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Research Article

Pattern of LRR in Endometrial Cancer and Identification of Predictive Factors

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Abstract

Background: Tailored adjuvant treatment is key to managing endometrial cancer effectively. Understanding prognostic factors of loco-regional failure and the impact of adjuvant treatment can help in treatment de-escalation without compromising survival outcomes.

The aim of this study was to assess the pattern of failure in endometrial cancer patients and to determine predicting Loco-Regional Recurrence (LRR) factors.

Patients and methods: Data were collected from 214 patients treated for endometrial cancer between 2005 and 2012 in Salah Azaiez Institute in Tunisia. All patients underwent upfront surgery followed by adjuvant brachytherapy with or without external beam radiation. The median follow-up period was 44 months. Univariate and multivariate analyses were performed to identify prognostic factors for LRR.

Results: The 5-year overall survival rate was 78.1%, and the 5-year progression-free survival rate was 80.1%. LRR occurred in 25 patients (11.6%), with a median recurrence time of 29 months (range 4 months - 46 months). Pelvic relapse was the most common site, occurring in 10 patients. Vaginal relapses were observed in 9 patients, and retro-peritoneal relapses were observed in 6 cases. FIGO stage, tumor grade, histologic type, Lympho-Vascular Space Invasion (LVSI), and delays in adjuvant treatment were significant predictors of LRR.

Conclusion: Identifying prognostic factors for LRR in endometrial cancer is crucial for optimizing adjuvant treatment strategies. Higher FIGO stages and the presence of LVSI were independent predictive factors for LRR. Tailored adjuvant treatment, taking these prognostic factors into account, is essential to improve patient outcomes and minimize unnecessary treatment-related toxicity.

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Keywords: Endometrial cancer; Loco-regional recurrence; Predictive factors; FIGO stage; Lympho-vascular space invasion; Adjuvant treatment

Abbreviations: LRR: Loco-Regional Recurrence; FIGO: International Federation of Gynecology and Obstetrics; LVSI: Lympho-Vascular Space Invasion; EBRT: External Beam Radiation Therapy; HDR: High-Dose Rate; OS: Overall Survival; PFS: Progression-Free Survival; RR: Relative Risk; CI: Confidence Interval; CTV: Clinical Target Volume; MRI: Magnetic Resonance Imaging; ESMO: European Society of Medical Oncology; APA: American Psychological Association; SPSS: Statistical Package for the Social Sciences

Introduction

Endometrial cancer is the most frequent gynecological malignancy in women after breast cancer in Europe and the USA [1], with a rising incidence globally. In Tunisia, the incidence has increased from 1.75 cases per 100,000 women per year in 1998 to 3.94 cases per 100,000 women per year in 2008 [1]. Despite advancements in treatment, approximately 13% of endometrial cancer cases relapse within two years of follow-up [2]. These recurrences significantly impact survival, with a median survival of less than 12 months upon relapse [3]. Loco-Regional Recurrences (LRRs) are particularly challenging, as they are often associated with distant metastases in three-quarters of cases [4]. Currently, no salvage therapy for recurrent endometrial cancer has demonstrated curative efficacy, underscoring the importance of identifying prognostic factors to guide adjuvant treatment.

Loco-regional recurrence is defined as the reappearance of cancer in the vaginal, pelvic, or retro-peritoneal regions after initial treatment [2]. Factors such as tumor grade, histologic subtype, lymphovascular space invasion (LVSI), and FIGO stage have been identified as significant predictors of LRR [5,6]. Specifically, high-grade tumors and type II histologic subtypes, including serous and clear-cell carcinomas, are associated with poorer outcomes [5,6].

This study aims to assess the patterns of LRR in endometrial cancer patients treated with upfront surgery followed by adjuvant brachytherapy, with or without External Beam Radiation Therapy (EBRT). By identifying the key predictive factors for LRR, we seek to inform better clinical decision-making and optimize adjuvant treatment strategies to improve patient outcomes.

Material and methods

We reviewed 214 cases treated in a single cancer institute between 2005 and 2012. Inclusion criteria were: Histologically proven epithelial primary tumor of the endometrium, initial workup consisting of a full-body scan, and upfront surgery. Exclusion criteria were: primary sarcomas and other rare primary endometrial tumors, distant metastases at diagnosis, vaginal primary adenocarcinoma, R2 type resection, and local progression at referral.

Tumor classification was established with the 2009 International Federation of Gynecology and Obstetrics (FIGO) classification for all the patients including those treated between 2005 and 2008. Stage I was subdivided into low, intermediate, and high risk following the revised FIGO staging [7]. Type I endometrial cancer was defined by the presence of an endometrioïd adenocarcinoma in 95% of the tumor or more including the material of curettage, this category also included squamous differentiation. Type II endometrial cancer was defined by the presence of a serous or mucinous or clear-cell or mixed-cell component in more than 5% of the tumor including the material of curettage.

All the patients had a uterine curettage proving an endometrial cancer before upfront surgery. Surgery consisted of at least a hysterectomy and a bilateral oophorectomy. Pelvic lymph node dissection was omitted in patients with an MRI showing a tumor invading less than 50% of the uterine wall and no pelvic lymph node involvement or in patients unfit for complete staging. Omentectomy, appendectomy, and retroperitoneal lymph node dissection were considered in type II endometrial cancer, with signs of involvement in baseline body scan and prop findings. Pelvic exenteration was performed in stage IVa patients depending on bladder and/or rectal invasion.

External Beam Radiation Therapy (EBRT) was performed in all stage II, III, and IV patients when deemed feasible. In stage I patients, all patients with type II histologic cancer, Lympho-Vascular Space Invasion (LVSI), and invasion of more than 50% of the uterine wall were considered for EBRT.

The technique used was conventional radiation therapy in all cases using Cobalt 60 gamma rays and 18 MV X-photons in case of obesity. In the case of pelvic irradiation, 4-field box therapy was used with the Clinical Target Volume (CTV) encompassing the tumor bed, and regional lymph nodes (external, internal, and common iliac nodes and presacral nodes). CTV comprised lumbar nodes in case of a documented histologic infiltration. The prescribed dose was 45 to 50.4 Gy, 1.8 to 2 Gy, and 5 fractions a week. Chemotherapy was used in stage III and IV. The protocol used was 3-week Cisplatine-Adriamycine in Mullerian tumors and Carboplatine-Paclitaxel in the other histologic subtypes. It consisted of a total of 3 to 4 infusions.

Vaginal vault High-Dose-Rate (HDR) brachytherapy was indicated in all patients. The isotope used was Iridium 192. Prior to treatment, a Nucletron GM1 1004160 applicator was placed. The prescription point was 5 mm deep.

After the completion of the treatment, a periodic follow-up was scheduled. Patients were seen every 3 months the first 2 years after treatment, every 6 months the 3 following years, and annually until death or loss of contact. Clinical examination was performed at every consultation, and pelvic ultrasonography and chest X-rays were performed twice a year in the first 2 years, then annually in the 3 following years. In case of an anomaly on these exams or new symptoms, appropriate explorations were indicated in case by case.

Loco-Regional Recurrence (LRR) was defined as a relapse in the vaginal and/or the pelvic area and/or in the retro-peritoneal area after 3 months of the completion of the treatment. Any other event within 3 months of the last treatment was considered to be a failure to control the disease. Vaginal relapses were all explored with appropriate biopsies. Retroperitoneal, pelvic, and distant recurrences were diagnosed with radiological exploration alone. Overall Survival (OS) was defined from the date of the diagnosis until death or the date of last contact. Progression-Free Survival (PFS) was calculated from the date of the diagnosis until documented progression.

Statistical analysis was performed using SPSS 17.0. OS and PFS were calculated using the Kaplan-Meier method. A Univariate Log-Rank test was used to identify prognostic factors with a risk of error $\alpha = 0.05$. Multivariate analysis used the Cox regression method to identify independent prognostic factors.

Results

The mean age was 58.9 ranging from 28 to 83. 177 of our patients (78%) were in menopause. Obesity was identified in 103 of our patients (48.1%) and 41 patients (19.1%) had a metabolic syndrome. Type I endometrial cancer was found in 162 patients (75.7%) and type II endometrial cancer in 52 patients (24.3%). LVSI was found in 23 patients (10.7%). 164 patients had stage I disease, 30 had stage II disease, 33 had stage III disease and 5 had stage IV disease. Among the 164 patients with stage I, 76 patients (46.3%) were in the low-risk group, 36 patients (21.9%) were in the intermediate-risk group and 34 patients (21.1%) were in the high-risk group. The patient's characteristics are shown in Table 1.

All the patients had an upfront surgery comprising at least a bilateral oophorectomy with a hysterectomy. In 15 cases (7%), omentectomy with appendectomy was performed in patients who had a histologic type II (7 cases), suspicious ovarian tumor (4 cases), and suspicion of limited peritoneal carcinomatosis (4 cases). The mean tumor greater dimension was 43.7mm on histologic findings. Surgery on pelvic lymph

Table 1: Patients' characteristics.

Characteristics		
Median age		58.9 (28 years - 83 years)
Mean tumor size		43.7 mm (15 mm - 180 mm)
Histologic subtype	Type I	162 (75.7%)
	Type II	52 (24.3%)
LVSI	Absent	191 (89.3%)
	Present	23 (10.7)
Uterine wall invasion> = 50%		68 (31.7%)
Cervix invasion		50 (23.3%)
Lymph-node dissection	Pelvic	165 (77.1%)
	Para-aortic	14 (6.5%)
FIGO Staging	I	146 (68.2%)
	II	30 (14%)
	III	33 (15.4%)
	IV	5 (2.3%)
Stage I subgroups	Low-risk	76 (51.3%)
	Intermediate-risk	36 (25.3%)
	High-risk	34 (23.2%)

nodes was performed in 165 cases (77.1%). In 138 cases (83.62%), it was a pelvic lymph node dissection and 27 cases (16.38%) had a pelvic lymph node sampling. In 14 cases, surgery on retro-peritoneal lymph nodes was performed. 9 patients had a retroperitoneal lymph node dissection and 5 had a retro-peritoneal lymph node sampling. Retro-peritoneal lymph node surgery was indicated in 9 cases for a type II histologic cancer, 4 cases for pre-op suspect lymph nodes, and 3 cases for radiological suspicion of retro-peritoneal lymph node involvement. The 5 patients with stage IV cancer had pelvic exenteration.

Half of the patients had EBRT. The clinical target volume encompassed at least the tumor bed and the external and internal iliac lymph nodes. 2 (1.8%) patients had retroperitoneal lymph node irradiation. Doses varied between 40 Gy and 50.4 Gy, with 5 weekly fractions of 1.8 to 2 Gy. The mean delay between adjuvant external beam radiation therapy and surgery was 4.35 months, with 55% of the cases receiving adjuvant radiation therapy more than 3 months after surgery. Treatment interruptions were observed in 33 cases (15.4%) and in 16 cases (7.4%) the interruption lasted more than 7 days.

HDR brachytherapy was performed for all of our patients. The 109 patients (50.9%) who did not receive external beam radiation therapy received 20 Gy in 4 weekly fractions. The 72 patients (33.7%) that were treated with 45 Gy or less with external beam radiation therapy received 8 Gy in 2 weekly fractions. The 37 patients (17.3%) that were treated with more than 45 Gy received a single 6 Gy fraction.

Fourteen patients (6.5%) received chemotherapy. 8 patients received a 3-weekly infusion of Paclitaxel-Carboplatin and 6 patients received a 3-weekly infusion of Doxorubicin-Cisplatin. Sequential chemotherapy was done in 11 cases and concomitant chemotherapy in 3 cases.

After a median follow-up of 44 months, 172 patients (80.8%) were in remission. 42 patients (19.1%) relapsed. 25 patients (11.6%) had an LRR (LRR). In 9 cases (4.2%), the relapse was in the vaginal vault. In 10 cases (4.6%), the relapse was in the pelvic area, and in 6 cases (2.8%), the relapse was in the retro-peritoneum. The median delay to relapse in isolated loco-regional relapses was 29 months [4-46]. In the case of LRR associated with distant metastases, the median delay to relapse was 17 months [6-55]. 5-year Overall Survival (OS) was 78.1%. 5-year progression-free survival (PFS) was 84.9%.

Univariate analysis has shown that grade 2–3 endometrial cancer was associated with more loco-regional relapses than grade 1 (21% *vs.* 9%, $p = 0.01$). Type II was associated with more frequent loco-regional relapses than type I (21.1% *vs.* 8.6%, $p = 0.01$). LVSI was a predictive factor of LRR 3.6% *vs.* 78.2% $p = 0.0003$. FIGO stage was a predictive factor of LRR with 7.3% relapses in stage I-II and 28.9% of relapses in stage III-IV $p = 0.001$. Incomplete resection was associated with more frequent LRR than complete resections (50% *vs.* 9.8% $p = 0.0001$). The patients who received adjuvant treatment more than 3 months after surgery had more LRR than patients who were treated within 3 months of surgery (23.3% *vs.* 8% $p = 0.02$). Suboptimal treatment delivery defined by an interruption of treatment superior to 7 days was associated with a more frequent LRR than optimal treatment delivery (37.5% *vs.* 13.1% $p = 0.018$). Univariate analysis in Table 2.

Multivariate Cox analysis showed that FIGO stage was an independent LRR predictive factor (adjusted RR 4.6, 95% CI

Table 2: Univariate analysis results of LRR prognostic factors.

	Number	LRR (%)	*p*
Age < 60 years Age ⩾ 60ans	107 103	10 (9.3%) 15 (14.5%)	< 0.05
Stage I II III IV	146 30 33 5	8 (5.4%) 5 (16.6%) 10 (30.3%) 1 (20%)	0.0001
Low-risk Intermediate-risk High-risk	76 36 34	4 (5.2%) 3 (8.33%) 1 (3%)	< 0.05
Type I Type II	162 52	14 (8.6%) 11 (21.1%)	0.01
Grade1 Grade 2-3	102 60	12 (9%) 13 (21.6%)	0.01
< 50 % Uterine wall invasion ⩾ 50 % Uterine wall invasion	129 85	12 (9.3%) 13 (15.2%)	< 0.05
Tumor larger diameter < 4 cm Tumor larger diameter ⩾ 4cm	44 61	4 (9%) 11 (18%)	< 0.05
LVSI + LVSI -	23 191	18 (9.4%) 7 (3.6%)	0.0003
Lymph-node invasion Present Absent	 20 158	 6 (30%) 19 (12%)	0.0003
Complete resection Marginal resection	204 10	20 (9.8%) 5 (50%)	0.0001
Treatment halted⩾7 DAYS Treatment halted < 7 DAYS or no interruption	16 91	6 (37.5%) 12 (13.1)	0.018
Delay between surgery and adjuvant treatment ⩾ 3 months < 3 months	 60 49	 14 (23.3%) 4 (8%)	0.02

1,217 to 77.84, p = 0,03) and LVSI was also an independent LRR predictive factor (RR 4.31, 95% CI 1.07 to 9.84, p = 0.037). Multivariate analysis results are shown in Table 3.

In stage I patients, relapses were distant in 9 patients (4.1%), vaginal in 4 patients (2.7%), and pelvic in 3 patients (2%). In stage II patients, relapses were distant in 5 patients (16%), vaginal in 3 patients (10%), and pelvic in 1 patient (3.3%). In stage III patients, relapses were distant in 10 patients (30.3%), vaginal in 1 patient (3%), pelvic in 5 patients (15.1%), and retroperitoneal in 4 patients (12%). In stage IV patients, relapses were distant in 2 patients, vaginal and pelvic in 1 patient.

In stage I patients, the low-risk group experienced 1 vaginal relapse (1.3%), 2 pelvic relapses (2.6%), and 3 distant relapses (3.9%). The intermediate-risk group experienced 2 vaginal relapses (5.5%), 1 pelvic relapse (2.7%), and 1 distant relapse (2.7%). The high-risk group experienced 1 vaginal relapse (3%), no pelvic relapses, and 5 distant relapses (14.7%). Relapses by the FIGO stage are shown in Table 4.

5-year OS in patients with loco-regional relapses was significantly lower than patients free of relapse 16.9% vs 87.9% (p < 0.00001). 5-year distant relapse-free survival was significantly higher in patients achieving loco-regional control 88.4% *vs*. 55.5% (p < 0.00001).

Discussion

Around 20% of patients with endometrial cancer experience a relapse 15% in the vaginal, 35% in the pelvic area, and 50% in the retroperitoneum and distant metastases [8]. A review of 16 retrospective studies cumulating 2922 patients demonstrated that predictive factors for loco-regional control were: FIGO stage, histologic subtypes, histologic grade, uterine wall invasion, and lymph node involvement [2]. We elicited the FIGO stage, histologic subtypes, histologic grade, LVSI, suboptimal treatment delivery, and delayed adjuvant treatment as prognostic factors for loco-regional control. In our study, the FIGO stage and LVSI were identified as independent prognostic factors. FIGO staging is based on the assessment of uterine extension (uterine wall involvement, cervical invasion, or the adnexa of the uterus), local extra-uterine extension (parametrium, vagina, rectum, and bladder), and lymph node extension (pelvic and retro-peritoneal). All of these are well-established prognostic factors [9].

Table 3: Multivariate analysis of LRR prognostic factors.

Prognostic factors	p	Adjusted RR	95% CI
Histologic subtype	0.052	3.75	[0.976 - 67.27]
LVSI	0.037	4.31	[1.07 - 9.84]
Lymph-node invasion	0.066	3.37	[0.113 - 1.073]
Quality of resection	0.088	2.9	[0.83 - 14.58]

Table 4: Pattern of LRR by FIGO stage.

	Vaginal relapse (%)	Pelvic relapse (%)	Retroperitoneal relapse (%)
Stage I	2,7	2	0.6
Low-risk	1,3	2,6	1.3
Intermediate-risk	5,5	2,7	0
High-risk	3	0	0
Stage II	10	3,3	3,3
Stage III	3	15,1	12
Stage IV	1	1	0

Uterine wall invasion is an established loco-regional prognostic factor. Retrospective evaluation of PORTEC 1 and PORTEC 2 patients showed that the invasion of more than 50% of the uterine wall was associated with worse overall survival and loco-regional and distant control [10]. External beam radiation therapy was indicated in most of our patients with an invasion of more than 50% of the uterine wall and could explain why this factor did not impact loco-regional control. Analysis of the PORTEC 1 trial and GOG 99 trial data revealed that some patients in the stage I intermediate-risk group could benefit from external beam radiation therapy [10,11]. A stratification of the intermediate-risk group using age> 60 years, grade 3, and LVSI permitted to subdivide intermediate-risk group into two groups low-intermediate risk where EBRT reduced loco-regional failure from 20% to 5% and a high-intermediate risk where EBRT reduced loco-regional failure from 6% to 2% [11,12].

The presence of LVSI, and suboptimal treatment delivery (delays in adjuvant therapy and treatment interruptions) are significant predictors of poor loco-regional control. LVSI as a prognostic factor prompted the SFOG (Société Française d'Obstétrique et de Gynécologie- French Society of Obstetrics and Gynecology) to integrate all patients with LVSI in the high-risk group of the 2009 ESMO (European Society of Medical Oncology) classification [13]. It was demonstrated that LVSI is a loco-regional failure prognostic factor and correlated with lymph node involvement [14-16].

Recent ESMO recommendations subdivided the intermediate-risk group into low-intermediate risk and high-intermediate risk groups in an effort of therapeutic de-escalation following the results of Kong and all meta-analyses [12,17]. Low-intermediate-risk patients would not receive external beam radiation therapy. In our patients, we indicated EBRT in low-intermediate-risk patients taking into account uterine wall invasion> 50%.

We found limited data about isolated vaginal relapses. Type II histologic cancer, LVSI, and uterine wall invasion > 50% were identified as prognostic factors of local relapse [15,18]. A study led by Elliot et al. reported isolated vaginal relapse at 10 years of follow-up was 3% in stage I, grade 1–2 endometrial with uterine wall invasion < 33% *vs.* 15% at 10 years of follow-up in patients with stage I, grade 3 and/or uterine wall invasion > 33% [18]. This shows how much disparity exists in stage I patients.

LVSI (RR = 4.27, p < 0.01), pelvic lymph-node invasion

(RR = 3.43, p = 0.02), and cervix involvement (RR = 2.26, p = 0.04) were demonstrated to be independent prognostic factors of pelvic relapse in Marian et al study. In our patients, we found similar results without being able to demonstrate independent prognostic factors of lymph node relapse.

Tumor grade was shown to be a predictive factor of loco-regional control with 5 times more likely relapses in grade 3 patients compared to the same FIGO stage patients with grades 1-2 [19]. In our patients, tumor grade was shown to be a prognostic factor in univariate analysis but not in multivariate analysis mainly due to a tendency to be associated with more advanced loco-regional extension.

In our study, type II histologic cancer was associated with a worse prognosis than type 1 (61% of 5-year OS *vs.* 84% $p < 0.05$). Albertini, et al. reported a similar result with 80% of 5-year OS in patients with type I histologic cancer vs 40% with type II histologic cancer [20]. Serous carcinomas have shown a tendency to a fast and frequent peritoneal dissemination prompting the use of chemotherapy. Clear-cell carcinoma is also an aggressive subtype with a 5-year OS of 44% in stage I patients [20].

Apart from histologic characteristics, actual research is looking at many prognostic markers with promising results such as hormonal receptors (Estrogen receptors and Progesterone receptors), markers of genetic alteration (p53, c-erb2, Ki67, bcl-2), and alteration of genetic ploidy [21,22]. These emerging factors could shed new light on the outcome of treatment and lead to the development of efficient targeted therapies. Recently, L1CAM was shown to be a useful marker in decision-making for low-risk patients [23].

Recent studies have also emphasized the role of genetic and molecular factors in predicting endometrial cancer outcomes. For example, genetic markers such as p53, c-erbB-2, and L1CAM have been associated with prognosis and may inform personalized treatment approaches [22,23]. Immunohistochemical analysis has also provided insights into the behavior of different endometrial cancer subtypes, further aiding in the stratification of patients based on risk [19,24].

Recent research has highlighted the significance of genetic factors and immunohistochemical markers in the prognosis and treatment of endometrial cancer. Key genetic alterations, such as mutations in the PTEN, PIK3CA, ARID1A, and TP53 genes, have been identified as critical in the development and progression of endometrial cancer. These genetic mutations can affect cell signaling pathways, leading to uncontrolled cell growth and malignancy [25].

Immunohistochemical analysis has become a vital tool in the pathological evaluation of endometrial cancer. Markers such as Estrogen Receptors (ER), Progesterone Receptors (PR), p53, and Ki-67 are frequently assessed to provide prognostic information and guide therapeutic decisions. For example, overexpression of p53 and high Ki-67 labeling index are associated with high-grade tumors and poor prognosis, while positive ER and PR status generally indicate a better response to hormone therapy. L1 Cell Adhesion Molecule (L1CAM) is another emerging biomarker with prognostic significance. High expression of L1CAM has been correlated with aggressive tumor behavior and poor clinical outcomes. The assessment of L1CAM, along with other markers, can help stratify patients into different risk categories, thereby tailoring adjuvant treatment strategies more effectively [23].

Incorporating genetic and immunohistochemical analyses into the evaluation of endometrial cancer can enhance the understanding of tumor biology and improve personalized treatment approaches. Recent studies explore these biomarkers to validate their clinical utility and integrate them into routine clinical practice [26]. Biological and molecular findings in endometrial cancer focus on identifying biomarkers and molecular characteristics that can influence prognosis and guide treatment decisions. Traditionally, radiotherapy has been a key component in the treatment of endometrial cancer, particularly in cases where there is a higher risk of local recurrence. However, with the identification of molecular subtypes like those with POLE mutations, there is ongoing research into whether de-escalation of radiotherapy can be considered without compromising treatment outcomes [26]. For patients with endometrial cancer harboring POLE mutations and favorable prognostic features (such as low-grade tumors and absence of myometrial invasion), there is a discussion about whether adjuvant radiotherapy can be safely omitted or reduced in intensity. Several clinical trials are exploring the feasibility and safety of reducing or omitting radiotherapy in patients with favorable molecular profiles, including those with POLE mutations. These trials aim to determine if outcomes in terms of local control and overall survival remain favorable with reduced treatment intensity. It is crucial to balance the potential benefits of de-escalation (reduced treatment toxicity and morbidity) with the risk of undertreating cancer [27].

Conclusion

Identifying prognostic factors is pivotal in the effective management of endometrial cancer. Given the grim survival rates following relapse, it is crucial for physicians to exercise caution in reducing treatment intensity prematurely. Conversely, adjuvant therapies, such as brachytherapy or external beam radiation, carry notable risks of toxicity. The specific impact of external beam radiation therapy on intermediate-risk patients, the efficacy of brachytherapy in low-risk patients, and the potential contributions of emerging biomarkers remain uncertain. Addressing these uncertainties through well-designed clinical trials is imperative to guide treatment decisions and enhance outcomes in endometrial cancer management.

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