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Impact of the 2023 FIGO staging system on risk stratification in endometrial cancer: a retrospective cohort study

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Abstract

Objective To evaluate the prognostic value of the 2023 FIGO staging system for endometrial cancer (EC) by comparing it with the 2009 FIGO system, using data from Shanghai General Hospital.

Methods We retrospectively analyzed 331 EC patients (March 2016–August 2025) and re-staged them from the 2009 FIGO criteria to the 2023 FIGO criteria. Molecular subtyping was integrated where available ($N=86$). The Net Reclassification Improvement (NRI) was used to evaluate risk stratification. Prognostic factors were identified using logistic and Cox regression models.

Results Re-staging according to the 2023 FIGO criteria resulted in stage migration for 186 out of 331 patients (56.2%). In the subset with molecular data ($n=86$), reclassification occurred in 47 patients (54.7%). Compared to the 2009 system, the 2023 system demonstrated a significant NRI of 100.76% ($P<0.001$) for Stages I–II. Key clinicopathological factors independently associated with stage migration included non-endometrioid histology, high tumor grade (G3), and deep myometrial invasion.

Conclusion Compared with the 2009 FIGO staging, the 2023 FIGO system significantly improves risk stratification in EC. Its integration of molecular and refined pathological factors facilitates more precise prognostication and supports individualized treatment planning.

Keywords Endometrial cancer (EC), FIGO stage, Progression-free survival (PFS), Overall survival (OS), Net reclassification improvement (NRI)

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Background

Endometrial cancer (EC) ranks among the most common malignancies of the female reproductive system, accounting for 20%–30% of all gynecological cancers. Annually, approximately 417,000 new cases are diagnosed worldwide, with a notably higher incidence observed in high-income countries [1]. In 2022, data from the International Agency for Research on Cancer reported 97,370 deaths attributable to EC [2]. Surgical treatment yields a 5-year disease-free survival (DFS) rate that varies considerably by stage ranging from 74.2% to 90.8% in stage I/II to as low as 16% in metastatic disease [3]. According to the Danish Gynecological Cancer Group (www.DGCG.dk, accessed 2021–09–15), survival rates have shown modest improvement between 2005–2017 and 2016–2020, largely due to advances in the characterization of histological and molecular subtypes, alongside the development of targeted therapy, immunotherapy, and endocrine treatment.

The current diagnostic framework for EC integrates the 2009 International Federation of Gynecology and Obstetrics (FIGO) staging system, the 8th edition TNM (tumor, node, metastasis) staging by the American Joint Committee on Cancer (AJCC, 2018) [2], and the 5th edition World Health Organization (WHO) Classification of Tumors of the Female Reproductive Organs endorsed by the International Society of Gynecological Pathologists (ISGyP) [4]. These systems evaluate EC from clinical,

high-risk, and pathological perspectives. A major conceptual migration was introduced in the 2023 FIGO staging system, which now incorporates not only clinico-pathological and surgical findings but also high-risk prognostic factors and molecular subtype information (Fig. 1). Key updates include refined definitions of lymphovascular space invasion (LVSI) and the integration of molecular classification—such as POLE mutation (POLEmut), MMR deficiency (MMRd), p53 abnormality (p53abn), and non-specific molecular profile (NSMP)—into staging. This revision aims to enhance prognostic discrimination, reduce overtreatment in early-stage disease, and guide tailored strategies for advanced or recurrent EC. A validation study by Gravebrot et al. involving over 134,000 patients confirmed improved survival stratification under the updated system [5].

Nonetheless, the 2023 FIGO update has sparked debate [6]. Critics point to its increased complexity [7], the financial burden associated with molecular testing, and potential inter-center variability in pathological interpretation, which may lead to stage migration effects. Moreover, discrepancies among major classification systems WHO, FIGO, and International Collaboration on Cancer Reporting (ICCR) regarding specific pathological criteria, such as ovarian involvement, pose challenges for uniform clinical implementation. Reflecting these ongoing controversies, the 2025 NCCN guidelines continue to reference both the 2009 FIGO system and the 2023 update [8].

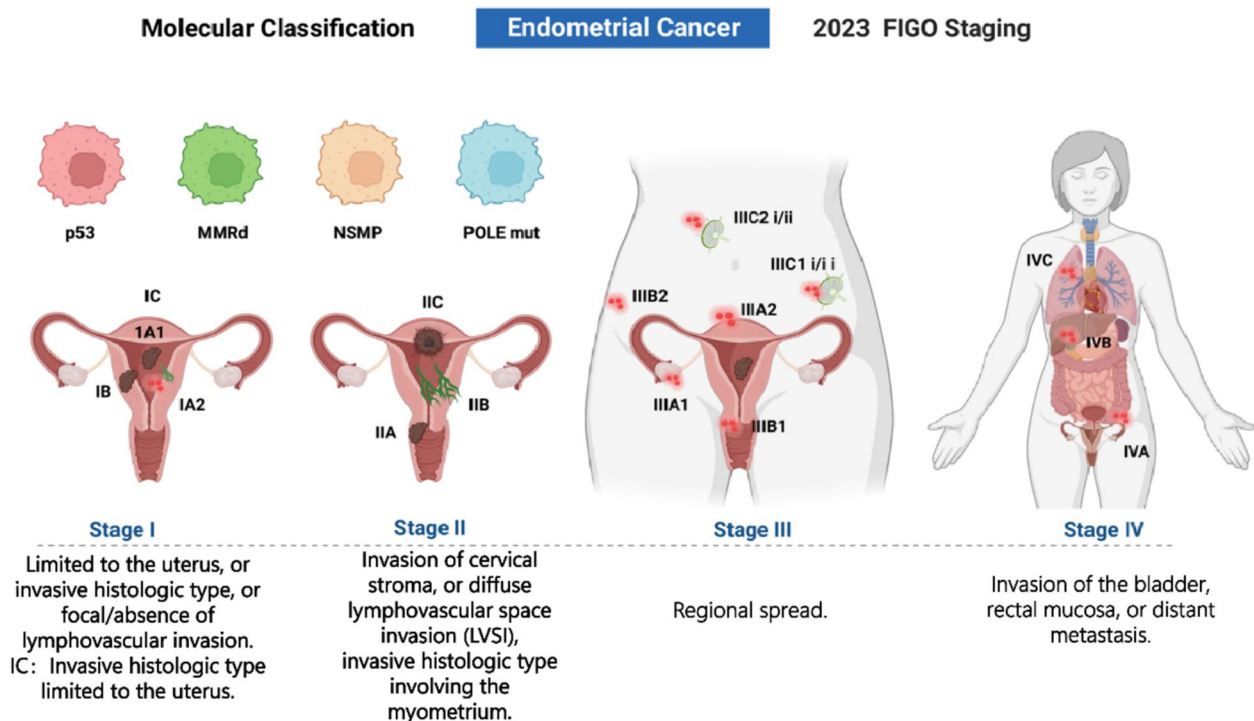


Fig. 1 Schematic diagram of the 2023 FIGO staging system for endometrial cancer, incorporating molecular classification (p53 abnormal, mismatch repair deficiency [MMRd], no specific molecular profile [NSMP], and POLE mutation)

Given these uncertainties, a systematic evaluation of the prognostic relevance and clinical applicability of the 2023 FIGO staging system is urgently needed. In this study, we retrospectively analyzed a cohort of EC patients from Shanghai General Hospital, reclassifying them according to the 2023 FIGO criteria integrated with molecular subtyping. We assessed stage migration between the 2009 and 2023 systems, identified factors associated with such migration, and developed a predictive model for recurrence and metastasis. Our objective is to validate the clinical necessity of the updated staging system and to provide evidence supporting individualized treatment strategies in EC management.

Patients and methods

Patients

Ethical considerations and study design

This study was approved by Chinese Clinical Trial Registry (ChiCTR2500104752) and Institutional Review Board of Shanghai General Hospital (2023SQ304) and conducted in accordance with the Declaration of Helsinki (Supplementary Material 1). Written informed consent was obtained from all participants. We performed a retrospective analysis of 331 EC patients treated between January 2016 and September 2025 (Fig. 2).

Patient selection

Inclusion required pathological confirmation of EC per the WHO 5th Edition classification. Exclusion criteria included severe comorbidities preventing staging surgery, patient withdrawal, loss to follow-up (> 24 months), or poor compliance.

Data collection and staging

Data completeness was ensured via standardized extraction protocols, with missing variables addressed through re-review of original records. Collected data comprised basic demographics, clinicopathological features, surgical details, FIGO 2009 and 2023 staging, molecular subtypes, and *BRCA1/2* mutation status where available.

Treatment

Treatment decisions for all patients in the institutional cohort were made following the standard-of-care guidelines, primarily based on the 2021 ESGO/ESTRO/ESP risk classification and the 2009 FIGO stage at initial diagnosis. The primary treatment consisted of total hysterectomy and bilateral salpingo-oophorectomy, with surgical staging (including pelvic and/or para-aortic lymphadenectomy or sentinel lymph node mapping) performed as indicated. Adjuvant therapy was administered based on the final pathological findings and assigned risk group.

Follow-up and outcomes

Patients were followed every 3 months (years 1–2), every 6 months (years 3–5), and annually thereafter. Progression-free survival (PFS) and overall survival (OS) were assessed at 3 and 5 years through medical records, clinic visits, and telephone calls. PFS was defined as the time from surgery to disease progression, recurrence, death, or last follow-up, with a median follow-up of 50.8 months.

Variable definitions

To ensure clarity in statistical modeling, the key variables used in regression analyses were operationally defined as follows:

Tumor diameter: The maximum diameter of the primary tumor, measured on preoperative MRI or from the pathological specimen report.

Histological type: Categorized according to the WHO Classification of Tumors of Female Reproductive Organs (5th Edition), primarily as endometrioid adenocarcinoma (EAC), serous carcinoma (SC), clear cell carcinoma (CCC), or other.

Tumor differentiation: Graded as G1, G2, or G3 based on the histopathological assessment of the resected tumor.

Myometrial invasion depth: Classified as either < 1/2 or ≥ 1/2 of the myometrial thickness, determined by pathological examination.

Risk group: Stratified according to the 2021 ESGO/ESTRO/ESP guidelines into low, intermediate, high-intermediate, high, and metastatic risk categories.

Statistical analysis

Analyses were conducted separately for the institutional cohorts. The median follow-up time was calculated using the reverse Kaplan–Meier method, with the interval defined from the date of surgery to the date of last contact or death. Patients' demographic characteristics and molecular subtype of FIGO stage migrations were analyzed by chi-square and t test. To address sparse data bias, Firth's penalized logistic regression was applied to estimate odds ratios with 95% confidence intervals for factors associated with FIGO stage migration. COX regression and Kaplan–Meier (KM) method were applied to assess the impact of these factors on EC recurrence and survival. The correlation between various factor in FIGO migration or patient survival was assessed using the Wilcoxon test and chi-square test. The log-rank test was applied to compare whether there were significant differences in survival curves between different groups. The “nri-cens” package (v1.6) was used for Net reclassification improvement (NRI) calculating. The NRI and its

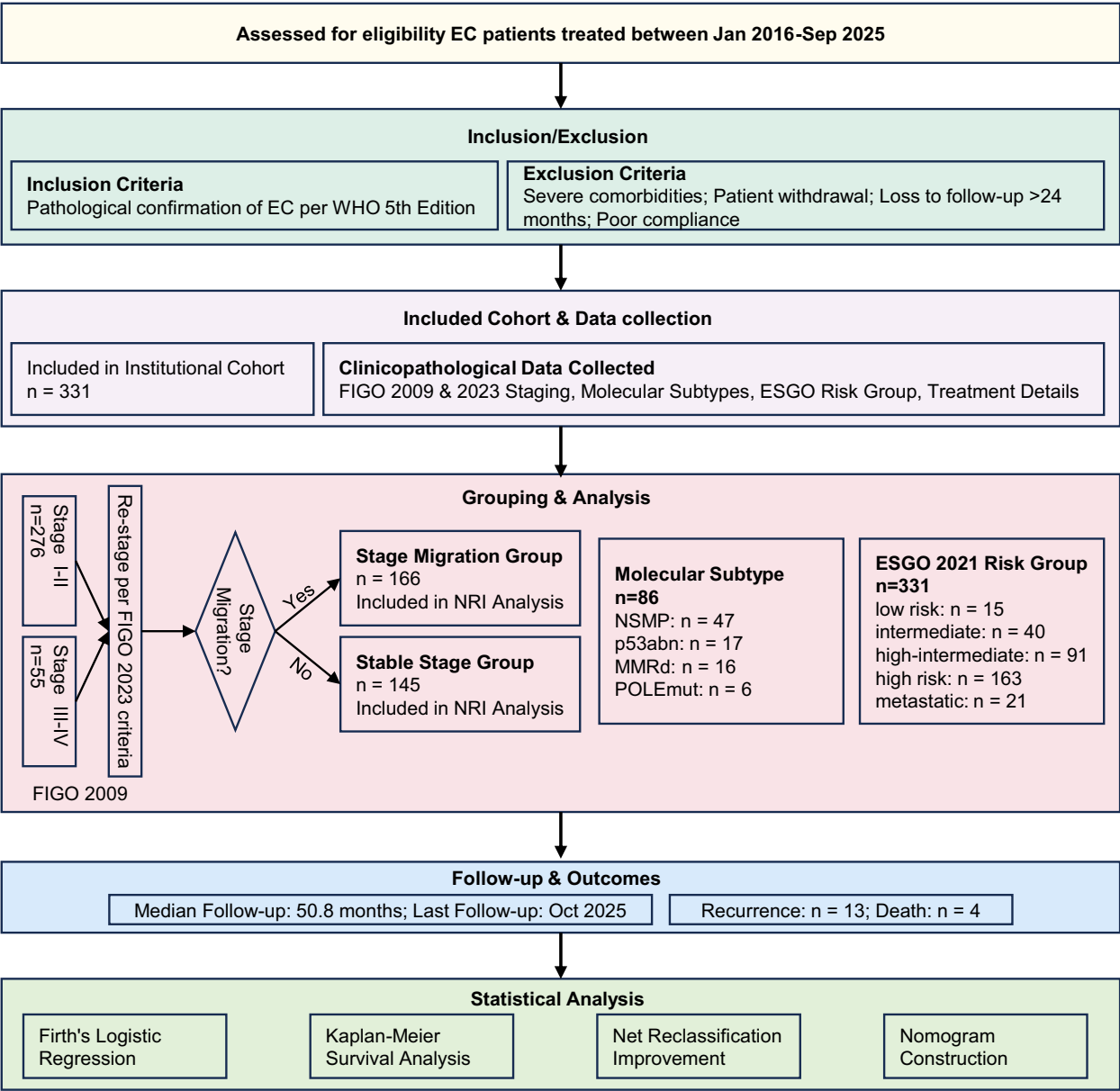


Fig. 2 Flow diagram of the institutional endometrial carcinoma cohort. This diagram illustrates the patient enrollment, data collection, grouping, and analysis process for the retrospective study. A total of 331 patients with endometrial carcinoma (EC) treated between January 2016 and September 2025 were assessed for eligibility and constituted the institutional cohort. Comprehensive clinicopathological data, including molecular subtypes and treatment details, were collected for all patients. The cohort was grouped and analyzed according to the FIGO 2009 and 2023 staging systems, the ESGO 2021 risk stratification, and the ProMisE molecular classification (available for $n=86$). The primary analyses included an assessment of stage migration and its impact using Net Reclassification Improvement (NRI), progression-free survival (PFS) and overall survival (OS) analysis, the development of a predictive nomogram. Patients were followed for a median of 50.8 months until October 2025. (NRI, Net Reclassification Improvement; PFS, Progression-Free Survival; OS, Overall Survival; ESGO, European Society for Gynaecological Oncology)

95% confidence intervals were calculated using the asymptotic method for the difference in proportions, as recommended by Pencina et al. The “survminer” package (v0.4.9) was used for visualization, generating KM curves. Nomograms were plotted using the “rms” package (v6.7–1) to visualize prediction results by C-index, and the model’s predictive ability was assessed through calibration curves. The “maftools”

package (v2.18.0) was used to read gene mutation data from samples, and ggplot2 (v3.5.0) was utilized to create a waterfall plot, displaying clinically significant mutation types sorted by mutation frequency. Statistical significance was determined using a cutoff p -value of <0.05 . All statistical analyses were conducted using SPSS version 29.0 and R 4.3.3 with RStudio.

Results
Basic characteristics of FIGO stage migrations in EC patients in the institutional cohort

A total of 331 EC patients were enrolled and numbered, the mean age at onset was 57 ± 10.7 years, with 51.4% (170/331) of patients aged between 27 and 57 years and 48.6% (161/331) aged between 56 and 91 years. Among the patients, 87.6% (290/331) had endometrioid histology, including 48.3% with Grade 1 (G1) EAC (160/331) and 28.4% with G2 EAC (94/331), and 10.6% with G3 EAC (35/331). Non-endometrioid histology were found in 12.4% of patients (41/331), comprising 6.3% with SC (21/331), 2.1% with CCC serous cancer (7/331), and 3.9% with other types of cancer (13/331). Based on the 2021

ESGO risk stratification, 4.5% of patients (15/331) were classified as low-risk, 12.1% (40/331) as intermediate-risk, 27.5% (91/331) as high-intermediate-risk, 49.2% (163/331) as high-risk, and 6.3% (21/331) were in the terminal metastatic stage. The last follow-up was conducted in October 2025. With a median follow-up duration of 50.8 months, 13 cases of recurrence and 4 deaths were recorded.

We re-staged EC patients previously diagnosed according to the 2009 FIGO staging system using the 2023 FIGO staging criteria. Following this re-staging, 56.2% of patients (186/331) experienced a migration in their stage (Fig. 3). The number of Stage I patients decreased from 256 to 241, while Stage II patients increased, and Stage III

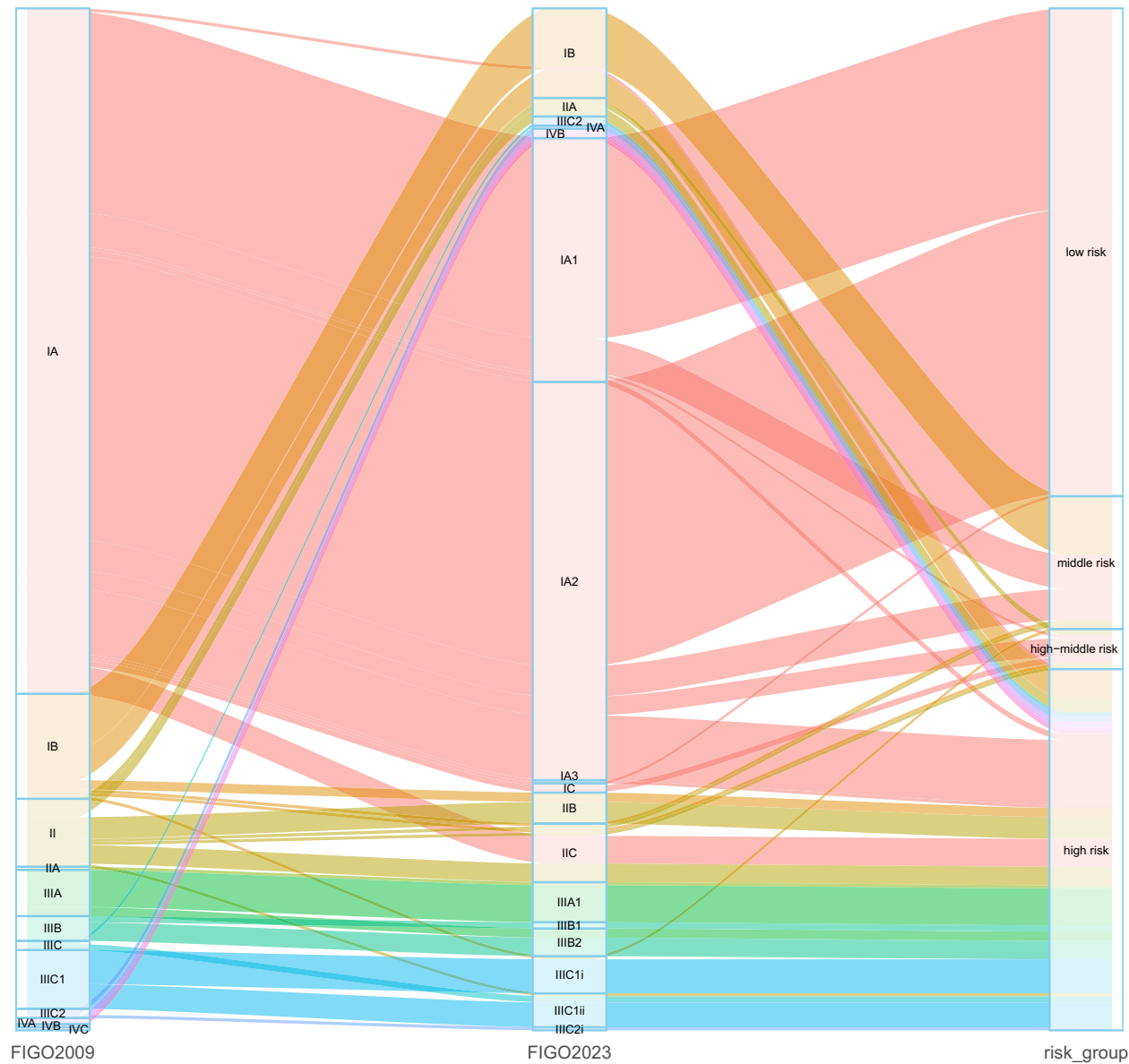


Fig. 3 Sankey diagram illustrating the redistribution of cases between the 2009 and 2023 FIGO staging systems (FIGO2009 and FIGO2023, respectively), categorized by associated risk group

patients decreased. Following re-staging, significant stage migration was observed, with the majority of changes occurring in patients initially diagnosed with Stage I or II disease under the 2009 system, while revisions in Stages III and IV primarily involved subcategory refinements. The most frequent pattern of upstaging was from Stage IA to IA2 (129 patients), underscoring the impact of the revised criteria for assessing myometrial invasion. Other notable transitions, detailed in the Interactive Sankey diagram (Supplementary Material 2). In contrast, 145 patients retained their original FIGO stage. Assessment of the drivers for stage migration revealed that key pathological parameters prompted reclassification in 48 patients. Concerning myometrial invasion depth, 19 patients originally staged as IA, IB, or II were upstaged to IIC. One patient was upgraded from Stage II to IIIC1ii due to the presence of pelvic lymph node metastasis and LVSI. Consistent with the ESGO risk categorization, all patients in Stages III and IV were classified as high-risk, while risk stratification for Stage I and II patients demonstrated greater flexibility.

The NRI to evaluate the FIGO stage migration

The NRI of the updated FIGO 2023 staging system compared to the 2009 version was evaluated for FIGO I–II and III–IV stages based on risk thresholds derived from the reclassification tables. For stages I–II ($N=276$), using risk thresholds of $<10\%$ (low risk), $<30\%$ (intermediate risk), and $\geq 30\%$ (high risk), the FIGO 2023 system reclassified cases significantly. The reclassification table for all subjects showed that 28 cases migrated from FIGO 2009's intermediate risk (10–20%) to low risk ($<10\%$), 86 cases from high risk ($\geq 30\%$) to low risk, and 5 cases from intermediate risk to high risk, while 156 cases remained classified as high risk. This resulted in an NRI improvement of 100.76% (95% CI: 67.73–104.28%; $P<0.001$), demonstrating substantial reclassification enhancement. For the FIGO Up subgroup (cases with stage migration upward), the NRI was 2.5% (95% CI: -0.57 – 5.38% ; $P=0.093$), which was not significant, while for the FIGO Stable subgroup, the NRI was 98.26% (95% CI: 66.67–100%; $P<0.001$), indicating strong improvement in non-migrated cases. For stages III–IV ($N=55$), applying risk thresholds of $<50\%$ (low risk), $<70\%$ (intermediate risk), and $\geq 70\%$ (high risk), the reclassification table for all subjects revealed that 5 cases were reclassified from FIGO 2009's low risk ($<50\%$) to high risk ($\geq 70\%$), 3 cases from intermediate risk (50–70%) to low risk, and 2 cases from intermediate risk to high risk, while 16 cases remained in high risk. This yielded an NRI improvement of 38% (95% CI: 0–67.24%; $P<0.05$). In the FIGO Up subgroup, the NRI was 28% (95% CI: 0–52.28%; $P<0.05$), showing significant reclassification for upstaged cases, whereas for the FIGO Stable subgroup, the NRI was 10% (95% CI:

0–24.14%; $P=0.131$), which was not significant. These results underscore the differential impact of the FIGO 2023 system on reclassification across stage groups and migration subgroups, highlighting its refined utility in risk stratification (Table 1).

Analysis of factors associated with migrations in FIGO stage

To identify clinicopathological factors associated with FIGO stage migration, Firth's penalized logistic regression was performed, with the non-migrating group serving as the reference. This approach was employed to reduce sparse data bias and improve estimate reliability. The analysis identified several factors significantly associated with stage migration: non-endometrioid histology (serous carcinoma: OR=8.50; clear cell carcinoma: OR=16.84), advanced tumor grade (G3 vs. G1: OR=15.33), deep myometrial invasion (non-invasion vs. $>1/2$: OR=64.26; $<1/2$ vs. $>1/2$: OR=8.81), fallopian tube involvement (OR=0.10), nerve invasion (OR=8.81), and higher risk category (middle risk vs. low risk: OR=8.73; high-middle risk vs. low risk: OR=5.21) (all $p<0.05$) (Fig. 4A, Supplementary Table 1).

The association between these stage migration-related factors and progression-free survival was assessed using Cox proportional hazards regression. Kaplan–Meier analysis showed that median survival was not reached in any subgroup, indicating that over half of patients remained progression-free during the study period. Several pathological features, including nerve invasion, pelvic or abdominal lymph node involvement, positive ascites cytology, and LVSI, were significantly associated with reduced survival probability (all log-rank $P<0.05$; Fig. 4B–F). Positive ascites cytology demonstrated the strongest adverse effect on survival outcomes.

The relationship between molecular subtype and FIGO stage migrations in EC patients

Molecular classification of the 86-patient cohort revealed NSMP as the most prevalent subtype (54.7%, 47/86), followed by p53abn (19.8%, 17/86), MMRd (18.6%, 16/86), and POLEmut (7.0%, 6/86). The integration of molecular data with the 2023 FIGO criteria prompted stage migration in over half of the cohort (54.7%, 47/86), with reclassification occurring across all molecular subgroups (Table 2, Supplementary Table 2).

An exploratory analysis of clinical outcomes following molecular-integrated reclassification revealed distinct trends across subtypes. All six patients with POLEmut tumors were down-staged to stage Ia_m and remained recurrence-free without adjuvant therapy, suggesting a favorable prognosis consistent with this subtype. In contrast, tumors with p53abn alterations appeared to be associated with more aggressive behavior, exemplified by

Table 1 NRI for FIGO I-II and III-IV stages

FIGO I-II stages				FIGO III-IV stages			
Reclassification Table for all subjects		P<0.001		Reclassification Table for all subjects		P<0.05	
Estimate	Std.Error	95%CI: Lower	95%CI: Upper	Estimate	Std.Error	95%CI: Lower	95%CI: Upper
1.0076087	0.122681632	0.677269285	1.04284536	0.38	0.174741456	0	0.6724138
FIGO 2023				FIGO 2023			
FIGO 2009	Low Risk < 0.1	Middle Risk < 0.3	High Risk > = 0.3	FIGO 2009	Low Risk < 0.5	Middle Risk < 0.7	High Risk > = 0.7
< 0.1	0	0	0	< 0.5	27	1	5
< 0.2	28	0	5	< 0.7	3	0	2
> = 0.3	86	0	156	> = 0.7	0	1	16
Reclassification Table for FIGO Up		P=0.093		Reclassification Table for FIGO Up		P<0.05	
Estimate	Std.Error	95%CI: Lower	95%CI: Upper	Estimate	Std.Error	95%CI: Lower	95%CI: Upper
0.0250000	0.014898959	-0.005747886	0.05379175	0.28	0.136705888	0	0.5227743
FIGO 2023				FIGO 2023			
FIGO 2009	Low Risk < 0.1	Middle Risk < 0.3	High Risk > = 0.3	FIGO 2009	Low Risk < 0.5	Middle Risk < 0.7	High Risk > = 0.7
< 0.1	0	0	0	< 0.5	1	1	5
< 0.2	0	0	5	< 0.7	0	0	2
> = 0.3	1	0	154	> = 0.7	0	1	15
Reclassification Table for FIGO Stable		P<0.001		Reclassification Table for FIGO Stable		P=0.131	
Estimate	Std.Error	95%CI: Lower	95%CI: Upper	Estimate	Std.Error	95%CI: Lower	95%CI: Upper
0.9826087	0.113770711	0.666666667	1.00000000	0.10	0.063905817	0	0.2413793
FIGO 2023				FIGO 2023			
FIGO 2009	Low Risk < 0.1	Middle Risk < 0.3	High Risk > = 0.3	FIGO 2009	Low Risk < 0.5	Middle Risk < 0.7	High Risk > = 0.7
< 0.1	0	0	0	< 0.5	26	0	0
< 0.2	28	0	0	< 0.7	3	0	0
> = 0.3	85	0	2	> = 0.7	0	0	1

Net Reclassification Improvement (NRI) analysis for the 2023 FIGO staging system compared to the 2009 FIGO staging system, stratified by early (I–II) and advanced (III–IV) stages. The table presents NRI estimates, standard errors, and 95% confidence intervals (CIs) for all subjects, as well as for subgroups with FIGO stage migration (upstaging) and those with stable staging. Reclassification tables cross-tabulate risk categories based on predicted probabilities under each staging system, with distinct probability thresholds applied for early (low risk: < 0.1, middle risk: < 0.3, high risk: ≥ 0.3) and advanced stages (low risk: < 0.5, middle risk: < 0.7, high risk: ≥ 0.7). P-values indicate the statistical significance of the NRI

one case (Case 23) that was upstaged to IIc2m-p53abn despite conventional low-risk features.

Recurrences (*n* = 8) were observed only in the NSMP and p53abn subgroups, and all recorded deaths (*n* = 3) occurred among patients with NSMP, MMRd, or p53abn subtypes. Illustrative cases highlighted heterogeneous recurrence patterns: one NSMP patient (Case 179) initially staged as IA2 (G1) later developed widespread metastases, while a p53abn patient (Case 193) with nodal micrometastases (IIIC1i) experienced rapid progression. Comprehensive data for all recurrent cases are provided in Supplementary Table 2.

Predictive model for migrations in FIGO stage

A nomogram was constructed based on multivariate logistic regression analysis to predict the probability of migration between the 2009 and 2023 FIGO stages (Fig. 5A, Supplementary Table 3). The model incorporated key clinicopathological variables based on 2025 NCCN guidelines and literature evidence, including

tumor diameter, tumor differentiation, menopausal status, cervical stromal invasion, fallopian tube involvement, ovarian invasion, vaginal bleeding, nerve invasion, presence of ascites, myometrial invasion, age, histological type, and abdominal lymph node involvement. Each variable was assigned a score on the point scale, with the sum of all scores corresponding to the predicted probability of stage migration. Myometrial invasion, histological type, tumor differentiation and fallopian tube involvement were identified as the most influential predictors in the model.

The nomogram demonstrated apparent strong discriminative ability in our cohort, with a C-index of 0.886 and a bootstrap-corrected C-index of 0.86 (Fig. 5B), suggesting potential utility in identifying patients at high probability of stage migration. The model also showed good calibration (Hosmer–Lemeshow test, *P* < 0.05) and a Brier score of 0.1267.

To apply this nomogram in clinical practice, the clinician obtains the patient's clinicopathological data

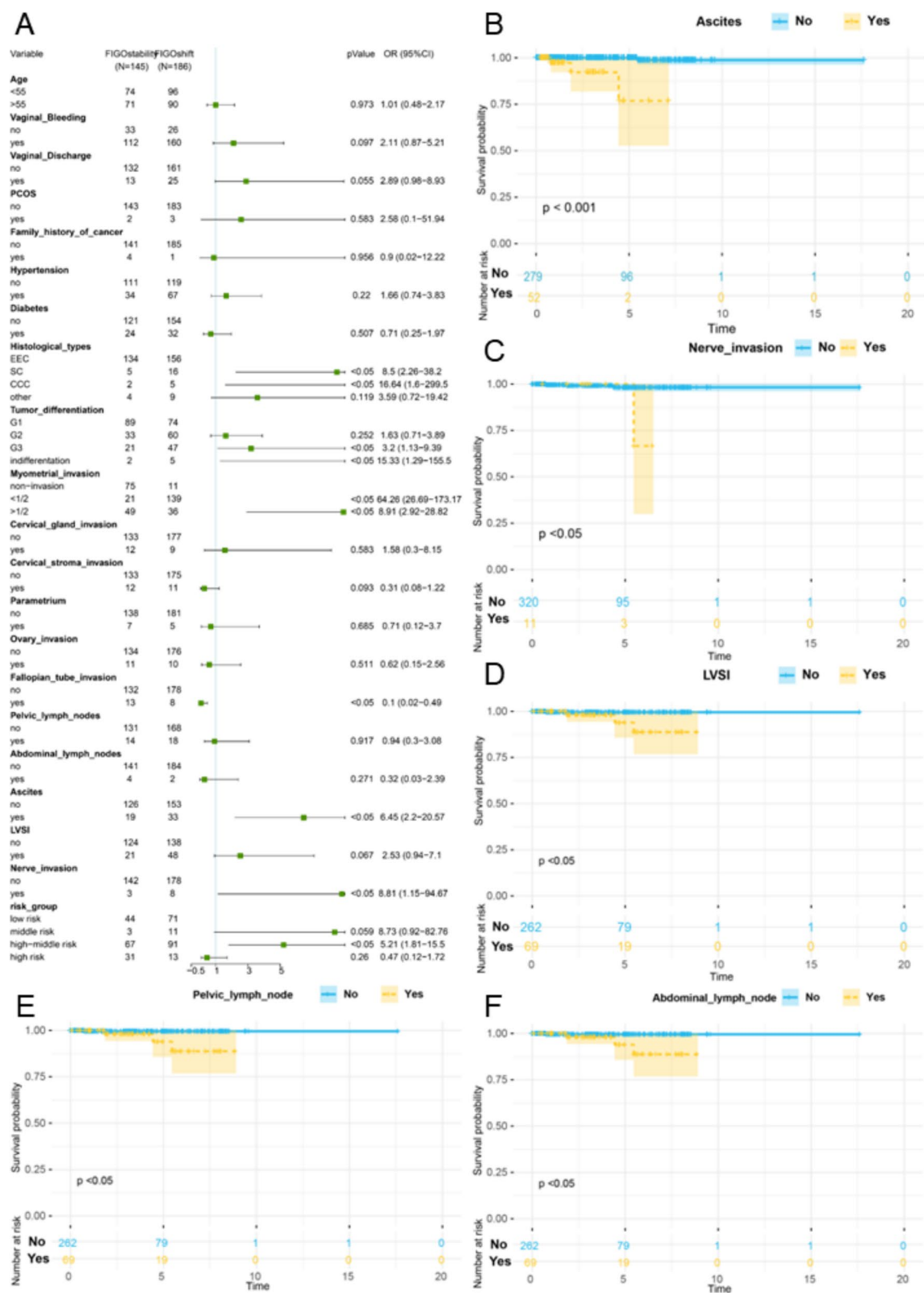


Fig. 4 Determinants influencing the shift between the 2009 and 2023 FIGO staging systems for endometrial cancer. **A** Baseline characteristics and univariate analysis comparing the FIGO-stable group (N= 145) and FIGO-migration group (N= 186). Categorical variables are presented as counts. Forest plot of factors significantly associated with FIGO migration, showing odds ratios (ORs) with 95% confidence intervals (CIs) and corresponding p-values from univariate logistic regression. **B-F** Kaplan–Meier (K-M) survival curves for the entire cohort (N= 331), stratified by the presence or absence of ascites, nerve invasion, LVSI, pelvic lymph node, abdominal lymph node with log-rank p-values indicated

Table 2 Molecular Subtypes and Stage Migration in Endometrial Cancer (N=86)

Molecular Subtype	Prevalence n (%)	Cases with Stage Migration	Stage Migration Rate within Subtype
NSMP	47 (54.7%)	23	48.9%
p53abn	17 (19.8%)	11	64.7%
MMRd	16 (18.6%)	11	68.8%
POLEmut	6 (7.0%)	2	33.3%
All Subtypes	86 (100%)	47	54.7%

This table details the distribution of molecular subtypes and the associated incidence of stage migration in the study cohort (N=86). The four molecular subtypes are as follows: NSMP (no specific molecular profile), p53abn (p53 abnormal), MMRd (mismatch repair deficient), and POLEmut (POLE ultramutated). For each subtype and the overall cohort, the table presents the number of cases (n), the prevalence as a percentage, the absolute number of cases that experienced stage migration, and the corresponding stage migration rate (calculated as the percentage of cases within each subtype that underwent stage migration). The total stage migration rate for the entire cohort was 54.7% (47/86)

Abbreviations: NSMP no specific molecular profile, p53abn p53 abnormal, MMRd mismatch repair deficient, POLEmut POLE mutated

for each variable included in the model. For each variable value, a corresponding score is obtained from the “Points” scale at the top of the nomogram (Fig. 5A). The scores for all variables are summed, and this total score is then projected downward to the “Total Points” axis. Finally, by drawing a line from the total points to the bottom “Probability of Stage Migration” axis, the clinician can read the patient’s individualized probability of being reclassified under the 2023 FIGO system. The detailed clinicopathological profiles of four representative cases MMRd (case110, Fig. 6A), POLEmut (case270, Fig. 6B), p53abn (case166, Fig. 6C), and NSMP (case41, Fig. 6D) subtypes are provided, allowing clinicians to practice the calculation process and verify the model’s predictive accuracy against actual staging outcomes (Fig. 6E, Supplementary Table 2). This tool may aid in preemptive clinical decision-making, such as prioritizing comprehensive molecular testing for patients with a high probability of stage migration.

Discussion

Over the past decade, advancements in pathology and molecular research have revealed limitations in the 2009 FIGO staging system for endometrial cancer (EC). Specifically, it did not incorporate histological subtypes, overlooked lymphovascular space invasion (LVSI), lacked granularity in defining lymph node metastasis size, provided ambiguous staging for endometrioid carcinoma involving both the endometrium and ovaries, and excluded molecular classification [8]. The 2023 FIGO update aimed to address these gaps by enabling more accurate patient stratification, thereby refining clinical decision-making and prognostic guidance, ultimately serving as a more precise predictor of survival.

Nevertheless, the update has attracted critique, encapsulated by titles such as “FIGO 2023 endometrial cancer staging: too much, too soon?” [9] and “Not too soon, but maybe too much” [7]. Primary concerns include: (1) potentially redundant development of risk models, (2) limited applicability and adoption by stakeholders, (3) insufficient supporting evidence for core modifications—for example, the reintroduction of superficial versus absent myometrial invasion assessment lacks citation of recent evidence—and (4) inadequate consultation with the pathology community during development. Notably, committee representation included only a single pathologist, and no gynecological pathologists were involved in the key publications. A collaborative survey by the International Society of Gynecological Pathologists (ISGyP) and the International Gynecological Cancer Society (IGCS), which included 172 pathologists and 135 clinicians, found that after excluding neutral responses, a majority of clinicians (67%) and pathologists (58–65%) supported incorporating histologic type, molecular classification, and LVSI into the staging system, based on a 75% agreement threshold [10]. McCluggage et al. [9] further highlighted the critical issue of interobserver variability in assessing key features such as superficial myometrial invasion, uterine serosal involvement, and LVSI quantification.

In a study of 547 EC patients, the FIGO 2023 system resulted in stage migration for 26.9% of cases, primarily in early-stage disease due to molecular reclassification. The 3-year progression-free survival (PFS) for Stage I was higher under FIGO 2023 (95.3%) than under FIGO 2009 (92.7%), whereas Stage II PFS decreased, particularly in the IIC and IIC2m-p53abn substages [11].

Our findings confirm that the 2023 FIGO system offers superior prognostic stratification compared to its predecessor. This revision represents the latest step in the ongoing evolution of EC classification, contrasting with the relative stability of FIGO systems for other gynecologic cancers like cervical or ovarian carcinoma. The substantial stage migration rate of 56.2% observed in our cohort underscores the system’s successful integration of molecular features with traditional clinicopathological parameters, building upon foundational frameworks such as The Cancer Genome Atlas (TCGA) molecular classification and subsequent clinical algorithms [8]. This continuous refinement reflects a growing consensus that optimal risk stratification requires a combination of histologic, clinical, and molecular parameters, as evidenced in prior studies where ESMO risk emerged as a strong prognostic predictor [12].

LVSI is a well-established independent prognostic factor for poor outcomes in EC [13]. However, consensus is lacking on the definition of “substantial LVSI”—specifically whether it refers to 3–4, ≥5, or more foci in a

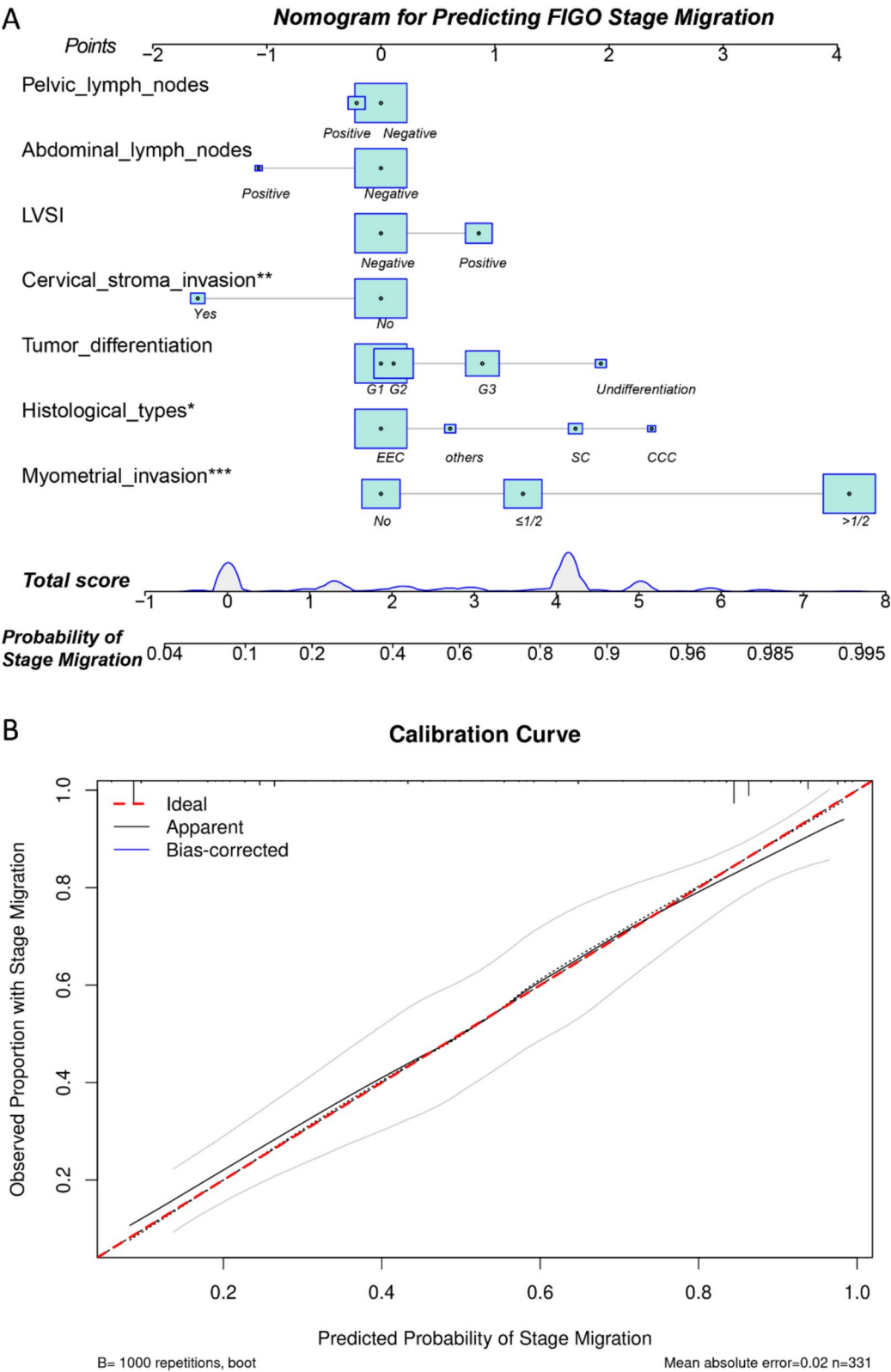


Fig. 5 (See legend on next page.)

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Fig. 5 Development and validation of a predictive model for FIGO stage migration between the 2009 and 2023 staging systems in endometrial cancer. **A** Nomogram for Predicting FIGO Stage Migration (2023 vs. 2009). A nomogram incorporating seven clinicopathological variables to predict the probability of FIGO stage migration from the 2009 to the 2023 staging system. For each variable, the corresponding point value is obtained by drawing a vertical line upward to the “Points” scale. The sum of all points is plotted on the “Total Points” axis, and a vertical line drawn downward to the “Probability of Stage Migration” axis yields the individual predicted probability. EEC, endometrioid adenocarcinoma; SC, serous carcinoma; CCC, clear cell carcinoma; G1–G3, grade 1–3; LVSI, lymphovascular space invasion. **B** Calibration plot of the nomogram, comparing predicted probabilities of stage migration with observed outcomes. The dashed line represents the ideal fit, the solid curve shows the apparent accuracy of the model, and the bias-corrected curve (based on 1000 bootstrap repetitions, $B=1000$) indicates the validated performance after internal validation. The mean absolute error (MAE) was 0.037 in the cohort ($N=331$)

single hematoxylin and eosin (H&E) section [14, 15]. LVSI should be evaluated at the tumor’s leading edge and is independent of myometrial invasion depth. Concerns persist regarding the reliability of current LVSI scoring criteria. For instance, Pifer et al. [13], studying 335 patients with Stage I endometrioid EC, found no significant impact of LVSI extent on 2-year overall survival using a cutoff of ≥ 4 vessels as defined by Peters et al. [16]. In contrast, the 2023 FIGO guidelines adopt a World Health Organization (WHO) cutoff of ≥ 5 vessels, complicating direct comparisons with earlier literature. Another study of 1,555 patients associated both focal and substantial LVSI with increased progression risk, reporting 5-year PFS rates of 90.7% for no invasion, 70.5% for focal LVSI, and a slightly higher risk for substantial LVSI [17]. Yet, substantial LVSI does not uniformly predict poorer survival compared to focal LVSI [18]. A recent meta-analysis of nine studies (4,456 patients) concluded that substantial LVSI is indeed associated with worse prognosis [17].

Endometrial cancer encompasses histologically and molecularly distinct diseases with varied clinical courses [19]. Endometrioid adenocarcinoma (EAC) accounts for approximately 80% of cases, is typically low-grade (G1–G2), and carries a favorable prognosis [15]. High-grade subtypes (G3 EAC, serous carcinoma [SC], clear cell carcinoma [CCC]) are more frequent in advanced or recurrent disease. High-grade EEC is particularly heterogeneous and benefits significantly from molecular classification. The FIGO 2023 system formally integrates molecular data, wherein POLEmut and p53abn subtypes directly influence Stage I/II assignment; without such testing, POLEmut tumors risk inappropriate upstaging.

Under this molecular-informed framework, POLEmut tumors are typically downstaged, while p53abn tumors are upstaged. Consistent with this, ESGO-ESTRO-ESP and ESMO guidelines advise against adjuvant therapy for uterus-confined POLEmut EC but classify p53abn disease with myometrial invasion as high-risk, warranting platinum-based chemotherapy. Schwameis et al. [20] identified Stage I_{am}-POLEmut and II_{C2m}-p53abn as subgroups with excellent (100% 5-year PFS) and poor (56% 5-year PFS) outcomes, respectively—a trend corroborated by Kobayashi et al. [21]. This pattern aligns with the stage shifts observed in our cohort, although limited molecular

data precluded a detailed analysis of these specific sub-stages. It is noteworthy that a minority of POLEmut tumors can metastasize or recur [22]. Although they constitute only ~1% of recurrent/metastatic EC, clinical research on immunotherapy for this subgroup remains scarce [23]. Conversely, approximately 46% of p53abn tumors exhibit homologous recombination deficiency (HRD), suggesting potential sensitivity to poly (ADP-ribose) polymerase (PARP) inhibitors. The upstaging of this group, however, raises legitimate concerns regarding potential overtreatment. Quantitatively, the enhanced discriminatory power of the new system is evidenced by an NRI of 100.76% for Stages I–II, confirming its superior risk stratification capacity. This finding is consistent with reports from other populations showing similar magnitudes of stage migration [24], validating the global relevance of this updated staging approach.

Analysis of reclassification patterns within our cohort identified specific drivers of stage migration. The most frequent change involved the reclassification of 129 patients from Stage IA to IA2, primarily driven by the refined assessment of myometrial invasion. Multivariate analysis further identified non-endometrioid histology, high tumor grade (G3), and deep myometrial invasion as key independent predictors of stage migration [12]. These factors are established proxies for aggressive tumor biology, confirming that the updated system effectively captures biologically meaningful disease characteristics [25].

Molecular integration, available for a subset of 86 patients, provided critical refinement across all subtypes. The consistent downstaging of POLEmut cases (all to stage I_{am}, remaining recurrence-free without adjuvant therapy) illustrates the system’s potential to prevent overtreatment, whereas the upstaging of p53abn cases appropriately flags high-risk disease. These findings corroborate previous studies on the prognostic significance of molecularly defined stages [5, 12, 20, 21, 24, 26] while also highlighting implementation challenges. These include the risk of overtreatment in upstaged p53abn cases and the current lack of standardized testing methodologies. This underscores the urgent need for refined, molecularly informed adjuvant therapy protocols to ensure treatment intensification is reserved for patients most likely to derive genuine benefit [22, 27].

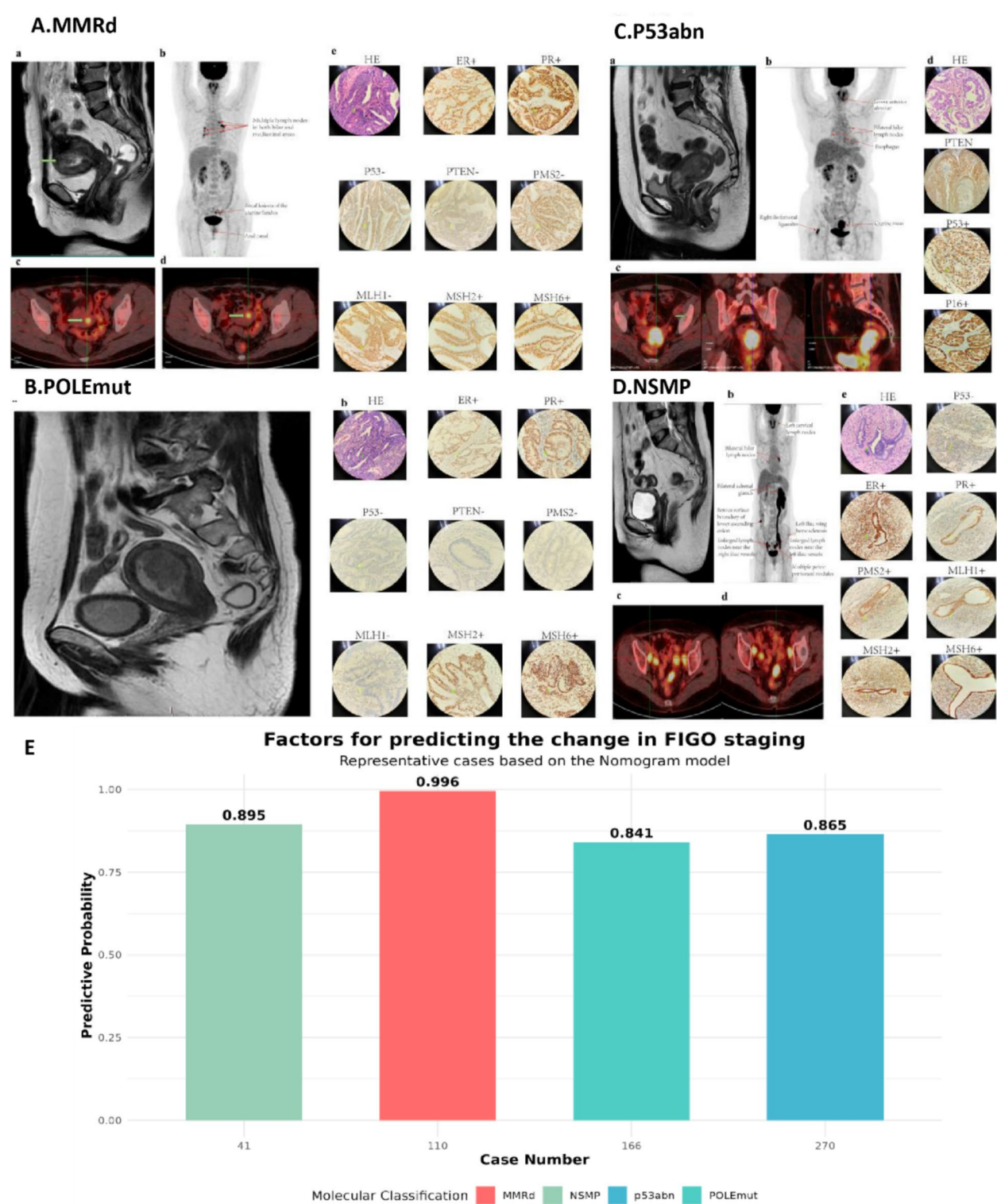


Fig. 6 Representative multi-modal patient characteristics – including pathological, imaging, and molecular features – for the four molecular subtypes of endometrial cancer according to the 2023 FIGO staging system. **A** Mismatch repair deficient (MMRd): (a) Magnetic resonance imaging (MRI); (b–d) Positron emission tomography–computed tomography (PET–CT), with green arrows indicating lesions; (e) Immunohistochemistry (IHC). **B** POLE exonuclease domain mutated (POLEmut): (a) MRI; (b) IHC. **C** p53 abnormal (p53abn): (a) MRI; (b–c) PET–CT, with green arrow indicating a lesion; (d) IHC. **D** No specific molecular profile (NSMP): (a) MRI; (b–d) PET–CT; (e) IHC. **E** The bar graph below illustrates the predicted probability of FIGO stage migration, as calculated by the nomogram, for one representative case from each molecular subtype

Our study contributes to the growing literature on the implementation of the 2023 FIGO system by providing data from a Chinese clinical setting, thereby complementing reports from other populations [20, 24, 26]. Furthermore, the developed nomogram (C-index: 0.886) addresses an unmet clinical need by offering a practical tool for estimating the probability of stage migration, which may help optimize the prioritization of molecular testing and resource allocation in routine practice [11].

Limitation

Several study limitations warrant consideration. First, the molecularly characterized subgroup was modest in size (*n* = 86), which constrained robust analysis of rare molecular subtypes. Second, the single-center, retrospective design may limit the generalizability of our findings. The potential for geographic, ethnic, or institutional variations in pathological assessment and patient management suggests that external validation in diverse, multicenter cohorts is essential. Third, regarding the predictive model, although we employed Firth's penalized regression and internal validation via bootstrapping to mitigate overfitting, the ratio of predictors to outcome events necessitates caution, and residual overfitting remains a possibility. Therefore, our findings, including the nomogram, should be considered hypothesis-generating. Finally, the clinical implications drawn from our data require prospective validation before they can be recommended for integration into standard clinical decision-making pathways. Future prospective studies with larger, independent cohorts are warranted to externally validate the nomogram's predictive performance and to further refine its clinical applicability.

Conclusion

In conclusion, the 2023 FIGO system represents a significant advancement in endometrial cancer classification, enabling more biologically grounded and personalized management. Our validation in a Chinese cohort confirms its improved prognostic stratification and identifies key drivers of stage migration, while highlighting both the promises and challenges of molecular integration in routine clinical practice. Prospective validation of the developed nomogram in multicenter settings will be essential to confirm its clinical utility and support its adoption in guiding personalized treatment decisions.

Abbreviations

EC	Endometrial cancer
FIGO	International Federation of Gynecology and Obstetrics
TCGA-UCEC	The Cancer Genome Atlas- Uterine Corpus Endometrial Carcinoma
TNM	Tumor, node, metastasis
AJCC	American Joint Committee on Cancer
WHO	World Health Organization

ISGyP	The International Society of Gynecological Pathologists
LVSI	Lymphovascular space invasion
POLEmut	POLE mutation
MMRd	MMR deficiency
P53abn	P53 abnormality
NSMP	Non-specific molecular profile
PFS	Progression-free survival
OS	Overall survival
ProMisE	The Proactive Molecular Risk Classifier for Endometrial Cancer
MSI-H	Microsatellite Unstable Hypermutated
EAC	Endometrioid adenocarcinoma
SC	Serous carcinoma
CCC	Clear cell carcinoma
NRI	Net reclassification improvement
HRD	Homologous recombination deficiency

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12957-026-04306-6>.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3: Supplementary Table 1. Univariate analysis of clinicopathological variables associated with FIGO stage migration (FIGOshift) versus stage stability (FIGOstability) between the 2009 and 2023 International Federation of Gynecology and Obstetrics (FIGO) staging systems for endometrial cancer. Analysis was performed using Firth logistic regression to address potential separation issues. Data are presented as counts for categorical variables, with odds ratios (ORs), 95% confidence intervals (CIs), and corresponding p-values. Variable categories include patient demographics, symptomatology, comorbidities, histology (Endometrioid Adenocarcinoma [EEC], Serous Carcinoma [SC], Clear Cell Carcinoma [CCC], other), tumor grade (G1, G2, G3, indifferentiation), patterns of local invasion (myometrial, cervical gland, cervical stroma, parametrium, ovary, fallopian tube, lymphovascular space invasion [LVSI], nerve), lymph node status (pelvic, abdominal), presence of ascites, and risk groups based on integrated staging.

Supplementary Material 4: Supplementary Table 2. Clinicopathological characteristics and follow-up data of the endometrial carcinoma cohort, stratified by molecular classification. The table includes patient demographics, symptomatology, comorbidities, surgical procedure type (Open Surgery [OS] or Laparoendoscopic Single-Site Surgery [LESS]), detailed pathological features, 2023 International Federation of Gynecology and Obstetrics (FIGO) stage, 2009 FIGO stage, FIGO stage migration status (Upgrade, Stable), and oncological outcomes (vital status, relapse). Molecular classifications are: Mismatch Repair Deficient (MMRd), POLE exonuclease domain mutated (POLEmut), p53 abnormal (p53 abn), and No Specific Molecular Profile (NSMP). Pathological characteristics encompass tumor diameter, histological type (predominantly Endometrioid Adenocarcinoma [EEC]), tumor differentiation grade (G1-G3), myometrial invasion depth, patterns of local invasion (cervical gland, cervical stroma, parametrium, ovary, fallopian tube, lymphovascular space invasion [LVSI], nerve), lymph node status (pelvic, abdominal), and presence of ascites.

Supplementary Material 5: Supplementary Table 3. Individual patient predictions of FIGO stage migration using the developed nomogram model. The table lists the case identifier, molecular classification (where available; including No Specific Molecular Profile [NSMP], POLE exonuclease domain mutated [POLEmut], Mismatch Repair Deficient [MMRd], and p53 abnormal [p53 abn]), the assigned 2023 and 2009 International Federation of Gynecology and Obstetrics (FIGO) stages, the observed FIGO change category (upgrade or stable), the total points calculated by the nomogram, and the corresponding predicted probability of FIGO stage upgrade. This detailed prediction data demonstrates the application of the model at the individual patient level.

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Authors' contributions

YY, MML and JYX conceived and designed the study. LC, FC and AYT were involved in data interpretation and manuscript writing. FC and LJH prepared Figs. 1, 2, 3, 4, 5 and 6. YYZ and YL recruited patients and collected clinical data. All authors reviewed the manuscript and approved the final version.

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Data availability

The original contributions presented in the study are included in the article. Further information is available from the corresponding author upon request.

Declarations

Ethics approval and consent to participate

This study was approved by the Institutional Review Board of Shanghai General Hospital (Approval No. 2023SQ304) and the Chinese Clinical Trial Registry (Approval No. ChiCTR2500104752). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Written informed consent for publication was obtained from the patient (or from the parent/legal guardian/next of kin in the case of a minor). A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare no competing interests.

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