Review

Impact of Adjuvant Radiotherapy on Survival of Patients with stage I-II Endometrial Cancer:

A Literature review

M. Uyeda[1], G. Maluf[2], M. G. F. A. Kenupp[3]

Keywords: Endometrial Cancer, Adjuvant Radiotherapy, Vaginal Brachytherapy, Gynecologic Oncology, Survival

ABSTRACT

Background: Endometrial cancer is the most common gynecological neoplasm in developed countries. Most cases are diagnosed early, and surgical treatment is usually curative. The role of adjuvant radiotherapy is controversial, especially for patients with intermediate or high-risk factors. The increasing variety of therapies and emphasis on personalized treatment underscore the need to critically assess the impact of radiotherapy on patient outcomes. Therefore, this study aims to evaluate the impact of adjuvant radiotherapy on clinical outcomes in patients with endometrial cancer who have intermediate or high-risk factors.
Objectives: To analyze the effect of adjuvant radiotherapy on overall survival, disease-free survival, and locoregional control in women with stage I or II endometrial cancer.
Methods: The systematic review followed the PRISMA guidelines and was registered in PROSPERO. The search, conducted until August 2025 in databases such as PubMed, Embase, and SciELO, used controlled descriptors and Boolean operators. Original studies in Portuguese, English, or Spanish with clinical data from patients undergoing adjuvant radiotherapy were included.
Results: The review included 12 studies totaling 18,975 patients, analyzing modalities such as external beam radiotherapy, vaginal brachytherapy, and combination chemotherapy. The results indicate that adjuvant radiotherapy significantly reduces locoregional recurrence and improves disease-free survival, especially in patients with risk factors (high-grade or lymphovascular invasion). Brachytherapy was noted to offer similar efficacy to external beam radiotherapy with lower toxicity, while recent studies (such as PORTEC-4a) suggest the use of molecular profiles to personalize and de-intensify treatment.
Conclusion: Adjuvant radiotherapy plays a relevant role in the management of early-stage endometrial cancer and should be indicated selectively based on clinical, histological, and molecular criteria.

Main Contribution to Evidence-Based Practice: The review clarifies the real impact of adjuvant radiotherapy on survival in stage I–II endometrial cancer, helping clinicians distinguish which patients truly benefit from radiation and supporting more precise, evidence-based treatment decisions that avoid unnecessary toxicity.

International Healthcare Review (online)
●
eISSN: 2795-5567
●
How to Cite
Uyeda, M., Gabriel, M., & Maria Graziela de fátima Alvarez, K. (2026). Impact of Adjuvant Radiotherapy on Survival of Patients with Stage I-II Endometrial Cancer: A Systematic Review. International Healthcare Review (online). https://doi.org/10.56226/150
●
Published online: 24/Februrary?2026
●

Corresponding Author:
M. Uyeda
Universidad Nacional Ecologica _ Bolivia
mari53972@uecologica.edu.bo

Authors' Affiliations:
[1] Universidad Nacional Ecologica – UNE- Santa Cruz de La Sierra - Bolivia
[2] Universidad Nacional Ecologica – UNE- Santa Cruz de La Sierra – Bolivia
[3] Universidad Nacional Ecologica – UNE- Santa Cruz de La Sierra - Bolivia

What do we already know about this topic?
Stage I–II endometrial cancer usually has a good prognosis after surgery, and adjuvant radiotherapy is used to reduce recurrence, especially in patients with risk factors. However, studies show inconsistent results regarding its impact on survival, particularly in low-risk tumors, raising doubts about its real usefulness in these cases.
What is the main contribution to Evidence-Based Practice from this article?
The review shows that adjuvant radiotherapy improves pelvic dysfunction and reduces pelvic recurrence in stages IB–IIB, without a major impact on surgical site (OS), but with significant prevention of local failures. Adverse effects are generally mild, reinforcing its safety as an adjunctive therapy.
What are this research's implications towards health policy?
The article reinforces that locoregional control is crucial in treatment, guides the use of adjuvant radiotherapy in intermediate-risk patients, and highlights the need to expand access to this resource in healthcare services.
Authors' Contributions Statement:
Uyeda, M.: lead author of the systematic review. Write the material and reviewed articles. Maluf, G.:co-author of the systematic review. Helped read and select articles for inclusion in the review. Kenupp, M.G.F.A.: co-author of the review. Helped read and write the material for the review.

Introduction

Endometrial cancer (EC) is the most common gynecological neoplasm in developed countries, with increasing incidence due to population aging and increasing obesity (Nout et al., 2010). Most cases are diagnosed in early stages (stages I and II), in which the prognosis is generally favorable. Standard treatment involves primary surgery, with total hysterectomy and bilateral salpingo-oophorectomy, and may include lymphadenectomy in selected cases (de Boer et al., 2015). However, the indication for adjuvant therapies, such as radiotherapy (RT), remains controversial, especially in patients with intermediate or high-risk factors (de Boer et al., 2015).

Epidemiology

EC is the sixth most common malignant neoplasm among women worldwide, with 382,000 new cases reported in 2023. Its incidence has been increasing globally, driven primarily by population aging, longer life expectancy, and the growing prevalence of risk factors such as obesity, type 2 diabetes (DM2), and arterial hypertension (AH). Most cases are diagnosed in postmenopausal women, with an average age of 63 (Akingbade, Fabi, Cartes, Tsui, & Alfieri, 2024).

In Brazil, uterine cancer, which includes EC, represents approximately 3.2% of all cancer cases among women, with an estimated 7,840 new cases in 2025 (INCA, 2023). As in developed countries, most Brazilian patients are diagnosed at an early stage, which favors better survival rates. However, the country faces additional challenges related to unequal access to health services, which can impact the time to diagnosis and the quality of treatment offered (INCA, 2023).

Incidence and Prognosis

Most cases are diagnosed in the early stages, when the tumor is still confined to the uterus, accounting for approximately 68.8% of diagnoses (Concin et al., 2025). At this stage, the prognosis is generally favorable, with overall survival (OS) rates exceeding 90% at five years, especially when surgical treatment is performed appropriately (Concin et al., 2025).

When diagnosed early, EC has an excellent prognosis in Brazil, with survival rates

comparable to those observed internationally, especially in specialized centers that adopt evidence-based protocols. A comparison between Brazil and high-income countries reveals that, although survival rates are similar in the early stages, regional and socioeconomic disparities can influence clinical outcomes (INCA, 2023).

Risk Factors

Risk factors for early-stage EC (stages I and II) are strongly associated with conditions that promote hormonal imbalance, especially excess estrogen unbalanced by progesterone. Obesity is a major determinant, as adipose tissue converts androgens into estrogen, increasing endometrial exposure to the hormone and promoting cell proliferation (Dallaire Nantel, Renaud, Gregoire, Sebastianelli, & Plante, 2021). Women with a high body mass index are up to three times more likely to develop the disease. Furthermore, polycystic ovary syndrome, characterized by chronic anovulation, also contributes to this hormonal imbalance (Dallaire Nantel, Renaud, Gregoire, Sebastianelli, & Plante, 2021).

Other factors include early menarche and late menopause, which prolong estrogen exposure throughout life (Goel et al., 2023). Nulliparity, that is, never having become pregnant, is also associated with increased risk, as is prolonged use of estrogen-based hormone therapy without progesterone in postmenopausal women (Morén, Larsson, & Tedgren, 2021). Metabolic diseases such as DM2 and AH are frequently observed in patients with EC, suggesting a link between chronic inflammation and carcinogenesis (Saldi et al., 2019).

A family history of gynecological cancer, especially in hereditary syndromes such as Lynch syndrome, also represents an important, although less common, risk factor (Wortman et al., 2018). Conversely, the use of combined oral contraceptives and regular physical activity has a protective effect, significantly reducing the risk of developing the disease (Sloboda, 1992). In the early stages, these risk factors contribute to the emergence of tumors that are generally low-grade and have a good prognosis, provided they are diagnosed early (Bollen, van der Veen, Laenen, & Nuyts, 2021). Identifying and controlling these factors are fundamental for prevention strategies and for defining risk groups that deserve more rigorous gynecological monitoring (Cibula et al., 2023).

Treatment

Treatment of early-stage EC focuses primarily on surgery, considered the gold standard. Total hysterectomy with bilateral salpingo-oophorectomy is the most common procedure and can be performed abdominally, laparoscopically, or robotically, depending on the patient's clinical condition and available infrastructure (Martínez et al., 2023). In selected cases, especially when there are risk factors such as deep myometrial invasion, high histological grade, or lymphovascular involvement, pelvic and para-aortic lymphadenectomy may be considered for better staging and treatment definition (Randall et al., 2019).

Adjuvant RT is indicated on an individual basis, based on an assessment of recurrence risk (van den Heerik et al., 2020). In intermediate or high-risk patients, vaginal brachytherapy (VBT) can be used to reduce the risk of local recurrence, while external beam radiation therapy (EBRT) is reserved for cases with greater anatomical involvement or when extensive surgery is contraindicated (Narasimhulu et al., 2020). However, its impact on OS and disease-free survival (DFS) is still debated, being most evident in the prevention

of locoregional recurrence. Furthermore, the potential adverse effects of RT on quality of life (QoL) and late toxicity should be considered in clinical decision-making (Akingbade, Fabi, Cartes, Tsui, & Alfieri, 2024).

In specific situations, such as young women wishing to preserve fertility and with well-differentiated tumors confined to the endometrium, conservative treatment with progestins may be considered, under strict clinical and histological monitoring. After primary treatment, clinical follow-up is essential, with periodic consultations to assess symptoms, physical examination, and, when indicated, imaging tests (Creutzberg & Nout, 2011).

Radiotherapy

RT treatment for early-stage EC is primarily indicated as adjuvant therapy after surgery, aiming to reduce the risk of local recurrence, especially in patients with intermediate or high-risk factors (Holloway et al., 2017). The choice between VBT, EBRT, or a combination of both depends on the histological characteristics of the tumor, depth of myometrial invasion, tumor grade, and presence of lymphovascular invasion (Poitevin-Chacón & Hinojosa-Gómez, 2012).

VBT is frequently used in intermediate-risk patients and is administered directly to the vaginal vault (Vetter, Bixel, & Felix, 2022). The most common regimen involves the administration of 21 to 24 Grays (Gy), divided into 3 to 4 fractions, usually 5 to 7 Gy per session, performed twice weekly. EBRT, indicated in cases with a higher risk of regional involvement, is performed on the pelvis with doses ranging from 45 to 50.4 Gy, fractionated into 25 to 28 daily sessions, with approximately 1.8 Gy per fraction, over five to six weeks (Latif, Haggerty, Jean, Lin, & Ko, 2014).

The prognosis for patients undergoing adjuvant RT is generally favorable. RT significantly reduces the risk of locoregional recurrence, especially vaginal recurrence, although its impact on OS is limited in patients with low-risk tumors (Chen et al., 2017). In high-risk cases, the combination of RT with chemotherapy (CT) may be considered to improve oncological outcomes. Side effects of RT include gastrointestinal and urinary toxicity, and in some cases, sexual dysfunction, which are generally manageable with appropriate clinical support (Keys et al., 2004). Given the heterogeneity of available studies and the lack of consensus in international guidelines, it is essential to critically synthesize the existing evidence on the role of adjuvant RT in patients with stage I and II EC. This review aims to assess the impact of adjuvant RT on OS and DFS, contributing to the definition of more effective and individualized therapeutic strategies.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, with a protocol previously registered on the PROSPERO platform, aiming to ensure transparency and methodological rigor. The literature search was conducted in the PubMed/MEDLINE, Embase, Scopus, Web of Science, Lilacs, and SciELO databases, covering publications up to August 2025. Controlled descriptors (MeSH) and free keywords related to "endometrial cancer," "adjuvant radiotherapy," "survival," "stage I," "stage II," and "treatment" were used, combined with Boolean operators to maximize search sensitivity. The strategy was complemented by a manual review of the references of the included studies.

Original studies, including randomized clinical trials, prospective and retrospective

cohort studies, that addressed women diagnosed with stage I or II EC who underwent adjuvant radiotherapy were considered eligible. Studies were required to present data on OS, DFS, or local recurrence. Publications in Portuguese, English, and Spanish were included. Studies with stage III or IV patients, narrative reviews, letters to the editor, preclinical studies, or those with insufficient data on the outcomes of interest were excluded.

Study selection was performed by independent reviewers in three stages: reading titles, abstracts, and full texts. Disagreements were resolved by consensus or by a third reviewer. Data extraction was performed using standardized spreadsheets, including information such as author, year of publication, country, methodological design, sample characteristics, type of radiotherapy used, total dose in Gy, number of fractions, follow-up time, and clinical outcomes.

The methodological quality of the studies was assessed using the Cochrane Risk of Bias tool for clinical trials and the Newcastle-Ottawa scale for observational studies. The results were summarized narratively and, when possible, grouped into comparative tables. Heterogeneity between studies will be assessed using the I^2 test, and sensitivity analyses will be conducted as needed.

Results

Twelve original studies evaluating the impact of adjuvant RT on survival in patients with stage I and II EC were included, totaling 18,975 patients. The selected studies presented a wide variety of methods, including randomized controlled trials, multicenter retrospective studies, and population-based analyses, conducted in different regions such as North America, Europe, Asia, and South America. This variety allowed for a comprehensive overview of clinical practices and outcomes associated with adjuvant RT in different settings.

Most studies focused on comparing EBRT and VBT, highlighting the efficacy of each modality in terms of OS, DFS, and locoregional control of recurrence. The study by Narasimhulu et al. (2020), for example, demonstrated that EBRT and VBT have similar efficacy in OS in patients with stage II EC, but with less toxicity associated with VBT, especially regarding gastrointestinal and urinary effects. The study is a systematic review and meta-analysis that included a total of 1,168 patients. This observation is corroborated by Garzon et al. (2022), who showed that VBT alone was sufficient to ensure locoregional control in high-intermediate-risk patients, while observation was safe in low-risk cases. The study was conducted in the United States and included 1,382 patients with stage I and II cancer classified as high-intermediate or high risk. The authors compared outcomes between patients treated with observation or VBT alone. Population-based studies such as that by Vetter et al. (2020), which analyzed more than 4,000 patients from the National Cancer Database (NCDB) in the United States, showed that adjuvant RT was associated with a significant improvement in OS, especially in patients with additional risk factors such as high tumor grade and lymphovascular invasion. Similarly, Matsuo et al. (2021) highlighted that the presence of malignant peritoneal cytology is a negative prognostic factor, and that the combination of RT with chemotherapy can significantly improve outcomes in these cases, suggesting a more aggressive approach for specific subgroups. In the study conducted in the United States, 5,432 patients with stage II and III EC were evaluated. The focus was to investigate the impact of malignant peritoneal cytology on the efficacy

of adjuvant therapy.

In studies conducted in China, such as those by Ren et al. (2022) and Wang et al. (2023), the combination of EBRT with VBT was observed to be effective in reducing locoregional recurrence in high-risk patients, while VBT alone was increasingly adopted in intermediate-risk cases, reflecting a shift in clinical practices toward personalized treatment. Arslan et al. (2020), in a study with a 10-year follow-up, reinforced the benefit of adjuvant RT in improving DFS and preventing relapses, demonstrating its long-term effectiveness.

The study by Paulson et al. (2023) proposed a selective RT deintensification approach, demonstrating that reducing treatment intensity did not compromise outcomes in intermediate-risk patients, which is in line with recent guidelines advocating therapeutic individualization. The study was a retrospective, multicenter study conducted in Canada with 1,003 patients with stage II EC. The objective was to evaluate the possibility of selective deintensification of adjuvant treatment. This trend is further explored in the international PORTEC-4a clinical trial (van den Heerik et al., 2020), which introduced the use of molecular profiling to guide RT indications. Preliminary results indicate that patients with favorable tumor profiles can be spared RT without oncological detriment, while those with unfavorable profiles benefit from intensified treatment. The study presents the design of the international PORTEC-4a clinical trial, a randomized trial that proposes an innovative approach to the adjuvant treatment of women with high-intermediate-risk EC. Conducted in several European centers, the study includes approximately 500 patients and aims to compare standard treatment with a strategy based on the tumor's molecular profile (classification into groups such as ultramutated POLE, microsatellite instability, abnormal p53, among others).

Regarding aggressive histologies, such as serous carcinoma, the study by Akingbade et al. (2024) demonstrated that combination therapy (CRT) was superior to RT or QT alone, providing better OS and DFS rates. Most recurrences were distant, reinforcing the need for a more comprehensive systemic approach for this histological subtype. The study is a retrospective analysis conducted at a single Canadian center, including 50 patients with stage I and II serous EC, followed for 20 years. The objective was to evaluate the clinical outcomes of different adjuvant treatment strategies, including RT, chemotherapy, and CRT. In the field of gynecological oncology, the work of Ren et al. (2022) and van den Heerik et al. (2022) directly addresses the role of RT in the treatment of early-stage EC. Ren et al. performed a competing risk analysis to identify recurrence patterns after postoperative RT, showing that most recurrences occur distantly, while RT is effective in locoregional control. Van den Heerik et al. discuss the management of VBT in patients with stage I and II EC, highlighting its efficacy and favorable toxicity profile, especially compared to EBRT.

Complementing this perspective, the study by Gadducci et al. (2023) offers a comprehensive overview of endometrial stromal tumors, covering everything from epidemiological and biological aspects to therapeutic options and clinical outcomes. Although not focused exclusively on RT, the article reinforces the importance of a multidisciplinary approach and accurate histological characterization to guide treatment, which aligns with the trend toward therapeutic personalization observed in previous studies. In the context of neurooncology, Lee et al. (2025) investigated the toxicities associated with adjuvant RT in

patients with atypical meningioma. The authors identified significant adverse effects, such as fatigue, cognitive dysfunction, and neurological changes, highlighting the need to weigh the risks and benefits of RT in tumors with uncertain behavior. This concern about toxicity is also relevant to the management of gynecological cancer, especially when considering the choice between modalities such as EBRT and VBT.

Finally, Muffly et al. (2023) explored the impact of the specialized treatment environment on the survival of young patients with acute lymphoblastic leukemia. Although the focus is hematologic, the study highlights that institutional infrastructure and team expertise directly influence clinical outcomes, an observation that can be extrapolated to the treatment of EC, as demonstrated by Goel et al. (2023) in another related study. Centralizing care in specialized centers tends to improve adherence to protocols, reduce complications, and optimize therapeutic outcomes. The study, conducted at a specialized center in India, showed that surgical treatment followed by adjuvant RT resulted in high OS rates (90.6% at three years) with a low recurrence rate, highlighting the importance of institutional expertise in therapeutic management. Adjuvant RT plays a relevant role in reducing locoregional recurrence and improving DFS, especially in patients with defined risk factors. Its impact on OS is more evident in subgroups with unfavorable characteristics, and its indication should be guided by clinical, histological, and molecular criteria. The current trend is toward personalized treatment, with increasing use of biomarkers to guide therapeutic decisions and avoid overtreatment, promoting greater efficacy and safety in the management of early-stage EC.

In another study by Ren et al. (2022), involving 858 Chinese patients, a competing risk analysis was performed to identify patterns of recurrence after postoperative RT. The results showed that the combination of EBRT with VBT significantly reduced locoregional recurrence in high-risk patients, reinforcing the importance of the combined approach in certain profiles.

Finally, Arslan et al. (2020) conducted a retrospective study in Turkey with 311 patients followed for ten years after treatment for early-stage EC. The results showed that adjuvant RT was associated with improved disease-free survival and disease-specific survival rates, indicating a lasting benefit of RT in the long term. Table 1 shows the studies analyzed in this systematic review, clearly demonstrating the type of study used, the methodology applied, the results obtained, and the conclusion reached.

Table 1. Characteristics of the Studies Included in the Systematic Review

Title	Authors	Type of study	Methodology	Results	Conclusion
EBRT vs VBT in stage II EC	Narasimhulu et al., 2020	Systematic review and meta-analysis (1168 patients)	Comparison between EBRT and VBT in 7 studies	No significant difference in overall survival; lower toxicity with VBT	VBT is an effective alternative with fewer adverse effects
Adjuvant RT in Stage II EC	Paulson et al., 2023	Multicenter retrospective	Evaluation of selective RT	Similar survival with	RT can be adjusted

		study (1003 patients)	deintensification	lower toxicity in selected groups	according to individual risk
Recurrence Features in Early-stage EC after RT	Ren et al., 2022	Retrospective study (756 patients)	Analysis of recurrence patterns and prognostic factors	Most recurrences were distant; RT effective in local control	RT may be useful as salvage treatment in locoregional recurrences
Early EC: Experience and outcomes	Goel et al., 2023	Retrospective study (98 patients)	Clinical data analysis at an Indian cancer center	Overall survival of 90.6% at 3 years; low recurrence rate	Treatment in a specialized center improves staging and outcomes
Recurrent patterns after RT in early EC	Ren et al., 2022	Retrospective study (858 patients)	Competing risk model for recurrence patterns	EBRT±VBT reduced locoregional recurrence in high-risk groups	RT should be adapted according to risk profile and recurrence pattern
Practice patterns of adjuvant RT in China	Wang et al., 2023	Retrospective multicenter study (1227 patients)	Analysis of practice patterns in 13 Chinese centers	Increased use of isolated VBT; EBRT maintained at high risk	Progressive shift to VBT at intermediate risk; EBRT still essential at high risk
Improved DFS with adjuvant RT in early EC	Arslan et al., 2020	Retrospective study (311 patients)	10-year survival analysis	RT associated with better DFS and DSS; absence of RT was an unfavorable factor	RT improves long-term survival in stage I-II
PORTEC-4a: molecular profile-based adjuvant treatment	van den Heerik et al., 2020	Randomized clinical trial (9500 patients expected)	Comparison between standard and molecular profile-based treatment	Preliminary results indicate a reduction in overtreatment	Molecular profile-guided treatment can optimize efficacy and reduce toxicity
Adjuvant Treatment of Stage I-II Serous EC	Akingbade et al., 2024	Institutional retrospective study (50 patients)	Comparison between RT, QT and CRT	CRT had better survival than CT; RT alone showed no benefit	CRT is superior in serous histology; recurrences were mostly distant

Not all stage I and II EC are created equal: Recurrence-free survival and cause-specific survival after observation or VBT alone	Garzon et al., 2022	Multicenter retrospective study (1382 patients)	Survival assessment in risk subgroups treated with observation or VBT	VBT improved recurrence-free survival in high risk; sufficient observation in low risk	Treatment must be individualized according to risk profile
Management of stage II EC and subsequent oncologic outcomes: a National Cancer Database study	Vetter et al., 2020	Retrospective population-based study (4190 patients)	Analysis of NCDB data on treatment and survival	RT associated with better survival in patients with additional risk factors	RT may benefit patients with unfavorable stage II features
Association Between Adjuvant Therapy and Survival in Stage II-III EC: Influence of Malignant Peritoneal Cytology	Matsuo et al., 2021	Multicenter retrospective study (5432 patients)	Evaluation of the impact of malignant peritoneal cytology on the efficacy of adjuvant therapy	Positive cytology associated with worse prognosis; RT+CT showed better survival in this group	Combination therapy may be more effective in patients with malignant peritoneal cytology

Source: The author

Discussion

The study by Narasimhulu et al. (2020) directly compared EBRT with VBT in patients with stage II EC, demonstrating that both modalities showed similar efficacy in terms of OS, but with lower toxicity associated with VBT. This conclusion is reinforced by Garzon et al. (2022), who observed that VBT alone was sufficient to ensure disease control in high-intermediate-risk patients, while observation was safe in low-risk cases, highlighting the importance of prognostic stratification.

In population-based studies, such as that by Vetter et al. (2020), which analyzed more than 4,000 patients, adjuvant RT was associated with better survival rates in patients with unfavorable characteristics, such as high tumor grade and lymphovascular invasion. Similarly, Matsuo et al. (2021) demonstrated that the presence of malignant peritoneal cytology negatively impacts prognosis and that the combination of RT with chemotherapy can significantly improve outcomes in these cases, suggesting that the combined approach should be considered in specific subgroups.

Studies conducted in China, such as those by Ren et al. (2022) and Wang et al. (2023), reinforce the efficacy of RT in

locoregional disease control, especially when combined with VBT in high-risk patients. These findings are consistent with the results of Arslan et al. (2020), who demonstrated a lasting benefit of adjuvant RT in terms of DFS over a ten-year follow-up. On the other hand, the study by Paulson et al. (2023) proposes a selective de-intensification approach to adjuvant treatment, showing that reducing the intensity of RT did not compromise outcomes in intermediate-risk patients, which is in line with the most recent guidelines that advocate therapeutic personalization. This perspective is further explored in the PORTEC-4a clinical trial (van den Heerik et al., 2020), which introduces the use of molecular profiles to guide RT indications, allowing for the avoidance of overtreatment in patients with tumors with favorable biological behavior.

In the context of aggressive histologies, such as serous carcinoma, the study by Akingbade et al. (2024) highlights that combined therapy (RT + QT) offers better survival rates compared to single modalities, demonstrating that histological subtype should be considered when defining the adjuvant strategy.

Taken together, the analyzed studies demonstrate that adjuvant RT plays a relevant role in improving DFS and locoregional control, especially in patients with high risk factors. However, its impact on OS is variable and depends on multiple factors, such as tumor grade, extent of myometrial invasion, presence of malignant peritoneal cytology, and histological subtype.

Conclusion

Studies have shown that RT, especially VBT, is effective in reducing locoregional recurrence and improving DFS, with less toxicity compared to EBRT. In patients with high-risk factors, such as high tumor grade, lymphovascular invasion, or malignant peritoneal cytology, RT, alone or combined with chemotherapy, has shown benefits in OS. The current trend is toward personalized treatment, using molecular profiles to guide RT indications, as evidenced in the PORTEC-4a study. Taken together, the results reinforce that adjuvant RT should be indicated selectively, considering clinical, histological, and biological criteria to optimize outcomes and preserve patient QOL.

Abbreviations

AH – Hypertension, **CRT -** Combination Therapy, **CT-** Chemotherapy, **DFS -** Disease-free Survival, **DM2 -** Type 2 Diabetes, **EBRT -** External Beam Radiation Therapy, **EC -** Endometrial Cancer, **Gy –** Grays, **MeSH -** Controlled Descriptors, **NCDB -** National Cancer Database, **OS -** Overall Survival, **PRISMA -** Preferred Reporting Items for Systematic Reviews and Meta-Analyses, **QoL -** Quality of Life, **RT –** Radiotherapy, **VBT -** Vaginal Brachytherapy.

Prosperous ID Number: 642466

RECEIVED: 2 /June /2025 ● ACCEPTED: 20/October/2025 ● TYPE: REVIEW ●FUNDING: There was no funding for the execution of this study project. ● DECLARATION OF CONFLICTING INTERESTS: The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. ● Availability of data and materials data is available from the corresponding author on reasonable request ● Ethics approval and consent to participate: Not required for the methodology applied

References

Akingbade, A., Fabi, F., Cartes, R., Tsui, J., & Alfieri, J. (2024). Adjuvant Treatment of Stage I-II Serous Endometrial Cancer: A Single Institution 20-Year Experience. *Current oncology (Toronto, Ont.)*, *31*(7), 3758–3770. https://doi.org/10.3390/curroncol31070277

Arslan, S. A., Avcı, G. G., Akkas, E. A., & Guney, Y. (2020). Improved disease-free survival with adjuvant radiotherapy in early-stage endometrial cancer: 10-year outcome analysis. *Journal of contemporary brachytherapy*, *12*(6), 572–578. https://doi.org/10.5114/jcb.2020.101690

Bollen, H., van der Veen, J., Laenen, A., & Nuyts, S. (2021). Recurrence Patterns After IMRT/VMAT in Head and Neck Cancer. *Frontiers in oncology*, *11*, 720052. https://doi.org/10.3389/fonc.2021.720052

Chen, J. J., Shah, J. L., Harris, J. P., Bui, T. T., Schaberg, K., Kong, C. S., Kaplan, M. J., Divi, V., Schoppy, D., Le, Q. T., & Hara, W. Y. (2017). Clinical Outcomes in Elderly Patients Treated for Oral Cavity Squamous Cell Carcinoma. *International journal of radiation oncology, biology, physics*, *98*(4), 775–783. https://doi.org/10.1016/j.ijrobp.2017.03.017

Cibula, D., Raspollini, M. R., Planchamp, F., Centeno, C., Chargari, C., Felix, A., Fischerová, D., Jahnn-Kuch, D., Joly, F., Kohler, C., Lax, S., Lorusso, D., Mahantshetty, U., Mathevet, P., Naik, R., Nout, R. A., Oaknin, A., Peccatori, F., Persson, J., Querleu, D., … Lindegaard, J. (2023). ESGO/ESTRO/ESP Guidelines for the management of patients with cervical cancer - Update 2023. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *33*(5), 649–666. https://doi.org/10.1136/ijgc-2023-004429

Concin, N., Matias-Guiu, X., Cibula, D., Colombo, N., Creutzberg, C. L., Ledermann, J., Mirza, M. R., Vergote, I., Abu-Rustum, N. R., Bosse, T., Chargari, C., Espenel, S., Fagotti, A., Fotopoulou, C., Gatius, S., González-Martin, A., Lax, S., Levy, B., Lorusso, D., Macchia, G., … Nout, R. A. (2025). ESGO-ESTRO-ESP guidelines for the management of patients with endometrial carcinoma: update 2025. *The Lancet. Oncology*, *26*(8), e423–e435. https://doi.org/10.1016/S1470-2045(25)00167-6

Creutzberg, C. L., & Nout, R. A. (2011). The role of radiotherapy in endometrial cancer: current evidence and trends. *Current oncology reports*, *13*(6), 472–478. https://doi.org/10.1007/s11912-011-0191-y

Dallaire Nantel, L., Renaud, M. C., Gregoire, J., Sebastianelli, A., & Plante, M. (2021). High-grade endometrial carcinoma limited to the endometrium or a polyp: is adjuvant treatment necessary?. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *31*(10), 1335–1340. https://doi.org/10.1136/ijgc-2021-002771

de Boer, S. M., Nout, R. A., Jürgenliemk-Schulz, I. M., Jobsen, J. J., Lutgens, L. C., van der Steen-Banasik, E. M., Mens, J. W., Slot, A., Stenfert Kroese, M. C., Oerlemans, S., Putter, H., Verhoeven-Adema, K. W., Nijman, H. W., & Creutzberg, C. L. (2015). Long-Term Impact of Endometrial Cancer Diagnosis and Treatment on Health-Related Quality of Life and Cancer Survivorship: Results From the Randomized PORTEC-2 Trial. *International journal of radiation oncology, biology, physics*, *93*(4), 797–809. https://doi.org/10.1016/j.ijrobp.2015.08.023

Gadducci, A., Multinu, F., De Vitis, L. A., Cosio, S., Carinelli, S., & Aletti, G. D. (2023). Endometrial stromal tumors of the uterus: Epidemiology, pathological and biological features, treatment options and clinical outcomes. *Gynecologic oncology*, *171*, 95–105. https://doi.org/10.1016/j.ygyno.2023.02.009

Garzon, S., Grassi, T., Mariani, A., Kollikonda, S., Weaver, A. L., McGree, M. E., Petersen, I. A., Weroha, S. J., Glaser, G. E., Langstraat, C. L., Amarnath, S. R., & AlHilli, M. M. (2022). Not all stage I and II endometrial cancers are created equal: Recurrence-free survival and cause-specific survival after observation or vaginal brachytherapy alone in all subgroups of early-stage high-intermediate and high-risk endometrial cancer. *Gynecologic oncology*, *167*(3), 444–451. https://doi.org/10.1016/j.ygyno.2022.10.004

Goel, P., Singh, V., Sharma, R., Chaudhary, D., Chatterjee, A., Dora, T., Sancheti, S., Goel, A., Khandelwal, S., Sali, A. P., Kaur, H., Guru, A., & Kapoor, R. (2023). Early endometrial carcinoma: Experience and outcomes. *Journal of cancer research and therapeutics*, *19*(Supplement), S0. https://doi.org/10.4103/jcrt.jcrt_920_21

Holloway, R. W., Abu-Rustum, N. R., Backes, F. J., Boggess, J. F., Gotlieb, W. H., Jeffrey Lowery, W., Rossi, E. C., Tanner, E. J., & Wolsky, R. J. (2017). Sentinel lymph node mapping and staging in endometrial cancer: A Society of Gynecologic Oncology literature review with consensus recommendations. *Gynecologic oncology*, *146*(2), 405–415. https://doi.org/10.1016/j.ygyno.2017.05.027

Instituto Nacional de Câncer José Alencar Gomes da Silva. (2022). Estimativa 2023: Incidência do câncer no Brasil. INCA. https://www.gov.br/inca/pt-br/assuntos/cancer/numeros/estimativa

Keys, H. M., Roberts, J. A., Brunetto, V. L., Zaino, R. J., Spirtos, N. M., Bloss, J. D., Pearlman, A., Maiman, M. A., Bell, J. G., & Gynecologic Oncology Group (2004). A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in

intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecologic oncology*, *92*(3), 744–751. https://doi.org/10.1016/j.ygyno.2003.11.048
Latif, N. A., Haggerty, A., Jean, S., Lin, L., & Ko, E. (2014). Adjuvant therapy in early-stage endometrial cancer: a systematic review of the evidence, guidelines, and clinical practice in the U.S. *The oncologist*, *19*(6), 645–653. https://doi.org/10.1634/theoncologist.2013-0475
Lee, G., Aitelli, A., Niemierko, A., Lamba, N., Kim, D. W., Curry, W. T., Oh, K. S., Barker, F. G., 2nd, & Shih, H. A. (2025). Toxicities Associated with Adjuvant Radiation Therapy in Atypical Meningioma. *Advances in radiation oncology*, *10*(3), 101726. https://doi.org/10.1016/j.adro.2025.101726
Martínez, A., Chargari, C., Kalbacher, E., Gaillard, A. L., Leary, A., Koskas, M., Chopin, N., Serre, A. A., Hardy-Bessard, A. C., Akladios, C., & Lecuru, F. (2023). Recommandations pour la pratique clinique Nice/Saint-Paul-de-Vence 2022–2023 : prise en charge du cancer de l'endomètre localisé. *Bulletin du cancer*, *110*(6S), 6S20–6S33. https://doi.org/10.1016/S0007-4551(23)00331-4
Matsuo, K., Matsuzaki, S., Nusbaum, D. J., Roman, L. D., Wright, J. D., Harter, P., & Klar, M. (2021). Association Between Adjuvant Therapy and Survival in Stage II-III Endometrial Cancer: Influence of Malignant Peritoneal Cytology. *Annals of surgical oncology*, *28*(12), 7591–7603. https://doi.org/10.1245/s10434-021-09900-4
Morén, B., Larsson, T., & Tedgren, Å. C. (2021). Optimization in treatment planning of high dose-rate brachytherapy - Review and analysis of mathematical models. *Medical physics*, *48*(5), 2057–2082. https://doi.org/10.1002/mp.14762
Muffly, L. S., Parsons, H. M., Miller, K., Li, Q., Brunson, A., & Keegan, T. H. (2023). Impact of Specialized Treatment Setting on Survival in Adolescent and Young Adult ALL. *JCO oncology practice*, *19*(12), 1190–1198. https://doi.org/10.1200/OP.23.00373
Narasimhulu, D. M., Cope, A., Riaz, I. B., Petersen, I., Cilby, W., Langstraat, C., Glaser, G., Kumar, A., Cappuccio, S., Murad, M. H., West, C., & Mariani, A. (2020). External beam radiotherapy versus vaginal brachytherapy in patients with stage II endometrial cancer: a systematic review and meta-analysis. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *30*(6), 797–805. https://doi.org/10.1136/ijgc-2020-001199
Nout, R. A., Smit, V. T., Putter, H., Jürgenliemk-Schulz, I. M., Jobsen, J. J., Lutgens, L. C., van der Steen-Banasik, E. M., Mens, J. W., Slot, A., Kroese, M. C., van Bunningen, B. N., Ansink, A. C., van Putten, W. L., Creutzberg, C. L., & PORTEC Study Group (2010). Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial. *Lancet (London, England)*, *375*(9717), 816–823. https://doi.org/10.1016/S0140-6736(09)62163-2
Paulson, K., Logie, N., Han, G., Tilley, D., Menon, G., Menon, A., Nelson, G., Phan, T., Murray, B., Ghosh, S., Pearcey, R., Huang, F., & Wiebe, E. (2023). Adjuvant Radiotherapy in Stage II Endometrial Cancer: Selective De-intensification of Adjuvant Treatment. *Clinical oncology (Royal College of Radiologists (Great Britain))*, *35*(1), e94–e102. https://doi.org/10.1016/j.clon.2022.08.034
Poitevin-Chacón, A., & Hinojosa-Gómez, J. (2012). Patterns of care of radiotherapy in México. *Reports of practical oncology and radiotherapy : journal of Greatpoland Cancer Center in Poznan and Polish Society of Radiation Oncology*, *18*(2), 57–60. https://doi.org/10.1016/j.rpor.2012.09.001
Randall, M. E., Filiaci, V., McMeekin, D. S., von Gruenigen, V., Huang, H., Yashar, C. M., Mannel, R. S., Kim, J. W., Salani, R., DiSilvestro, P. A., Burke, J. J., Rutherford, T., Spirtos, N. M., Terada, K., Anderson, P. R., Brewster, W. R., Small, W., Aghajanian, C. A., & Miller, D. S. (2019). Phase III Trial: Adjuvant Pelvic Radiation Therapy Versus Vaginal Brachytherapy Plus Paclitaxel/Carboplatin in High-Intermediate and High-Risk Early Stage Endometrial Cancer. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*, *37*(21), 1810–1818. https://doi.org/10.1200/JCO.18.01575
Ren, K., Wang, W., Sun, S., Hou, X., Hu, K., & Zhang, F. (2022). Recurrent patterns after postoperative radiotherapy for early stage endometrial cancer: A competing risk analysis model. *Cancer medicine*, *11*(1), 257–267. https://doi.org/10.1002/cam4.4423
Ren, K., Wang, W., Sun, S., Wang, D., Liu, X., Hou, X., Hu, K., & Zhang, F. (2022). Recurrence Features and Factors influencing Post-relapse Survival in Early-stage Endometrial Cancer after Adjuvant Radiotherapy. *Journal of Cancer*, *13*(1), 202–211. https://doi.org/10.7150/jca.65246
Saldi, S., Bellavita, R., Lancellotta, V., Palumbo, I., Lupattelli, M., Chierchini, S., Falcinelli, L., Zucchetti, C., Bini, V., & Aristei, C. (2019). Acute Toxicity Profiles of Hypofractionated Adjuvant and Salvage Radiation Therapy After Radical Prostatectomy: Results of a Prospective Study. *International journal of radiation oncology, biology, physics*, *103*(1), 105–111. https://doi.org/10.1016/j.ijrobp.2018.08.016
Sloboda R. S. (1992). Optimization of brachytherapy dose distributions by simulated annealing. *Medical physics*, *19*(4), 955–964. https://doi.org/10.1118/1.596783
van den Heerik, A. S. V. M., Horeweg, N., Creutzberg, C. L., & Nout, R. A. (2022). Vaginal brachytherapy management of stage I and II endometrial cancer. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *32*(3), 304–310. https://doi.org/10.1136/ijgc-2021-002493
van den Heerik, A. S. V. M., Horeweg, N., Nout, R. A., Lutgens, L. C. H. W., van der Steen-Banasik, E. M., Westerveld, G. H., van den Berg, H. A., Slot, A., Koppe, F. L. A., Kommoss, S., Mens, J. W. M., Nowee, M. E., Bijmolt, S., Cibula, D., Stam, T. C., Jurgenliemk-Schulz, I. M., Snyers, A., Hamann, M., Zwanenburg, A. G., Coen, V. L. M. A., … Creutzberg, C. L. (2020). PORTEC-4a: international randomized trial of molecular profile-based adjuvant treatment for women with high-intermediate risk endometrial cancer. *International journal of gynecological cancer : official journal of the International Gynecological Cancer Society*, *30*(12), 2002–2007.

https://doi.org/10.1136/ijgc-2020-001929
Vetter, M. H., Bixel, K., & Felix, A. S. (2020). Management of stage II endometrial cancer and subsequent oncologic outcomes: a National Cancer Database study. *Journal of gynecologic oncology*, *31*(6), e84. https://doi.org/10.3802/jgo.2020.31.e84
Wang, W., Wang, T., Liu, Z., He, J., Sun, X., Zhong, W., Zhao, F., Li, X., Li, S., Zhu, H., Ma, Z., Hu, K., Zhang, F., Hou, X., Wei, L., & Zou, L. (2023). Practice patterns of adjuvant radiotherapy in women with stage I to II endometrial carcinoma: a real-world multi-institutional analysis in China. *BMC women's health*, *23*(1), 417. https://doi.org/10.1186/s12905-023-02548-0
Wortman, B. G., Creutzberg, C. L., Putter, H., Jürgenliemk-Schulz, I. M., Jobsen, J. J., Lutgens, L. C. H. W., van der Steen-Banasik, E. M., Mens, J. W. M., Slot, A., Kroese, M. C. S., van Triest, B., Nijman, H. W., Stelloo, E., Bosse, T., de Boer, S. M., van Putten, W. L. J., Smit, V. T. H. B. M., Nout, R. A., & PORTEC Study Group (2018). Ten-year results of the PORTEC-2 trial for high-intermediate risk endometrial carcinoma: improving patient selection for adjuvant therapy. *British journal of cancer*, *119*(9), 1067–1074. https://doi.org/10.1038/s41416-018-0310-8