Am J Transl Res 2026;18(1):336-347
www.ajtr.org /ISSN:1943-8141/AJTR0169049

Original Article

Hormone receptor status score is negatively correlated with adverse pathological features and serves as an independent prognostic factor in endometrial carcinoma

Qingqing Hu, Ling Xu, Zheng Fu, Yuping Xiao

Department of Reproductive Medicine, The Affiliated Hospital of Southwest Medical University, Luzhou 646000, Sichuan, China

Received September 27, 2025; Accepted December 12, 2025; Epub January 15, 2026; Published January 30, 2026

Abstract: Objective: To investigate the effect of estrogen and progesterone receptor status score on the prognosis of endometrial cancer (EC) patients. Methods: We chose 187 endometrial cancer patients hospitalized in The Affiliated Hospital of Southwest Medical University between March 2021 and March 2023. The histologic score (H score) and the Allred score were used to evaluate and analyze their correlation with clinical pathological parameters and prognosis. Results: The hormone receptor status score was negatively correlated with lymph node metastasis (LNMs), differentiation degree, depth of invasion (DOI), and the clinical stage ($P<0.05$). The hormone receptor status score was significantly higher in the survival group compared to that in the dead group ($P<0.05$). According to multivariate logistic regression analysis, the hormone receptor status score was identified as an independent protective factor for endometrial cancer patient prognosis ($P<0.05$). Conclusion: The hormone receptor status score has a definite correlation with LNMs, DOI, differentiation degree, and clinical stage in EC patients, and is related to prognosis.

Keywords: Estrogen, progesterone, receptor status score, endometrial carcinoma, prognosis

Introduction

Endometrial cancer (EC), one of the most common gynecological cancers, accounts for over 90% of cancer cases in perimenopausal women [1]. Patients often present with abnormal uterine bleeding, which frequently aids in early detection [2]. The primary treatment involves surgery, usually supplemented by radiation or chemotherapy based on the disease stage.

Most endometrial cancers are endometrioid carcinomas, classified as Type I, caused by estrogen stimulation and associated with risk factors such as anovulation, infertility, unopposed estrogen therapy, and tamoxifen use [3]. Additionally, Type I EC is linked to other risk factors like diabetes, obesity, and hypertension [4]. In contrast, Type II cancers are not associated with excess estrogen and typically occur in older individuals. Approximately 10% of EC cases are Type II cancers, including serous and clear cell carcinomas [5]. Despite the increasing incidence of EC, multimodal treatments have improved survival rates for EC patients. When classifying molecular subgroups related to prognosis and considering treatment options, hormone receptor status becomes particularly important [6]. Immunohistochemistry is commonly used to assess protein expression levels and determine the need for anti-hormonal drugs. Several scoring systems, such as the Allred score and histologic score (H score), have been employed to measure hormone receptor status [7]. Based on the sum of percentage score (PS) and intensity score (IS), Allred and Fast scores are semiquantitative [8]. The Allred scoring system, a well-known method, has been clinically validated as successful. The optimal cutoff value for disease-free survival and overall survival (OS) is an Allred score greater than 2, equivalent to weak staining in more than 1% of tumor cells [9]. The H score is calculated by multiplying

https://doi.org/10.62347/YYJY9070

the fraction of tumor cells by the total staining intensity [10]. However, comprehensive comparative analyses of integrated scoring systems remain insufficient in most studies.

The innovation of this study lies in the simultaneous application and comparison of two immunohistochemical scoring systems, the H-score and Allred score, to evaluate the status of estrogen receptor (ER) and progesterone receptor (PR) in a well-defined cohort of endometrial cancer patients. We further analyzed the correlation between these receptor scores and various clinicopathological parameters, including lymph node metastasis, differentiation, myometrial invasion, and clinical staging. More importantly, this study explored the independent prognostic value of hormone receptor scores in the context of overall survival, providing potential evidence for refining risk stratification and personalized adjuvant therapeutic strategies.

This study aims to investigate the impact of ER and PR expression levels, measured by H score and Allred score, on the prognosis of EC patients. Our findings may help improve risk stratification for endometrial cancer patients and support personalized treatment strategies.

Data and methods

Case selection

We chose 187 endometrial cancer patients hospitalized in The Affiliated Hospital of Southwest Medical University between March 2021 and March 2023. The inclusion criteria were: (1) Patients who met the diagnostic criteria for EC [11]; (2) The clinical data of the patients were complete. The exclusion criteria were: (1) Patients with gynecological inflammation; (2) Patients with other combined malignant tumors; (3) Pregnant patients; (4) Follow-up dropouts.

This study was a retrospective analysis that utilized only de-identified patient data. All data were de-identified prior to analysis to ensure that individual patients could not be traced, thereby protecting the patient privacy. Since this study did not influence or intervene in patient treatment and all data were anonymized, it was approved by The Affiliated Hospital of Southwest Medical University's Institutional Review Board to waive the requirement for informed consent. We strictly adhered to relevant ethical guidelines and data protection regulations to ensure that the research process met the highest ethical standards and protected patient rights. All research activities were conducted under the supervision of The Affiliated Hospital of Southwest Medical University's IRB to ensure the legality and ethical integrity of the study.

Data collection

Immunohistochemical staining: All tumor tissue samples included in the analysis were sourced from archived formalin-fixed, paraffin-embedded (FFPE) tissue blocks of patients who underwent surgical treatment and were diagnosed with endometrial cancer at our hospital. Fresh tissue samples obtained from patients during surgery were immediately fixed in neutral-buffered formalin and embedded in paraffin according to standard operating procedures after completing the gross examination and sampling required for routine pathological diagnosis. These prepared FFPE tissue blocks, as part of the diagnostic archive, are stored long-term by the hospital's pathology department for potential future clinical, diagnostic, or research use.

Reagents: Mouse anti-human ER monoclonal antibody (1D5) and progesterone receptor polyclonal antibody were purchased from Beijing Zhong Shan - Golden Bridge Biological Technology Co., Ltd. P53 monoclonal antibody (DO-7), pika general secondary antibody and diaminobenzidine (DAB) chromogenic kit were purchased from Dako Company. Tissue samples that had been formalin-fixed and paraffin-embedded were further cut into 4 μm sections with a microtome and placed on slides. Tissue section-containing slides were dewaxed at 75°C, and cell conditioning with ethylenediaminetetraacetic acid (EDTA) solution was carried out at 100°C for 4 min. The incubation with the primary antibody was for 20 minutes. The slides were then stained with the automatic Ventana Benchmark Ultra system. (1) Allred score: Two knowledgeable pathologists evaluated the stained slides and assigned the ER and PR Allred ratings. Allred scores were calculated by adding the PS (range 0 to 5) and the IS (range 0 to 3). (2) The H score: A pathologist noted the whole invasive tumor region and inspected all ER and PR immunostaining slides.

Table 1. Hormone receptor status scores

Index	Average value/ Proportion
Age	58.43±8.22
BMI	23.56±2.38
Hypertension	39 (20.86%)
Diabetes Mellitus	13 (6.95%)
Disease Duration (months)	12.59±1.89
ER H score	251.65±35.98
PR H score	198.58±31.98
ER Allred score	7.47±2.87
PR Allred score	6.27±1.98

BMI: body mass index; ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

The hormone receptor immunohistochemistry staining findings were quantified using a QuantCenter image analyzer, and translated to H scores. The H-score scoring system: H-score = positive intensity × the number of positive cells in 100 cells. The four categories included: negative (0 points), weakly positive (1 point), moderately positive (2 points), and strongly positive (3 points) for positive intensity. A multiplication result of ≤50 was considered as -; 51 to 100 was considered as +; 101 to 200 was considered as ++, and 201 to 300 was considered as +++.

Data collection and follow-up: Clinical data of patients such as the age at diagnosis, lymph node metastasis (LNMs), and tumor stage were collected. The follow-up was done for 2 years by telephone and outpatient or inpatient reexamination to understand the survival of patients. The follow-up time was up to March 2022. Based on the follow-up results, patients were divided into survival (n=125) and dead (n=62) groups.

Statistical methods

The experimental data were examined using SPSS 21.0. The measurement data, which followed a normal distribution, were represented by X±SD, and an independent sample t-test was used to compare the two groups. The chi-square test was used to compare the two groups from the count data, which were reported as the number of instances or rate. Correlation analysis was performed using the Spearman correlation technique. Multivariate analysis was conducted using an MLR model, and factors having statistical significance in univariate analysis were included. Statistical significance was at P<0.05.

Results

Hormone receptor status scores

Table 1 presents the average values for hormone receptor status scores, including patient age and relevant scores for ER and PR. The average age of the patients was 58.43±8.22 years, with a mean Body Mass Index (BMI) of 23.56±2.38 kg/m^2. Among the cohort, hypertension was present in 39 cases (20.86%), while diabetes mellitus was observed in 13 cases (6.95%). The mean disease duration was 12.59±1.89 months. The mean ER H score was 251.65±35.98, reflecting the intensity and distribution of estrogen receptor expression in tumor tissues. The mean PR H score was 198.58±31.98, indicating the level of progesterone receptor expression. Additionally, the ER Allred score averaged 7.47±2.87, while the PR Allred score averaged 6.27±1.98, providing a semi-quantitative assessment of receptor positivity that combines the proportion of positive cells and staining intensity.

Relationship between the hormone receptor status score and clinical characteristics of patients with endometrial cancer

For ER H score, patients in Stage III-IV had significantly lower scores compared to those in Stage I-II (P<0.001), indicating a decrease in estrogen receptor expression with advancing disease stage (**Figure 1**). Similarly, PR H scores were also significantly lower in Stage III-IV patients compared to Stage I-II patients (P= 0.002), suggesting a reduction in progesterone receptor expression as the disease progresses. Regarding the ER Allred score, there was a significant difference between the two groups (P=0.023), with higher scores noted in Stage I-II patients. This trend continued for the PR Allred score, which also showed significantly higher values in Stage I-II patients compared to Stage III-IV patients (P=0.010).

For ER H score, patients with lymph node metastasis had significantly lower scores compared to those without lymph node metastasis (P=0.001), indicating reduced estrogen receptor expression in patients with LNM (**Table 2**). Similarly, PR H scores were significantly lower

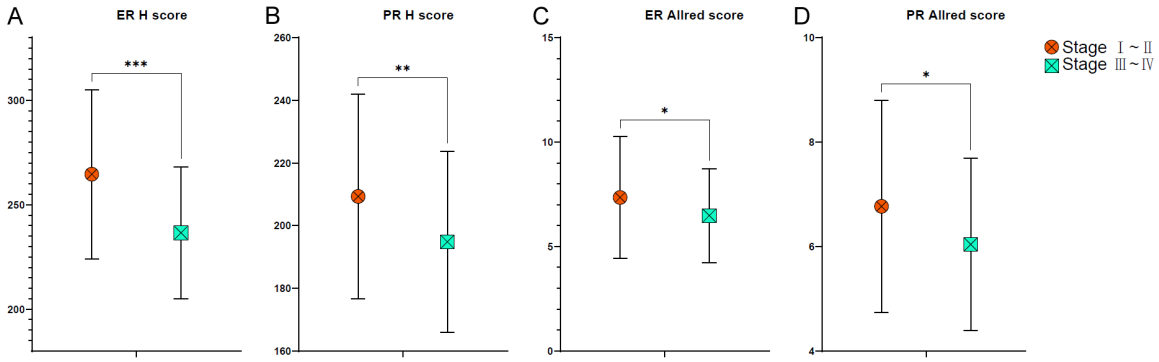

Figure 1. The relationship between the hormone receptor status score and clinical stages of patients with endometrial cancer. A: ER H score; B: PR H score; C: ER Allred score; D: PR Allred score. *: P<0.05; **: P<0.01; ***: P<0.001. ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

Table 2. The relationship between the hormone receptor status score and lymph node metastasis of patients with endometrial cancer

Index	Lymph node metastasis (n=17)	No lymph node metastasis (n=170)	t	P
ER H score	234.22±30.19	270.43±44.21	3.297	0.001
PR H score	188.94±27.05	213.76±32.98	3.001	0.003
ER Allred score	5.98±2.44	7.50±3.01	2.015	0.045
PR Allred score	5.36±1.78	6.73±2.12	2.559	0.011

ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

in patients with lymph node metastasis than in those without (P=0.003), suggesting decreased progesterone receptor expression in the presence of LNM. Regarding the ER Allred score, there was a significant difference between the two groups (P=0.045), with higher scores noted in patients without lymph node metastasis. This trend continued for the PR Allred score, which also showed significantly higher values in patients without lymph node metastasis compared to those with lymph node metastasis (P=0.011).

When comparing hormone receptor status scores between moderately differentiated and poorly differentiated (MDAPD) and well-differentiated groups, significant differences were observed across all evaluated parameters (**Figure 2**). The ER H score was significantly lower in the MDAPD group compared to the well-differentiated group (P=0.001), indicating higher estrogen receptor expression in well-differentiated cases. Similarly, the PR H score was also significantly lower in the MDAPD group than that in the well-differentiated group (P=0.002), suggesting greater progesterone receptor levels in better differentiated tumors. Additionally, both the ER Allred score (P=0.016) and PR Allred score (P<0.001) were significantly lower in the MDAPD group, reinforcing the association between higher hormone receptor expression and better tumor differentiation. These findings highlight the potential role of hormone receptor status as an indicator of tumor differentiation grade.

For ER H score, patients with invasion depth less than half the muscle layer had significantly higher scores compared to those with invasion depth greater than or equal to half the muscle layer (P=0.014), indicating higher estrogen receptor expression in less invasive tumors (**Table 3**). Similarly, PR H scores were significantly higher in patients with invasion depth less than half the muscle layer compared to those with deeper invasion (P=0.001), suggesting higher progesterone receptor expression in less invasive tumors. Regarding the ER Allred score, there was a significant difference between the two groups (P=0.008), with higher scores noted in patients with less deep invasion. This trend was also observed for the PR Allred score, which showed a highly significant difference (P<0.001) with substantially higher values in patients with less deep invasion compared to those with deeper invasion.

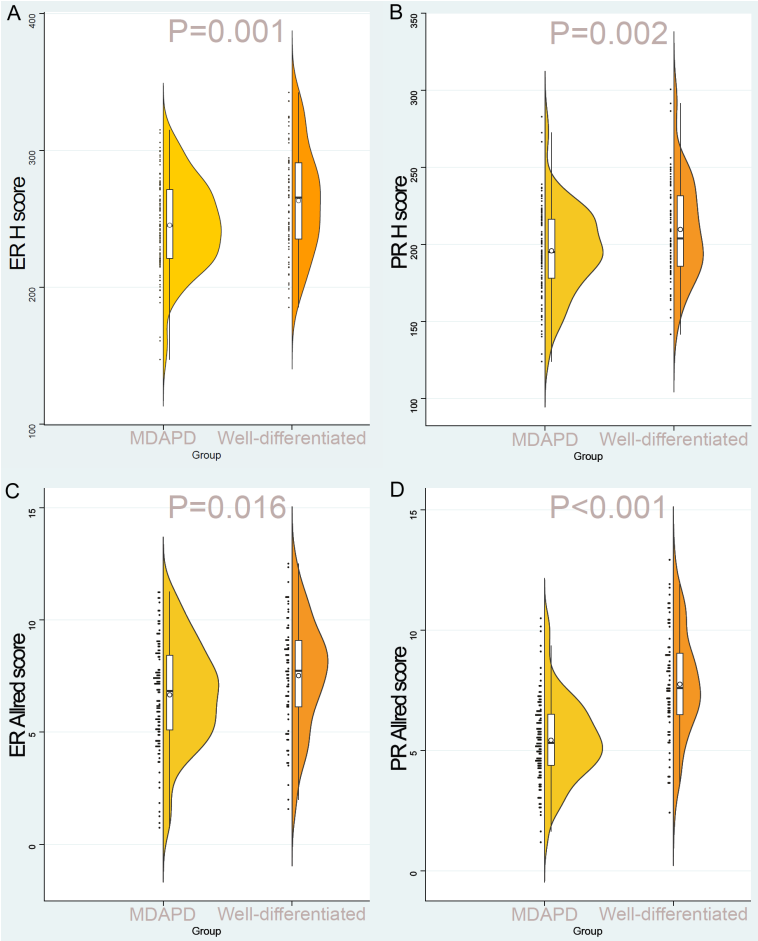

Figure 2. The relationship between the hormone receptor status score and differentiated degree of patients with endometrial cancer. MDAPD: Moderately differentiated and poorly differentiated; A: ER H score; B: PR H score; C: ER Allred score; D: PR Allred score.

Table 3. The relationship between the hormone receptor status score and depth of invasion of patients with endometrial cancer

Index	<1/2 muscle layer (n=69)	≥1/2 muscle layer (n=118)	t	P
ER H score	259.41±38.01	246.09±33.95	2.476	0.014
PR H score	206.85±26.16	194.91±22.24	3.318	0.001
ER Allred score	7.71±3.37	6.47±2.32	2.702	0.008
PR Allred score	6.99±2.21	5.88±1.68	3.603	<0.001

ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

Correlation analysis of the hormone receptor status score and clinical characteristics of patients with endometrial cancer

In the correlation analysis between hormone receptor status scores and clinical characteristics of EC patients, several significant relationships were observed (**Table 4**). For lymph node metastasis, both ER H score and PR H score showed a significant negative correlation (P<0.001 and P=0.002 respectively), indicating lower hormone receptor expression in patients with lymph node metastasis. Similarly, ER Allred score and PR Allred score also correlated negatively with lymph node metastasis (P=0.027 and P=0.012 respectively). Regarding differentiation degree, significant negative correlations were found between differentiation degree and both ER H score (P<0.001) and PR H score (P=0.001), suggesting higher hormone receptor expression in well-differentiated tumors. For ER Allred score and PR Allred score, significant negative correlations were also observed (P=0.043 and P<0.001 respectively), with the PR Allred score showing a particularly strong correlation. The differentiation grade (1 = well-differentiated, 2 = moderately differentiated, 3 = poorly differentiated) exhibited significant negative correlations with both ER H-score and PR H-score (P<0.001 and P=0.006, respectively), indicating lower hormone receptor expression in poorly differentiated tumors. ER Allred score and PR Allred score also showed significant negative correlations with clinical stage (P=0.015 and P=0.005 respectively). Depth of invasion demonstrated significant negative correlations with both ER H score and PR H score (P=0.024 and P=0.003 respectively), suggesting lower hormone receptor expression in deeper invasions. For ER Allred score and PR Allred score, significant negative correlations were noted (both P<0.001), indicating lower hormone receptor expression scores in cases of deeper tumor invasion.

Table 4. Correlation analysis between the hormone receptor status score and clinical characteristics of endometrial cancer patients

Clinical characteristics	ER H score		PR H score		ER Allred score		PR Allred score	
	rho	P	rho	P	rho	P	rho	P
Lymph node metastasis	-0.244	<0.001	-0.222	0.002	-0.161	0.027	-0.184	0.012
Differentiation degree	-0.242	<0.001	-0.239	0.001	-0.148	0.043	-0.488	<0.001
Clinical stage	-0.364	<0.001	-0.200	0.006	-0.177	0.015	-0.204	0.005
Depth of invasion	-0.165	0.024	-0.214	0.003	-0.194	0.008	-0.240	<0.001

Table 5. Comparison of hormone receptor status scores between the survival group and the dead group

Index	Dead group (n=62)	Survival group (n=125)	t	P
ER H score	249.96±27.07	263.14±26.32	3.194	0.002
PR H score	195.02±28.32	208.53±25.85	3.259	0.001
ER Allred score	6.34±2.13	7.59±2.37	3.503	<0.001
PR Allred score	5.91±1.45	6.97±1.83	4.274	<0.001

ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

Table 6. Multivariate logistic analysis of factors affecting survival prognosis in endometrial cancer patients

Index	Coefficient	Std Error	Wald Stat	P	OR (95% CI)
ER H score	0.019	0.006	3.038	0.002	1.019 (1.007, 1.032)
PR H score	0.019	0.006	3.107	0.002	1.019 (1.007, 1.031)
ER Allred score	0.248	0.075	3.310	<0.001	1.282 (1.112, 1.495)
PR Allred score	0.373	0.102	3.657	<0.001	1.453 (1.199, 1.792)

ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

Comparison of the hormone receptor status scores between the survival group and the dead group

Significant differences were observed in hormone receptor status scores when comparing the dead group and the survival group (**Table 5**). The ER H score was significantly higher in the survival group compared to the dead group (P=0.002), indicating that higher estrogen receptor expression is associated with better survival outcomes. Similarly, the PR H score was also significantly elevated in the survival group relative to the dead group (P=0.001), suggesting a positive correlation between progesterone receptor levels and survival. Furthermore, both the ER Allred score (P<0.001) and PR Allred score (P<0.001) were notably higher in the survival group, reinforcing the link between increased hormone receptor expression and improved survival outcomes. These findings underscore the potential prognostic value of hormone receptor status in predicting patient survival.

Multivariate logistic analysis and receiver operating characteristic analysis of factors affecting the prognosis of patients with endometrial cancer

In the multivariate logistic analysis of factors affecting survival prognosis in EC patients, several significant associations were identified (**Table 6**). Higher ER H score was associated with better survival prognosis (P=0.002, OR 1.019), indicating that it serves as a protective factor. Similarly, PR H score also showed a protective effect (P=0.003, OR 1.019). Furthermore, both ER Allred score (P=0.038, OR 1.158) and PR Allred score (P=0.001, OR 1.358) were significant predictors of survival, with higher scores correlating with improved survival outcomes, thus acting as protective factors. These findings suggest that increased hormone receptor expression levels are linked to better prognoses in EC patients, emphasizing their potential role as favorable indicators in patient survival.

Evaluating hormone receptor status as predictors of survival through receiver operating characteristic (ROC) analysis revealed that the PR Allred score exhibited the highest area under the curve (AUC) value (0.756), with a sensitivity of 0.664 and specificity of 0.758, indicating its superior discriminatory power for predicting survival outcomes (**Figure 3**). The PR H score also showed strong performance, achieving an

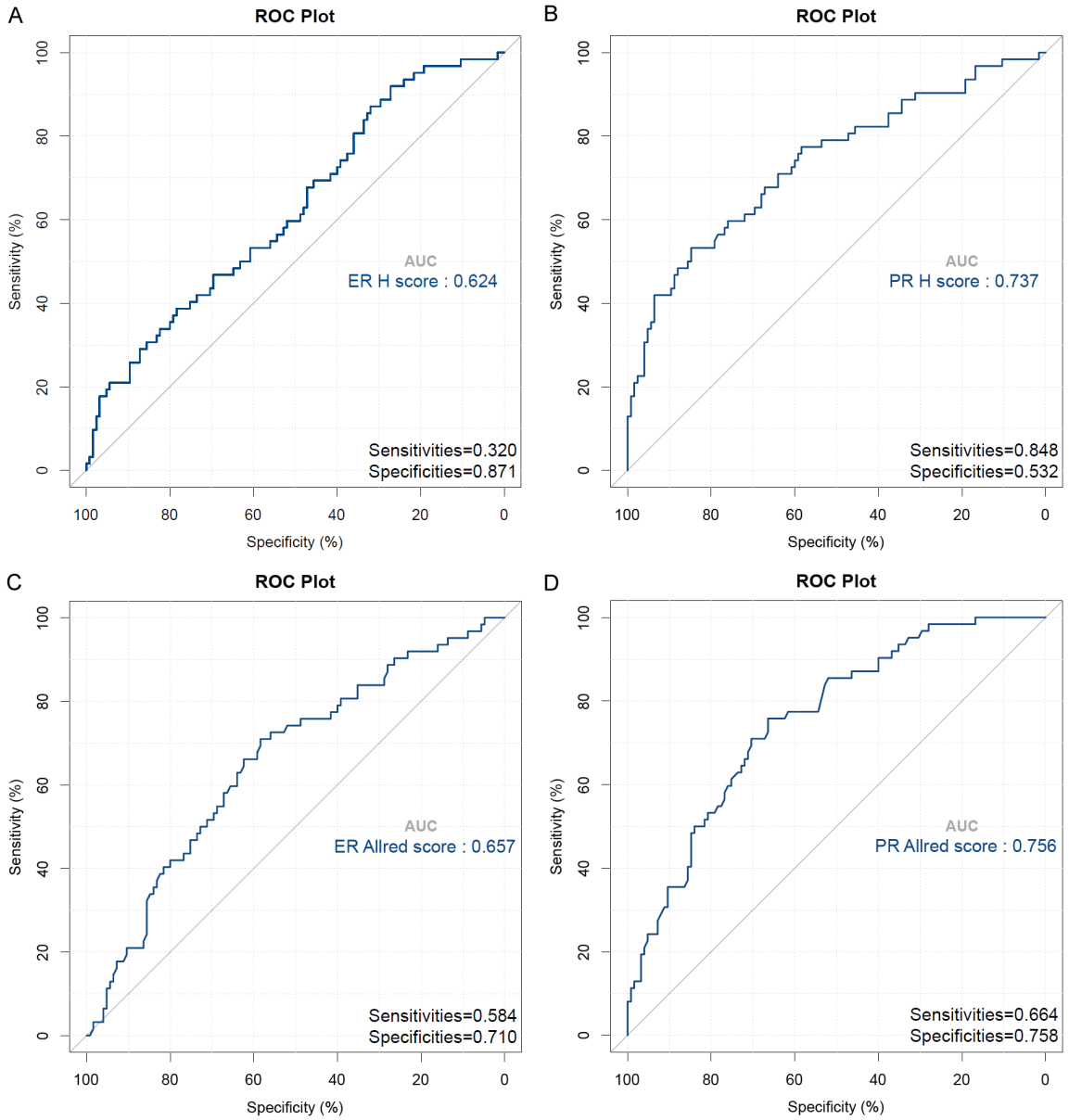

Figure 3. Evaluation of hormone receptor status as predictors of survival using receiver operating characteristic analysis. A: ER H score; B: PR H score; C: ER Allred score; D: PR Allred score. ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

AUC of 0.737, along with a sensitivity of 0.848 and specificity of 0.532, suggesting that it serves as another robust predictor in this context. The ER Allred score had an AUC of 0.657, with a sensitivity of 0.584 and specificity of 0.710, indicating moderate predictive capacity. In contrast, the ER H score exhibited the lowest AUC (0.624) among the evaluated parameters, with a sensitivity of 0.320 and specificity of 0.871, suggesting limited utility in distinguishing between survival outcomes. These results highlight the potential of PR-related scores as more effective indicators for survival prognosis in this patient cohort.

Within the risk threshold of 0-0.7, especially in the moderate-to-low risk range of 0.2-0.6, the net benefit of the four scoring models, ER H-score, PR H-score, ER Allred score, and PR Allred score was significantly higher than that of the two baseline strategies of “treat all” and “treat none” (**Figure 4**). This indicates that

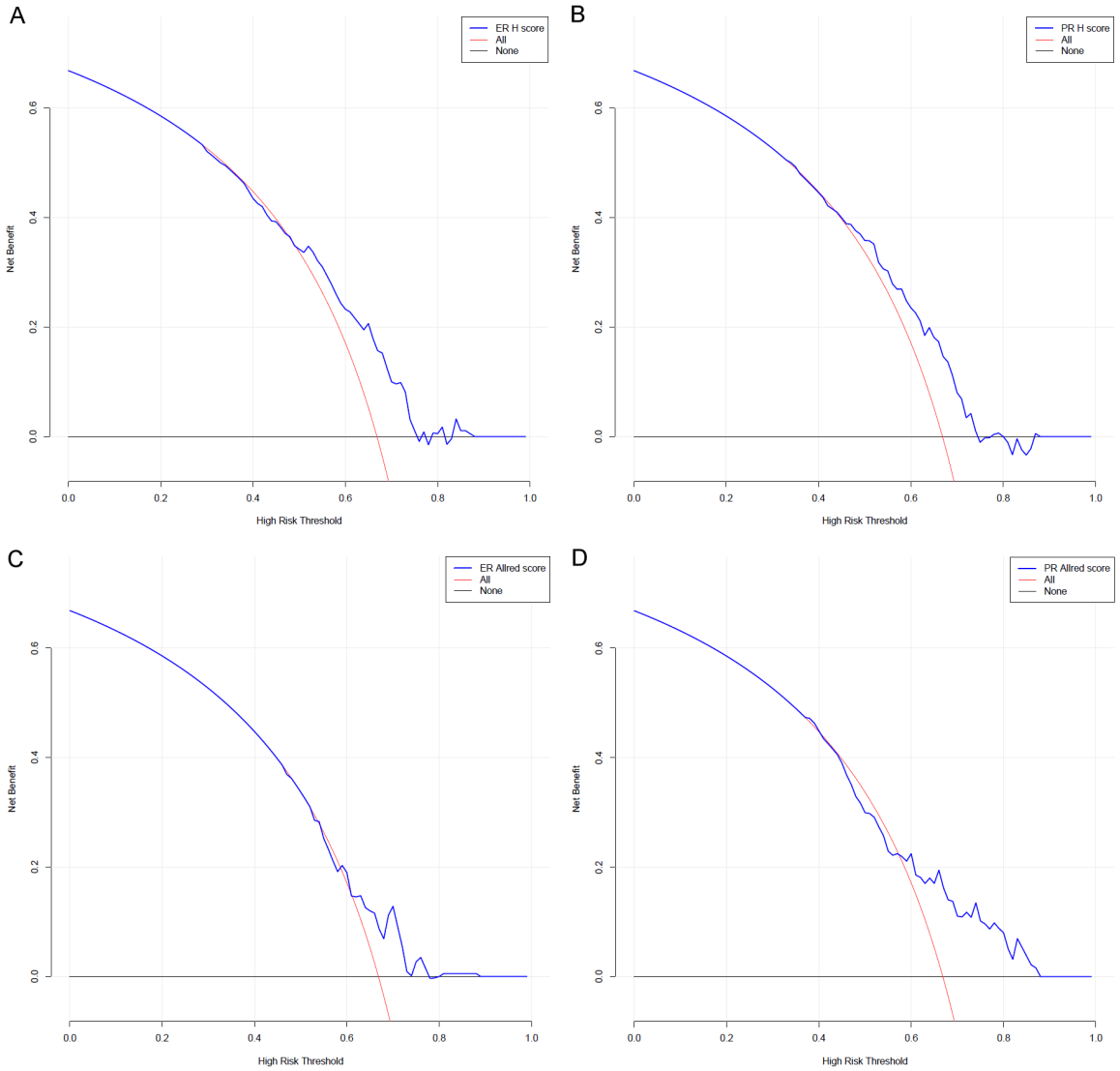

Figure 4. Decision curve analysis to evaluate hormone receptor status as a prognostic factor for survival. A: ER H score; B: PR H score; C: ER Allred score; D: PR Allred score. ER: estrogen receptor; PR: progesterone receptor; H score: histologic score.

these scoring models can more accurately identify high-risk patients who require intervention, thereby enhancing the effectiveness of personalized treatment decisions and avoiding both overtreatment and undertreatment.

Discussion

This study applied both the H-score and Allred scoring systems to quantify the expression of ER and PR in endometrial cancer. It explored the relationship between these hormone receptor scores and patients' clinicopathological features and prognosis. We found that hormone receptor scores were markedly negatively correlated with lymph node metastasis, tumor differentiation, myometrial invasion depth, and clinical stage. In multivariate analysis, these scores were confirmed as independent protective factors for patient prognosis. These results reinforced the critical role of hormone receptors in the biological behavior of endometrial cancer and highlighted the importance of incorporating standardized scoring systems into routine pathological assessments. Doing so could enhance the precision of risk stratification and guide personalized treatment decisions, showing significant clinical value.

First, this study found that hormone receptor scores were negatively correlated with clinical staging. Patients with advanced stages (III-IV)

showed markedly lower ER and PR expression levels compared to those in early stages (I-II). This finding aligned well with the classical understanding of endometrial cancer biology, where tumors tend to lose their hormone dependency as they progress and dedifferentiate, leading to reduced ER and PR expression [12]. Previous studies also reported similar trends, indicating that the loss of hormone receptors marks increased aggressiveness of the disease [13]. For instance, low or absent ER/PR expression is commonly observed in aggressive subtypes like serous carcinoma or high-grade endometrioid carcinoma [14, 15]. Both scoring systems used in this study confirmed this pattern, demonstrating the robustness of the findings regardless of the scoring method. The underlying biological mechanisms likely involve epigenetic changes, abnormal activation of signaling pathways such as PI3K/AKT/mTOR, and epithelial-mesenchymal transition (EMT) during tumor progression [16, 17]. These molecular events collectively contribute to the inactivation of hormone receptor pathways.

In terms of lymph node metastasis, this study showed that patients with lymph node involvement had markedly lower hormone receptor scores. This finding closely correlated with the tumor's metastatic potential [18, 19]. Estrogen promotes cell proliferation and survival through ER signaling, while progesterone typically induces differentiation and inhibits proliferation via PR signaling [20]. When PR expression is lost, the proliferative effects of estrogen may proceed unchecked, increasing the invasiveness and migration capacity of tumor cells, thus promoting lymphovascular invasion and distant spread. Previous studies suggested that reduced PR expression correlates with higher rates of vascular and lymphovascular invasion [21]. The results of this study further supported this view and extended the prognostic value of PR to include lymph node metastasis, a critical clinical event.

Regarding tumor differentiation, this study observed that moderately to poorly differentiated tumors had markedly lower hormone receptor scores compared to well-differentiated tumors. While this result seemed straightforward, it required deeper interpretation in the context of contemporary molecular subtyping [22, 23]. According to TCGA molecular classification, the p53 abnormal subtype, often associated with serous carcinoma or high-grade cancers, typically showed low differentiation and very low hormone receptor expression. In contrast, some NSMP (no specific molecular profile) or MMRd (mismatch repair deficient) subtypes of lower-grade endometrioid carcinomas might retain some hormone receptor expression [24]. The observed trend in this study, where "the poorer the differentiation, the lower the receptor score", likely reflected the distribution differences of various molecular subtypes at the histological level [25].

Myometrial invasion depth is a crucial indicator in the surgical-pathological staging of endometrial cancer. This study confirmed that tumors with an invasion depth of ≥1/2 the myometrial thickness had significantly lower hormone receptor scores compared to those with less invasive tumors. This finding aligned with the understanding that myometrial invasion directly reflects the tumor's invasive capability [26]. Lower ER/PR expression might allow tumor cells to escape the inhibitory effects of the hormone-regulated microenvironment, leading to enhanced local invasiveness. Basic research also indicated that activation of the PR signaling pathway could reduce the activity of matrix metalloproteinases (MMPs), thereby inhibiting extracellular matrix degradation and tumor invasion [27]. Therefore, the loss of receptor expression might be linked to mechanisms like EMT and increased cell motility, ultimately resulting in deeper myometrial invasion.

One of the key findings of this study was that hormone receptor status served as an independent prognostic factor for patient survival. In multivariate logistic regression analysis, higher receptor scores for both ER and PR, whether assessed by H-score or Allred scoring, consistently indicated a protective effect. This suggested that even after adjusting for traditional risk factors such as staging, grading, and myometrial invasion, hormone receptor levels still provided unique prognostic information. Notably, ROC analysis showed that PR-related scores, particularly the PR Allred score, had the best discriminative power in predicting survival, with the highest AUC values. This highlighted the central role of PR in the biology of endometrial cancer. The antiproliferative and pro-differentiation effects of progesterone likely

underpinned its protective effect. High PR expression might indicate greater sensitivity to endocrine therapy or suggest a more differentiated tumor state with lower malignant potential [28, 29]. These findings had direct clinical implications. For postoperative patients, quantifying PR expression could help identify those with a favorable prognosis who might benefit from less aggressive adjuvant treatments, allowing for more personalized therapy.

This study compared both the H-score and Allred scoring systems. The H-score offered a continuous variable, potentially better at capturing subtle differences in expression, while the Allred score, as a semi-quantitative system, was easier to use in clinical settings [30]. Results showed that both methods performed similarly in linking clinicopathological parameters and prognosis. However, ROC curves suggested that the Allred system, especially for PR, might have better predictive discrimination. This could be due to the Allred score's threshold for assessing the proportion of positive cells (>1%), which effectively distinguished biologically meaningful receptor expression. This comparison provided a reference for pathologists to choose practical and effective scoring methods in daily work. Standardizing scoring procedures would be key to promoting the quantitative application of hormone receptors in the future. It wasn't just about confirming the prognostic value of hormone receptors but also about establishing a standardized and optimized assessment method, a crucial step for implementing personalized treatment strategies. These findings offered a practical and innovative approach to enhancing postoperative risk assessment and could help develop more tailored treatment plans for cancer patients.

The results obtained from multivariate regression and ROC analysis provide strong evidence to address the primary objective of this study regarding prognosis. The identification of ER and PR scores as independent protective factors confirms that quantitative hormone receptor status is a fundamental determinant of survival in endometrial cancer patients. The superior performance of the PR Allred score, in particular, provides a clinically useful tool for prognostic stratification. This suggests that incorporating this score into postoperative pathological assessments can effectively distinguish between patients with favorable prognoses and those at high risk. Therefore, our study ultimately demonstrates that estrogen and progesterone receptor status scores have independent prognostic impacts on cancer patients.

Despite the meaningful findings of this study, several limitations needed to be addressed. First, this was a single-center retrospective study with a limited sample size and potentially biased patient selection, which restricted the generalizability of the conclusions to a broader population. Second, the retrospective design could not fully control for all confounding factors. Third, the follow-up period was relatively short. For a disease like endometrial cancer, where some patients might experience late recurrences, a shorter follow-up time might not capture all events related to long-term survival. This could affect the accurate assessment of prognostic factors.

Based on these findings and limitations, future research could explore several directions. The top priority would be to validate the prognostic thresholds and clinical applicability of hormone receptor scores, particularly the PR Allred score, in large, multicenter prospective cohorts. Second, researchers should delve deeper into the molecular mechanisms behind the downregulation of hormone receptors in aggressive endometrial cancers. Questions remain about whether specific gene mutations, epigenetic silencing, or microenvironment changes play a role. Third, from a translational perspective, future studies should aim to integrate hormone receptor status into existing molecular classification frameworks. Building composite prognostic models that combine morphological, immunohistochemical, and molecular information could offer more precise risk stratification. Additionally, exploring whether hormone receptor scores can guide endocrine therapy decisions for advanced or recurrent patients holds substantial clinical value. Finally, with the rise of digital pathology, developing automated, standardized algorithms for hormone receptor scoring could enhance the comparability and reproducibility of assessments across different institutions.

Conclusion

In summary, this study systematically applied both the H-score and Allred scoring systems to

confirm that quantitative assessment of estrogen receptor and progesterone receptor levels closely correlated with key clinicopathological features of endometrial cancer and served as independent predictors of patient prognosis. The findings emphasized the importance of incorporating standardized hormone receptor scores into routine pathology reports, providing valuable reference information for improving patient risk stratification and guiding adjuvant treatment decisions. Despite the limitations in study design, this research added new evidence to deepen our understanding of the role of hormone receptors in endometrial cancer and promoted the development of personalized treatment strategies.

Acknowledgements

This study was supported by the Key Laboratory Project of Medical Integration and Translational Medicine in Luzhou City (XGY202107).

Disclosure of conflict of interest

None.

Address correspondence to: Qingqing Hu, Department of Reproductive Medicine, The Affiliated Hospital of Southwest Medical University, No. 25 Taiping Street, Jiangyang District, Luzhou 646000, Sichuan, China. E-mail: huqingqing_lz@163.com

References

[1] Akçay A, Gültekin MA, Altıntaş F, Peker AA, Balsak S, Atasoy B, Toluk Ö and Toprak H. Updated endometrial cancer FIGO staging: the role of MRI in determining newly included histopathological criteria. Abdom Radiol (NY) 2024; 49: 3711-3721.

[2] Huang Z, Li X and Li L. Early recurrence after surgery in FIGO 2023 stage I-III endometrial cancer: characteristics and risk factors. Front Oncol 2024; 14: 1500658.

[3] Bassette E and Ducie JA. Endometrial cancer in reproductive-aged females: etiology and pathogenesis. Biomedicines 2024; 12: 886.

[4] Restaino S, Paglietti C, Arcieri M, Biasioli A, Della Martina M, Mariuzzi L, Andreetta C, Titone F, Bogani G, Raimondo D, Perelli F, Buda A, Petrillo M, Greco P, Ercoli A, Fanfani F, Scambia G, Driul L and Vizzielli G; The Udine Hospital Gynecological-Oncological Tumor Board Group. Management of patients diagnosed with endometrial cancer: comparison of guidelines. Cancers (Basel) 2023; 15: 1091.

[5] Leo E, Stanzione A, Miele M, Cuocolo R, Sica G, Scaglione M, Camera L, Maurea S and Mainenti PP. Artificial intelligence and radiomics for endometrial cancer MRI: exploring the whats, whys and hows. J Clin Med 2023; 13: 226.

[6] Mahdi H, Ray-Coquard I, Lorusso D, Mirza MR, Monk BJ and Slomovitz B. Evolving treatment paradigms in metastatic or recurrent low-grade endometrial cancer: When is hormonal-based therapy the preferred option? Int J Gynecol Cancer 2023; 33: 1675-1681.

[7] Das A, Mandal SK, Arya S, Samanta SK, Kumar A, Panchpuri M, Abdel-Gawad H, Dwibedi V, Das N, Bose S, Gupta JK, Jaitak V and Rath SK. Therapeutic approach for triple-negative breast cancer through poly (ADP-ribose) polymerase-1 inhibitors: current update. Bioorg Chem 2025; 163: 108558.

[8] Ahmad Fauzi MF, Wan Ahmad WSHM, Jamaluddin MF, Lee JTH, Khor SY, Looi LM, Abas FS and Aldahoul N. Allred scoring of ER-IHC stained whole-slide images for hormone receptor status in breast carcinoma. Diagnostics (Basel) 2022; 12: 3093.

[9] Jeon T, Kim A and Kim C. Automated immunohistochemical assessment ability to evaluate estrogen and progesterone receptor status compared with quantitative reverse transcription-polymerase chain reaction in breast carcinoma patients. J Pathol Transl Med 2021; 55: 33-42.

[10] Son SM, Woo CG, Lee OJ, Lee SK, Cho M, Lee YP, Kim H, Kim HK, Yang Y, Kwon J, Lee KH, Kim DH, Yun HY and Han HS. Discordance in claudin 18.2 expression between primary and metastatic lesions in patients with gastric cancer. J Gastric Cancer 2025; 25: 303-317.

[11] Koppikar S, Oaknin A, Babu KG, Lorusso D, Gupta S, Wu LY, Rajabto W, Harano K, Hong SH, Malik RA, Strebel H, Aggarwal IM, Lai CH, Dejthevaporn T, Tangjitgamol S, Cheng WF, Chay WY, Benavides D, Hashim NM, Moon YW, Yunokawa M, Anggraeni TD, Wei W, Curigliano G, Maheshwari A, Mahantshetty U, Sheshadri S, Peters S, Yoshino T and Pentheroudakis G. Pan-Asian adapted ESMO clinical practice guidelines for the diagnosis, treatment and follow-up of patients with endometrial cancer. ESMO Open 2023; 8: 100774.

[12] Waluyo ST, Tjokroprawiro BA and Rahaju AS. Estrogen receptor and programmed death ligand-1 expression in type 1 endometrial cancer and its associated clinicopathological characteristics. Cancer Treat Res Commun 2023; 37: 100766.

[13] Vermij L, Jobsen JJ, León-Castillo A, Brinkhuis M, Roothaan S, Powell ME, de Boer SM, Khaw P, Mileshkin LR Fyles A, Leary A, Genestie C, Jürgenliemk-Schulz IM, Crosbie EJ, Mackay HJ,

Nijman HW, Nout RA, Smit VTHBM, Creutzberg CL, Horeweg N and Bosse T; TransPORTEC Consortium. Prognostic refinement of NSMP high-risk endometrial cancers using oestrogen receptor immunohistochemistry. Br J Cancer 2023; 128: 1360-1368.

[14] Przewoźny S, Rogaliński J, de Mezer M, Markowska A, Markowska J and Żurawski J. Estrogen receptor (ER) and progesterone receptor (PgR) expression in endometrial cancer-an immunohistochemical assessment. Diagnostics (Basel) 2024; 14: 322.

[15] Noori AS and Ghafour KHA. Immunohistochemical expression of estrogen and progesterone receptors in endometrial carcinoma in relation to clinic-pathological parameters. Iraqi Postgraduate Medical Journal 2023; 22: 407-416.

[16] Chibbar R, Foerstner S, Suresh J, Chibbar R, Piche A, Kundapur D, Kanthan R, Kundapur V, Lee CH, Agrawal A and Lai R. Estrogen/progesterone receptor loss, CTNNB1 and KRAS mutations are associated with local recurrence or distant metastasis in low-grade endometrial endometrioid carcinoma. Appl Immunohistochem Mol Morphol 2023; 31: 181-188.

[17] Erkılınç G, Yüceer RO, Erdemoğlu E, Kaymak ZA, Darbaş ŞM, Bozkurt KK and Çiriş İM. The expression of stanniocalcin-1, estrogen receptor and progesterone receptor in endometrioid endometrial cancer. Turk J Obstet Gynecol 2023; 20: 8-15.

[18] Mosquim S, Zamore M, Vallon-Christersson J, Rydén L and Levander F. Multiomic profiling of metastatic potential in estrogen receptor-positive human epidermal growth factor-negative breast cancer. medRxiv 2025.

[19] Wang K, Li L, Franch-Expósito S, Le X, Tang J, Li Q, Wu Q, Bassaganyas L, Camps J, Zhang X, Li H, Foukakis T, Xiang T, Wu J and Ren G. Integrated multi-omics profiling of high-grade estrogen receptor-positive, HER2-negative breast cancer. Mol Oncol 2022; 16: 2413-2431.

[20] Dias Da Silva I, Wuidar V, Zielonka M and Pequeux C. Unraveling the dynamics of estrogen and progesterone signaling in the endometrium: an overview. Cells 2024; 13: 1236.

[21] Clusan L, Ferrière F, Flouriot G and Pakdel F. A basic review on estrogen receptor signaling pathways in breast cancer. Int J Mol Sci 2023; 24: 6834.

[22] Zhang Z, Cao Z, Wang J, Li Z, Wang T and Xiang Y. Serum protein N-glycome patterns reveal alterations associated with endometrial cancer and its phenotypes of differentiation. Front Endocrinol (Lausanne) 2023; 14: 1157487.

[23] Zhang X, Joseph S, Wu D, Bowser JL and Vaziri C. The DNA damage response (DDR) landscape of endometrial cancer defines discrete disease subtypes and reveals therapeutic opportunities. NAR Cancer 2024; 6: zcae015.

[24] Han KH, Park N, Lee M, Lee C and Kim H. The new 2023 FIGO staging system for endometrial cancer: what is different from the previous 2009 FIGO staging system? J Gynecol Oncol 2024; 35: e59.

[25] Ronchi S, Di Lauro E, Facco C, Raffone A, Fulgione C, Casarin J, Santoro A, Arciuolo D, Angelico G, Zannoni GF, La Rosa S and Travaglino A. Low-grade endometrial endometrioid carcinoma of the p53-abnormal group: case presentation and diagnostic issues. Pathologica 2024; 116: 320-323.

[26] Tong Y, Huang M, Chen L, Lei H, Lin H, Mao X and Sun P. ERRγ, a novel biomarker, associates with pathoglycemia of endometrial cancer to predict myometrial invasion. J Oncol 2022; 2022: 5283388.

[27] Shi L, Yang D, Dong H, Zhang X and Yang C. miR-34b-5p suppresses the epithelial-mesenchymal transition and metastasis in endometrial cancer AN3CA cells by targeting ZEB1. Int J Clin Exp Pathol 2024; 17: 137-150.

[28] Dodds LV, Sanchez-Covarrubias AP, Sowamber R, Milea A, Pinto A, Ban Y, Schlumbrecht M, Shaw PA and George SH. Hormone receptor expression and disease prognosis in high-grade serous ovarian cancer. medRxiv 2023.

[29] Kwak Y, Jang SY, Choi JY, Lee H, Shin DS, Park YH, Kim JY, Ahn JS, Chae BJ, Yu J, Lee JE, Kim SW, Nam SJ and Ryu JM. Progesterone receptor expression level predicts prognosis of estrogen receptor-positive/HER2-negative young breast cancer: a single-center prospective cohort study. Cancers (Basel) 2023; 15: 3435.

[30] Tsoneva E, Dimitrova P, Metodiev M, Shivarov V, Vasileva-Slaveva M, Yordanov A and Kostov S. Utility of expression of 4-hydroxynonenal tested by immunohistochemistry for cervical cancer. Prz Menopauzalny 2024; 23: 6-13.