, the study population consisted of patients with suspected endometrial lesions who underwent invasive diagnostic evaluation or surgery and subsequently received a definitive histopathological diagnosis. This selection process may have resulted in a higher proportion of malignant lesions and a different disease spectrum than that observed in general outpatient populations. Therefore,

the diagnostic performance of the proposed model should not be directly extrapolated to routine outpatient screening settings. Fifth, the analyses of high-risk pathological features were exploratory and involved relatively few events, particularly for cervical stromal invasion. Although Firth-penalized logistic regression was used with adjustment for age, BMI, and histologic type, residual confounding and limited statistical precision remain possible. These findings should therefore be interpreted as associations rather than causal or fully validated predictive effects. Finally, because of the retrospective nature of the study, complete molecular classification data were not available. Although p53 data were available, some patients lacked MMR or microsatellite instability (MSI) assessment, and POLE status and integrated molecular classification were not systematically collected. Therefore, this study was unable to evaluate the associations of PNI, CAR, and FAR with molecular subtypes within a complete classification framework, which may limit the interpretation of their value for risk stratification. Future studies should incorporate more complete molecular classification data to further validate these findings.

Conclusions

In summary, preoperative FAR, as a composite blood-based marker integrating coagulation-related alterations, nutritional depletion, and acute phase inflammatory responses, showed better overall performance than PNI and CAR for the preoperative differentiation of benign and malignant endometrial lesions. It also provided incremental discriminatory information beyond clinical risk factors and ultrasonographic morphological assessment. These findings suggest that FAR has the potential to serve as an auxiliary marker for preoperative risk stratification and may provide complementary discriminatory information in preoperative diagnostic and surgical settings. However, before broader clinical application, external validation in prospective multicenter studies is warranted, and its integration with modern molecular classification systems should be further explored.

Availability of Data and Materials

The data analyzed are available from the corresponding author upon reasonable request.

Author Contributions

Conception and design: JMH. Provision of study materials: YZ and MJS. Collection and assembly of data: JMH and YZ. Data analysis and interpretation: JMH and MJS. Manuscript writing: all authors. All authors have been involved in revising the manuscript critically for important intellectual content. All authors gave final approval of the version to be published. All authors have participated sufficiently in the work to take public responsibility for appro-

priate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was carried out in strict accordance with the ethical guidelines of the Declaration of Helsinki. It has been reviewed and approved by the Ethics Committee of Jinhua Municipal Central Hospital (Approval No. 2026-264). Because this was a retrospective study and all patient information was anonymized before analysis, the requirement for informed consent was waived by the Ethics Committee of Jinhua Municipal Central Hospital.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.62713/ai.c.4881>.

References

- [1] Patrizi L, Ticconi C, Borelli B, Finocchiaro S, Chiamonte C, Sesti F, et al. Clinical significance of endometrial abnormalities: an observational study on 1020 women undergoing hysteroscopic surgery. *BMC Women's Health*. 2022; 22: 106. <https://doi.org/10.1186/s12905-022-01682-5>
- [2] Kumari K, Paswan MK, Kundan M, Ambedkar SN. A prospective study of endometrial histopathology in post-menopausal women in Jharkhand. *Journal of Family Medicine and Primary Care*. 2024; 13: 1696–1700. https://doi.org/10.4103/jfmpe.jfmpe_1331_23
- [3] Yu J, Wang F, Chen L, Zhang J. Development and clinical evaluation of an ultrasound-based predictive model for early diagnosis of endometrial cancer. *Medicine*. 2026; 105: e47682. <https://doi.org/10.1097/MD.00000000000047682>
- [4] Guo X, Cheng Y, Du J. Clinical value of D-dimer combined with transvaginal ultrasonography in the postmenopausal population with endometrial carcinoma. *Scientific Reports*. 2025; 15: 27447. <https://doi.org/10.1038/s41598-025-12980-x>
- [5] Li X, Wang H, Wang T, Cui H, Wu L, Wang W, et al. Combining demographic data and transvaginal ultrasonography: a predictive model for endometrial carcinoma in postmenopausal patients. *BMC Women's Health*. 2024; 24: 539. <https://doi.org/10.1186/s12905-024-03374-8>
- [6] Ruan H, Chen S, Li J, Ma L, Luo J, Huang Y, et al. Development and Validation of a Nomogram Prediction Model for Endometrial Malignancy in Patients with Abnormal Uterine Bleeding. *Yonsei Medical Journal*. 2023; 64: 197–203. <https://doi.org/10.3349/ymj.2022.0239>
- [7] Zhao H, Wu L, Yan G, Chen Y, Zhou M, Wu Y, et al. Inflammation and tumor progression: signaling pathways and targeted inter-

- vention. *Signal Transduction and Targeted Therapy*. 2021; 6: 263. <https://doi.org/10.1038/s41392-021-00658-5>
- [8] Njoku K, Barr CE, Ramchander NC, Crosbie EJ. Impact of pre-treatment prognostic nutritional index and the haemoglobin, albumin, lymphocyte and platelet (HALP) score on endometrial cancer survival: A prospective database analysis. *PloS One*. 2022; 17: e0272232. <https://doi.org/10.1371/journal.pone.0272232>
- [9] Fang Y, Zheng T, Zhang C. Prognostic Role of the C-Reactive Protein/Albumin Ratio in Patients With Gynecological Cancers: A Meta-Analysis. *Frontiers in Oncology*. 2021; 11: 737155. <https://doi.org/10.3389/fonc.2021.737155>
- [10] Chen Y, Zhang J. Prognostic role of fibrinogen-to-albumin ratio in patients with gynecological cancers: a meta-analysis. *Frontiers in Oncology*. 2025; 15: 1580940. <https://doi.org/10.3389/fonc.2025.1580940>
- [11] Marin AG, Filipescu AG, Petca RC, Vlădăreanu R, Petca A. Clinical Correlations between Serological Markers and Endometrial Cancer. *Cancers*. 2024; 16: 1935. <https://doi.org/10.3390/cancers16101935>
- [12] Kinoshita A, Onoda H, Imai N, Iwaku A, Oishi M, Tanaka K, et al. The C-reactive protein/albumin ratio, a novel inflammation-based prognostic score, predicts outcomes in patients with hepatocellular carcinoma. *Annals of Surgical Oncology*. 2015; 22: 803–810. <https://doi.org/10.1245/s10434-014-4048-0>
- [13] Hwang KT, Chung JK, Roh EY, Kim J, Oh S, Kim YA, et al. Prognostic Influence of Preoperative Fibrinogen to Albumin Ratio for Breast Cancer. *Journal of Breast Cancer*. 2017; 20: 254–263. <https://doi.org/10.4048/jbc.2017.20.3.254>
- [14] Wolberg AS. Fibrinogen and fibrin: synthesis, structure, and function in health and disease. *Journal of Thrombosis and Haemostasis : JTH*. 2023; 21: 3005–3015. <https://doi.org/10.1016/j.jth.2023.08.014>
- [15] Zheng S, Shen J, Jiao Y, Liu Y, Zhang C, Wei M, et al. Platelets and fibrinogen facilitate each other in protecting tumor cells from natural killer cytotoxicity. *Cancer Science*. 2009; 100: 859–865. <https://doi.org/10.1111/j.1349-7006.2009.01115.x>
- [16] Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. *The New England Journal of Medicine*. 1999; 340: 448–454. <https://doi.org/10.1056/NEJM199902113400607>
- [17] Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. *Seminars in Dialysis*. 2004; 17: 432–437. <https://doi.org/10.1111/j.0894-0959.2004.17603.x>
- [18] Li B, Deng H, Lei B, Chen L, Zhang X, Sha D. The prognostic value of fibrinogen to albumin ratio in malignant tumor patients: A meta-analysis. *Frontiers in Oncology*. 2022; 12: 985377. <https://doi.org/10.3389/fonc.2022.985377>
- [19] Leone FPG, Timmerman D, Bourne T, Valentin L, Epstein E, Goldstein SR, et al. Terms, definitions and measurements to describe the sonographic features of the endometrium and intrauterine lesions: a consensus opinion from the International Endometrial Tumor Analysis (IETA) group. *Ultrasound in Obstetrics & Gynecology : the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2010; 35: 103–112. <https://doi.org/10.1002/uog.7487>
- [20] Van Den Bosch T, Verbakel JY, Valentin L, Wynants L, De Cock B, Pascual MA, et al. Typical ultrasound features of various endometrial pathologies described using International Endometrial Tumor Analysis (IETA) terminology in women with abnormal uterine bleeding. *Ultrasound in Obstetrics & Gynecology : the Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*. 2021; 57: 164–172. <https://doi.org/10.1002/uog.22109>
- [21] Song YJ, Kim HG, Yoon HJ, Choi KU, Suh DS, Kim KH. Preoperative Haematologic Markers for the Differentiation of Endometrial Cancer from Benign Endometrial Lesions in Postmenopausal Patients with Endometrial Masses. *Cancer Management and Research*. 2023; 15: 1111–1121. <https://doi.org/10.2147/CMAR.S430013>
- [22] Qin L. The predictive value of NLR, PLR and MLR in the differential diagnosis of benign uterine diseases and endometrial malignant tumors. *Discover Oncology*. 2024; 15: 91. <https://doi.org/10.1007/s12672-024-00956-8>
- [23] Ge L, Liu G, Hu K, Huang K, Zhang M, Zhou J, et al. A New Risk Index Combining d-Dimer, Fibrinogen, HE4, and CA199 Differentiates Suspecting Endometrial Cancer From Patients With Abnormal Vaginal Bleeding or Discharge. *Technology in Cancer Research & Treatment*. 2020; 19: 1533033819901117. <https://doi.org/10.1177/1533033819901117>
- [24] Li H, Liao H, Jing B, Wang Y. Effects of coagulation function indicators and tumor markers on diagnosis and clinicopathological characteristics of endometrial cancer. *The International Journal of Biological Markers*. 2023; 38: 214–222. <https://doi.org/10.1177/03936155231196253>
- [25] Hassan N, Efig J, Kiesel L, Bendas G, Götte M. The Tissue Factor Pathway in Cancer: Overview and Role of Heparan Sulfate Proteoglycans. *Cancers*. 2023; 15: 1524. <https://doi.org/10.3390/cancer15051524>
- [26] Mao S, Zhang Z, Li Y. Prognostic and clinicopathological role of prognostic nutritional index (PNI) in endometrial cancer: A meta-analysis. *Heliyon*. 2024; 10: e35211. <https://doi.org/10.1016/j.heliyon.2024.e35211>
- [27] Concin N, Matias-Guiu X, Vergote I, Cibula D, Mirza MR, Marantz S, et al. ESGO/ESTRO/ESP guidelines for the management of patients with endometrial carcinoma. *International Journal of Gynecological Cancer : Official Journal of the International Gynecological Cancer Society*. 2021; 31: 12–39. <https://doi.org/10.1136/ijgc-2020-002230>
- [28] Berek JS, Matias-Guiu X, Creutzberg C, Fotopoulou C, Gaffney D, Kehoe S, et al. FIGO staging of endometrial cancer: 2023. *Journal of Gynecologic Oncology*. 2023; 34: e85. <https://doi.org/10.3802/jgo.2023.34.e85>

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