SYMPOSIUM

CERVICAL CANCER

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Current treatment of cervical cancer: progress and prospects

Tratamiento actual del cáncer de cuello uterino: avances y perspectivas

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ABSTRACT

Standard treatment for early cervical cancer is mainly by laparotomy. Lymph node assessment is essential, utilizing sentinel lymph nodes and pelvic lymphadenectomy. If intraoperative lymph node involvement is identified, it is preferable to avoid dissection and opt for chemoradiotherapy. Radical type C hysterectomy is the usual approach, although extrafascial hysterectomy may be considered in low-risk patients. The SHAPE study suggests that there are no significant differences in recurrence-free survival between the two types of hysterectomy. In young women who wish to preserve their fertility, conization or radical trachelectomy are viable options in stages IA2-IB1. In stages IB3 and IIA2, concurrent chemoradiotherapy is preferred and has shown more favorable survival results. Neoadjuvant chemotherapy is applied in settings where radiotherapy is not available. For patients with early disease, radiotherapy may be an alternative if there are contraindications to surgery. Finally, adjuvant radiotherapy is recommended for patients with high-risk factors after surgery, while low-risk patients do not require additional treatment, thus allowing for a personalized approach based on individual patient characteristics.

Key words: Uterine cervical neoplasms, Laparoscopy, Hysterectomy

RESUMEN

El tratamiento estándar del cáncer de cuello uterino en estadios tempranos se realiza principalmente por laparotomía. La evaluación de los ganglios linfáticos es fundamental, determinada por los ganglios centinela y la linfadenectomía pélvica. Si se identifica compromiso ganglionar intraoperatorio, es preferible evitar la disección y optar por quimiorradioterapia. La histerectomía radical tipo C es el enfoque habitual, aunque en pacientes de bajo riesgo puede considerarse una histerectomía extrafascial. El estudio SHAPE sugiere que no hay diferencias significativas en la supervivencia libre de recurrencia entre ambos tipos de histerectomía. En las mujeres jóvenes que desean preservar su fertilidad, la conización o la traquelectomía radical son opciones viables en estadios IA2-IB1. En los estadios IB3 y IIA2 se prefiere la quimiorradioterapia concurrente, que ha mostrado resultados de supervivencia más favorables. La quimioterapia neoadyuvante se aplica en contextos donde la radioterapia no está disponible. Para pacientes con enfermedad temprana, la radioterapia puede ser una alternativa si existen contraindicaciones para la cirugía. Finalmente, se recomienda la radioterapia adyuvante para pacientes con factores de alto riesgo posterior a la cirugía, mientras que las pacientes de bajo riesgo no requieren tratamiento adicional, permitiendo así un enfoque personalizado en función de las características individuales de cada paciente.

Palabras clave. Neoplasias del cuello uterino, Laparoscopy, Histerectomía

Introducción

In recent years, significant changes have been made in the management of cervical cancer. In 2018, the LACC (Laparoscopy Approach for Cervical Cancer) study by Ramirez et al. reported a higher risk of death with laparoscopic surgery compared to laparotomy in cases of invasive cervical cancer in early clinical stages[1]. The recent publication of the SHAPE trial (Radical Versus Simple Hysterectomy and Pelvic Node Dissection in Patients With Low-Risk Early Stage Cervical Cancer) showed that simple hysterectomy is not inferior to radical hysterectomy in patients with tumor lesions < 2 cm with limited stromal invasion, in terms of survival and recurrence for the treatment of early stage cervical cancer[2]. The arrival of precision therapy, specifically with immunotherapy using pembrolizumab, has shown a substantially higher recurrence-free survival and overall survival compared to placebo in patients with locally advanced or metastatic cervical cancer[3,4].

Context and rationale

In recent years, the treatment of cervical cancer has undergone important advances driven by increasing and ongoing high-quality studies and robust scientific evidence. These developments have provided new tools to improve survival at different stages of the disease, whether in early, locally advanced, metastatic or recurrent stages.

One of the key principles in modern surgery for early clinical stages is the personalization of surgical radicality. Instead of applying a 'one-size-fits-all' solution to all cases, there has been a move towards individualized surgical approaches.

The current trend in radical surgery is the transition towards less invasive techniques, adapted to the specific characteristics of the risk.

In addition, fertility preservation has become a crucial aspect for women of childbearing age. Current techniques make it possible to achieve oncologic results comparable to those of radical hysterectomy, while offering an adequate rate of chances of pregnancy.

The aim of this section is to provide a clear and comprehensive view of the appropriate management of cervical cancer, considering the different clinical scenarios and stages.

Recommendations

1. **Centralization of care:** It is suggested that the management of cervical cancer be centralized in specialized centers and integrated oncologic networks at the national level.

2. **Multidisciplinary planning:** Implement multidisciplinary planning based on a comprehensive knowledge of the prognostic and predictive factors of oncologic outcomes.

3. **Comprehensive patient counseling:** Provide patients with counseling on available treatment alternatives, including a clear assessment of the associated risks and benefits.

4. **Promotion of clinical trials:** Promote the management of patients within clinical trials, facilitating access to innovative treatments and contributing to the advancement of research in this area[5].

Staging of cervical cancer

The staging of cervical cancer (Table 1) has evolved over the years, driven by a better understanding of the disease and of prognostic and predictive factors for recurrence and survival. Patients should be staged according to the 2021 AJCC (American Joint Committee on Cancer) TNM (Tumor-Node-Metastasis) classification[6] and the 2018 FIGO classification[7]. Documentation and integration of clinical, pathologic, and imaging findings is essential to ensure appropriate and personalized management of cervical cancer.

Stages and definitions according to FIGO (International Federation of Gynecology and Obstetrics)

- Stage I: The carcinoma is confined exclusively to the cervix (extension to the body of the uterus is not included).
  - IA: Invasive carcinoma detected solely by microscopy, with an invasion depth of ≤5 mm.
    - IA1: Stroma invasion ≤3 mm in depth.
    - IA2: Stromal invasion between 3 mm and 5 mm in depth.
  - IB: Carcinoma with invasion beyond 5 mm (beyond stage IA) but limited to the cervix, with the tumor size measured by its maximum diameter.
    - IB1: Stromal invasion >5 mm and tumor ≤2 cm in its greatest dimension.
    - IB2: Stromal invasion >2 cm and ≤4 cm in its greatest dimension.
    - IB3: Invasive tumor larger than 4 cm.
- Stage II: The carcinoma invades beyond the uterus but does not affect the lower third of the vagina or the pelvic wall.
  - IIA: Invasion limited to the upper two-thirds of the vagina without affecting the parametrium.
    - IIA1: Carcinoma ≤4 cm.
    - IIA2: Carcinoma >4 cm.

  - IIB: With involvement of the parametrium, but not reaching the pelvic wall.

- Stage III: The carcinoma affects the lower third of the vagina, extends to the pelvic wall, causes hydronephrosis or a non-functional kidney, or affects the pelvic and/or para-aortic lymph nodes.

  - IIIA: Invasion of the lower third of the vagina without reaching the pelvic wall.

  - IIIB: Extension to the pelvic wall and/or provocation of hydronephrosis or renal dysfunction (unless another cause is known).

  - IIIC: Involvement of pelvic and/or para-aortic lymph nodes, regardless of the size or extent of the tumor.

    - IIIC1: Metastasis only in pelvic lymph nodes.

    - IIIC2: Metastasis in paraaortic lymph nodes.

- Stage IV: The carcinoma extends beyond the pelvis or involves the mucosa of the bladder or rectum. The presence of bullous edema does not indicate this stage.

  - IVA: Propagation to nearby organs.

  - IVB: Propagation to distant organs.

Additional notes:

- To complement clinical findings, both imaging and pathology can be used, particularly regarding the size and extent of the tumor at any stage.

- The involvement of vascular and lymphatic spaces does not alter the classification, and the lateral extension of the lesion is not considered in this staging.

- Isolated tumor cells do not modify the stage, but their presence must be recorded.

- A notation "r" (for radiological findings) or "p" notation (for pathological findings) must be added in stage IIIC to document how lymph node involvement was determined. For example, IIIC1r if metastases are detected by imaging, or IIIC1p if confirmed by pathology. The method used to determine the stage must be documented.

Adapted from FIGO 2021[8]

Surgical treatment

Surgery is the main treatment modality for early-stage cervical cancer in early stages (stage IA-IIA). Surgical interventions include hysterectomy and lymphadenectomy. To more accurately describe the extent of surgical excision, the Querleu-Morrow (QM) classification offers a simple and universal tool for assigning different levels of radicality. Another relevant classification is that of Piver, published in 1974[9].

Querleu-Morrow (Q-M) Classification System: Published in 2008 and updated in 2017, the QM classification describes the degree of resection and nerve preservation in three-dimensional (3D) planes of resection (Table 2). This system includes two components: surgical grading of the uterus and lymph node dissection. Surgical staging is related to the extent of parametrectomy, which is divided according to specific anatomical structures.

Classification of lymph node dissection

The extent of retroperitoneal lymphadenectomy is divided into four levels according to the anatomical markers of the arteries. Obturator lymph nodes are routinely resected by default.

- **Level 1:** Removal of lymph node tissues from the external and internal iliac arteries. The boundary with grade 2 is marked by the bifurcation of the internal and external iliac arteries.

- **Level 2:** Excision of ganglionic tissues of the common iliac artery. The limit with grade 3 is marked by the bifurcation of the abdominal aorta.

- **Level 3:** Removal of para-aortic lymph node tissues up to the level of the inferior mesenteric artery.

- **Level 4:** Extirpation of para-aortic ganglionic tissues up to the level of the renal veins[11].

Early clinical stage disease: Early clinical stage disease refers to clinical-radiological stages IA to IIA1. Fertility-preserving surgical treatments are not recommended for non-HPV-associated adenocarcinomas and neuroendocrine tumors, due to their high-risk nature.

Microscopic (non-visible) invasive carcinoma disease: The diagnosis of clinical stage IA tumors is based on microscopic pathological examinations performed by an expert pathologist. This includes analysis of conization specimens with negative margins of invasive disease or high-grade dysplasia (HSIL).

Treatment of stage IA1 disease

No desire for fertility preservation

In situations where a conization has been performed, and provided there is no invasion in the lymphovascular space (LVS) or cancerous cells at the surgical margins, an extrafascial hysterectomy is suggested for women who have completed their reproductive stage or for older women. This intervention can be performed through abdominal, vaginal, or minimally invasive techniques[12].

Desire for fertility preservation

In fertility preservation, it is essential that the margins of the cone be negative and that there be no lymphovascular invasion. In the absence of these factors, observation may be a viable option. In patients with positive margins after conization, management options include cone biopsy to better assess depth of invasion (to rule out stage IA2/IB disease) or radical trachelectomy with intraoperative evaluation of surgical margins.

In studies of patients with positive margins after conization, predictors of residual disease include positive endocervical curettage, endocervical margin combined with endocervical curettage, and disease volume[15].

Treatment of stage IA2 disease

No desire for fertility preservation

In stage IA2, there is a small risk that the lymph nodes may have metastasis. If there is lymphovascular invasion (LVI), the risk of lymph node involvement increases from 1.3% in the absence of LVI to 12% when it is present. Therefore, it is important to perform an evaluation of the lymph nodes using the sentinel node technique or pelvic lymphadenectomy, along with a type B radical hysterectomy[16,17].

When ILV (lymphovascular space invasion) is evident, pelvic lymphadenectomy or sentinel lymph node evaluation should be considered, as the risk of lymph node involvement can reach up to 8.2%. If there is no ILV, the risk is less than 1%, along with the extrafascial hysterectomy[13,14,27].

For cases with low-risk criteria (no ILV and negative sentinel node), it is possible to consider a simple hysterectomy or a trachelectomy, combined with pelvic lymphadenectomy or sentinel node evaluation[18,28].

Desire for fertility preservation

If fertility preservation is desired, alternatives to standard treatment can be offered:

1. Cervical conization accompanied by pelvic lymphadenectomy or sentinel lymph node evaluation, either through open surgery or minimally invasive surgery.

2. Radical trachelectomy combined with pelvic lymphadenectomy, which can be performed via laparotomy, vaginal approach, or minimally invasive techniques[19,20].

Recommendation: The performance of minimally invasive surgery in trachelectomy should be discussed in a multidisciplinary team together with the patient. This should be considered in the context of the results of the prospective LACC study[1], which was not designed for fertility preservation surgery. It is also suggested to review the results of the IRTA study[21], a retrospective study comparing fertility preservation surgery with minimally invasive surgery, where no significant differences were found in cases of non-conized tumor. For conized lesions and free margins that do not meet the low-risk criteria, laparoscopic trachelectomy can be considered, in relation to the results of the SUCCOR CONO study[22], which showed a significantly lower risk of relapse and death.

Differences between NCCN and ESGO Guidelines

- NCCN (*Clinical Practice Guidelines in Oncology*): Unequivocally recommends modified radical hysterectomy with lymph node evaluation[23].
- ESGO (*European Society of Gynaecological Oncology*): In cases of negative ILV, suggests simple conization or extrafascial hysterectomy, with the possibility of sentinel node biopsy. Regarding ILV positivity, both guidelines suggest sentinel biopsy and simple hysterectomy[5].

Final recommendation: Decision-making should be based on the personalization and interpretation of risk factors. Consider the SHAPE study by Dr. Plante (2024), which compares radical versus extrafascial hysterectomy, including patients with low-risk criteria and without exclusion for ILV. She found similar results in recurrence-free survival at 3 years between both groups, in relation to the possibility of parametrial compromise and association with ILV[2].

Post-treatment follow-up: After fertility preservation surgery, the following follow-up protocol is recommended:

- **Pap smears:**
  - Every 3 months for the first 2 years.
  - Then semi-annually for the next 3 years.
- If after 5 years the follow-up is satisfactory, the patient can rejoin the routine screening program following national guidelines[24].
- **Additional tests:** Imaging tests are not routinely recommended; they can be performed, if necessary, on a case-by-case basis.

Recommendations

After completion of the desire for childbearing, hysterectomy may be recommended for patients who have received radical trachelectomy or fertility-sparing conization, especially in the following cases:

- Chronic and persistent HPV infection
- Persistent abnormal Pap smears
- Personal desire to perform the surgery[23].

MACROSCOPIC Invasive cervical carcinoma: FIGO IB1, IB2, IIA1

At these stages, the treatment of choice is surgical intervention. This treatment involves a radical hysterectomy type C along with pelvic lymphadenectomy[25].

FIGO stage IB1, IB2, IIA1 treatment

Recommendations

- **Approach route:** Surgery through laparotomy is suggested.
- **Lymph node evaluation:** Should be performed as the first step in surgical treatment, using:
  - Sentinel lymph node biopsy using frozen section technique.
  - Pelvic lymphadenectomy, with preference for the use of indocyanine green or combined technique with blue and radiocolloid as an alternative.
- **Suspected lymph node involvement:** In case of suspicion, an intraoperative frozen section evaluation should be performed.
- **Intraoperative lymph node involvement:** If detected, it is advisable to avoid both dissection and radical hysterectomy. Instead, the patient should be referred to chemoradiotherapy. Inframesenteric paraaortic lymphadenectomy and ovarian suspension can be considered if the patient is of reproductive age.
- **Type of radical hysterectomy:** The choice of the type of hysterectomy should be based on the preoperative evaluation of prognostic factors, such as tumor size and stromal invasion. This allows for preoperative assessment in high, intermediate, and low recurrence risk

groups. It is recommended to follow the modified 2017 version of the Querleu-Morrow classification for a detailed description of the surgical procedure[26].

Low-risk criteria

Stage IB1-IIA1 according to the FIGO classification is classified as low risk if the following criteria are met: the tumor size is less than 2 cm, stromal invasion does not exceed 50%, and no suspicious images of positive nodes are observed.

Standard Treatment

Radical hysterectomy type C: This is the standard treatment modality. However, in selected low-risk cases a modified radical hysterectomy may be recommended. It is essential to always include lymphadenectomy, since a high frequency of pelvic lymph node involvement is reported (21% in lesions smaller than 4 cm) and 3% at the para-aortic level[29,30].

Comparison of treatments: Dr. Plante's SHAPE study (2024) is a non-inferiority study comparing radical versus extrafascial hysterectomy in patients with low-risk criteria. No significant differences in recurrence-free survival at 3 years were found between the two groups[2].

Pelvic nerve sparing: In patients undergoing radical hysterectomy (type C1), as long as radical curability is maintained. Injuries to the intrapelvic autonomic nerves can cause alterations in urination, defecation, and sexual function[29].

Radical trachelectomy: In young women who wish to preserve fertility, it is possible to provide alternatives to standard treatment, such as performing a radical trachelectomy, which is done for tumors in stages IA2-IB1. In this procedure, the cervix and the parametrium are removed, followed by the reconnection of the uterus with the vagina. Trachelectomy can be performed through an open abdominal or vaginal approach.

Ovarian preservation: In premenopausal women younger than 45 years with early squamous cell carcinoma, the risk of ovarian metastasis is low (0.9%). Ovarian preservation may be considered in cases of HPV-related adenocarcinomas, although it is not recommended in HPV-unrelated adenocarcinomas. If the decision is made to preserve the ovaries, a bilateral salpingectomy is suggested[31].

FIGO stage IB2 and IIA1

In FIGO stages IB2 and IIA1 of cervical cancer, both surgery and radiotherapy can be initial treatment options depending on individual patient factors and the resources available at each center, as both approaches show comparable results.

Advantages of surgical treatment:

1. **Precise postoperative staging**: Surgery allows for an exact determination of the stage based on the final pathology findings, which facilitates the personalization of adjuvant treatment, depending on the risk characteristics of recurrence.

2. **Treatment of radiotherapy resistant cancers:** It offers the possibility of addressing tumors that might be less sensitive to radiotherapy.

3. **Preservation of ovarian function:** During the surgery, it is possible to perform an ovarian transposition considering the potential need for subsequent adjuvant treatment.

The preservation of both ovarian function and sexual function makes surgical treatment a preferred option in young patients. An essential component of the surgical procedure is pelvic lymphadenectomy, which includes the removal of pelvic lymph nodes, such as the parametric, obturator, external iliac, internal iliac, and common iliac nodes.

Surgical treatment can be performed through laparotomy or minimally invasive techniques, such as laparoscopy or robotic surgery. However, the LACC trial conducted in 2018, a multicenter and randomized study, demonstrated that minimally invasive techniques are associated with a reduction in overall survival, with a sixfold higher risk of mortality compared to laparotomy. The results of the 4.5-year follow-up of the LACC study, presented in May 2024, confirmed that these findings remain, showing a higher incidence of carcinomatosis in the minimally invasive treatment group, suggesting that laparotomy continues to be the standard of care[32].

Ongoing trials on minimally invasive surgery in cervical cancer

Currently, two prospective randomized trials are underway to investigate the role of minimally invasive surgery in the management of cervical cancer in stages.

- **Robot-assisted approach to cervical cancer (RACC):** It is a Swedish multicenter prospective trial where no uterine manipulator is used and suggests closing the vagina before colpotomy, although it is not a mandatory requirement. The completion of this trial is scheduled for 2027[33].

- **Randomized controlled trial in China:** This multicenter trial will evaluate the use of a uterine manipulator and the vaginal excision method, with a scheduled closing date for 2023[34].

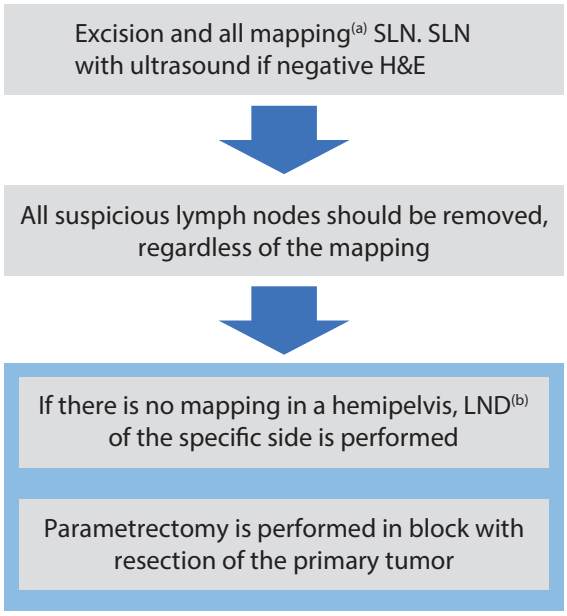
Sentinel node

The sentinel node is a prominent topic in the management of this neoplasm in early stages, incorporated into the NCCN guidelines since 2015. Since then, there has been an increased understanding of its role in staging, especially in the detection of atypical pathways and low-volume disease. Its implementation requires specialized gynecologic oncology centers and is posed as an alternative rather than a specific recommendation. According to NCCN 2024, sentinel node is considered for stages IA1 with lymphovascular invasion (LVI), IA2 and IB1 less than 2 cm. It is essential to properly follow the mapping algorithm (Figure 1) and to perform node evaluation by ultrastaging[35].

FIGO stages IB3 and IIA2

In these stages, the tumor size is greater than 4 cm and there is a high possibility of presenting high-risk factors, such as lymph node involvement, parametrial involvement, or affected surgical margins, which increases the risk of recurrence and makes adjuvant radiotherapy necessary after surgery. Other risk factors that increase the likelihood of pelvic recurrence, even without lymph node involvement, include tumor diameter greater than 4 cm, lymphovascular invasion (ILV) and stromal invasion[36]. In these scenarios, adjuvant pelvic radiotherapy has proven effective in reducing the rate of local failures and improving progression-free survival compared to those treated with surgery alone[37]. It is important that the use of combined treatment modalities can increase the risk of morbidity.

Figure 1. Surgical algorithm for early-stage cervical cancer.



Abbrevitions: SLN=sentinel lymph node, H&E=hematoxylin and eosin staining, LND=lymphadenectomy, a: Intracervical injection with:, b: Includes interiliac/ subaortic nodes
Adapted from: Cormier B, Diaz JP, Shih K, et al. Establishing a sentinel lymph node mapping algorithm for the treatment of early cervical cancer. Gynecol Oncol. 2011;122:275-280.

Therefore, the choice of treatment should be based on the available resources and factors related to the tumor as well as the patient. Concurrent platinum-based chemoradiotherapy (CONCURRENT QT+RT) is the treatment of choice for lesions in stages IB3 to IIA2, as it has been shown that the prognosis in terms of overall survival, progression-free survival, and reduction of local and distant recurrences is more favorable with CONCURRENT QT+RT compared to radical hysterectomy followed by adjuvant radiotherapy.

In places where access to radiotherapy is limited, neoadjuvant chemotherapy (NACT) has been used with the following objectives:

- Reduce the stage of the tumor, improving the possibility of radical and safe surgery.

- Inhibit the appearance of micrometastases and distant metastases.

There is no consensus on whether NACT has improved the prognosis compared to the standard treatment. Two randomized trials, EORTC 55994[38] and the study by Gupta et al[39], had mixed results. EORTC showed no significant difference in 5-year overall survival between NACT and concurrent chemoradiotherapy (CCRT), although chemotherapy-related toxicity was reported in the NACT group. On the other hand, the study by Gupta et al. showed superior disease-free survival in the CCRT group.

The extent of surgery after NACT remains the same, i.e. radical hysterectomy and pelvic lymphadenectomy. However, one should proceed with caution, as NACT can hide pathological findings and complicate the evaluation for adjuvant radiotherapy or CCRT. It is recommended to reserve NACT for research settings or in contexts where radiotherapy is not available, especially in patients with very large tumors or adenocarcinomas, which tend to have lower response rates[40].

Surgery in FIGO stage IVA or recurrent disease

In certain very rare scenarios, patients with stage IVA may present only central involvement, without involving the lateral pelvic wall or showing distant metastasis. In these cases, or in situations of recurrence with similar characteristics, pelvic exenteration with curative intent may be considered; however, it is generally associated with an unfavorable prognosis[41].

Radiotherapy

In low- and middle-income countries, most patients have locally advanced disease, where surgery has a limited role. In the last two decades, the development of advanced planning and delivery techniques, together with the introduction of imaging and computer technologies, have revolutionized the management of radiotherapy enhancing clinical outcomes and reducing toxicity[42]. Likewise, radiotherapy can be used for curative purposes as an adjuvant treatment in patients who have been operated on, with the aim of preventing regional recurrence. However, the use of the 'dual modality' of treatment is not recommended. It can also be used as palliative therapy to relieve severe symptoms in patients with advanced, incurable diseases.

Radiotherapy for early-stage disease (FIGO stages IA, IB1, IB2 and IIA1)

Surgery is the first option in the treatment of early-stage disease, although radiotherapy also offers equivalent results in terms of local control and survival, especially in cases where there are surgical or anesthetic contraindications. The choice of treatment should be based on a thorough evaluation of the patient's conditions, functional status, adverse events, anatomical and social characteristics.

In cases of microinvasive disease, intracavitary radiotherapy (ICRT) has proven to be effective, especially when medical conditions prevent surgical intervention. Additionally, some patients with very small stage IB1 tumors (less than 1 cm) may benefit from ICR alone, specifically if there are contraindications for external beam radiotherapy (EBRT). In general, a dose equivalent to 60-65 Gy is administered at point A. In these cases, the combination of EBRT and ICRT is also considered a viable option.

Adjuvant radiotherapy

After radical surgical treatment, adjuvant radiotherapy, with or without systemic management, is indicated for patients with a high risk of recurrence based on pathological findings. Patients are classified as high, intermediate, or low risk according to certain prognostic factors.

High-risk: In this group, external pelvic radiotherapy (EPRT) combined with chemotherapy is recommended. The GOG 109 trial demonstrated an improvement in overall survival in these cases[44]. This group includes those patients with positive surgical margins, lymph node metastasis, or parametrial invasion

Intermediate risk: These patients require only external pelvic radiotherapy (EPRT) without additional chemotherapy. This group includes those with two of the following three factors: tumors larger than 4 cm, lymphovascular invasion, or deep stromal invasion.

Low-risk: Patients who do not present the mentioned risk factors after radical hysterectomy are considered low risk and do not require adjuvant therapy.

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