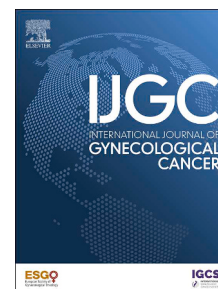


Management of radiation-induced gynecological toxicities: AFSOS-SFCE-GFRCP clinical practice guidelines

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HIGHLIGHTS

- Provides the first multidisciplinary clinical practice guidelines dedicated to radiation-induced gynecological toxicities.
- Proposes a 3-phase management model (before, during, after radiotherapy) tailored to gynecologic toxicities.
- Emphasizes sexual health, fertility preservation, and patient-centered supportive care.
- Introduces practical algorithms for the treatment of radiation-induced vulvovaginitis and vaginal stenosis.
- Integrates pediatric-specific recommendations and addresses premature ovarian failure.

ABSTRACT

Radiation-induced gynecological toxicities are frequently under-recognized, under-diagnosed, and insufficiently managed. These adverse effects negatively impact patients' quality of life and may compromise oncological outcomes by delaying or interrupting cancer treatment. This guideline aims to define best clinical practices for the prevention, identification, and management of both acute and late radiation-induced gynecological toxicities. The French Association for Supportive Care in Cancer (AFSOS) convened a multidisciplinary task force to perform a literature review and apply a consensus methodology to establish these guidelines. External validation was conducted by an independent panel of experts. Optimal management involves a 3-phase approach: before, during, and after radiotherapy. Patients should receive pre-treatment counseling on potential gynecological and sexual side effects, along with preventive hygienic and dietary guidance. During treatment, acute toxicities such as vulvitis, vaginitis, urethritis, and proctitis should be actively managed. Post-radiotherapy care must address vaginal dryness, stenosis, synechiae, premature menopause, lymphedema, and sexual dysfunction, with integration of onco-sexological support as needed. Awareness and proactive management of radiation-induced gynecological toxicities are critical for maintaining quality of life and ensuring treatment continuity. This guideline provides structured recommendations to support clinicians in delivering comprehensive, patient-centered supportive care.

Keywords:

Gynecology; Radiotherapy; Toxicity; Supportive Care; Prevention; Menopause; Sexual Health

INTRODUCTION

Radiation-induced gynecological toxicities remain frequently overlooked and insufficiently addressed within oncologic care, despite their substantial impact on the physical, sexual, and emotional well-being of patients. These adverse effects are often underestimated due to the prevailing emphasis on tumor control, which tends to overshadow patients' lived experiences, particularly in terms of intimate and urogenital function.^{1,2}

The current literature on the epidemiology and clinical management of these toxicities is limited. Radiation can affect all gynecologic organs, and adjacent urinary and digestive structures. With the increasing use of advanced techniques such as intensity-modulated radiation therapy (IMRT), there is a growing concern

regarding late effects, for which long-term data remain scarce. Left unaddressed, these complications may significantly diminish quality of life, not only for patients but also for their partners.^{3,4} Furthermore, they can disrupt clinical care by leading to premature discontinuation of treatment or complicating oncologic follow-up—vaginal stenosis, for example, can hinder adequate pelvic examination and delay the detection of tumor recurrence.⁵

Given these challenges, supportive care must be fully integrated throughout the continuum of cancer therapy. To date, no specific international clinical guidelines exist to address the comprehensive management of radiation-induced gynecological toxicities. The absence of such structured recommendations contributes to heterogeneity in clinical practice and may lead to underdiagnosis or

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suboptimal care. Developing dedicated guidelines is therefore essential to standardize practices, improve symptom recognition, and ensure consistent, high-quality supportive care across institutions.

This guideline, developed under the auspices of the French Association for Supportive Care in Cancer (AFSOS), aims to establish evidence-based best practices for the prevention, identification, and management of both acute and late gynecological toxicities induced by pelvic radiotherapy.

METHODS

These clinical practice guidelines were developed under the coordination of AFSOS, through a collaborative effort involving a multidisciplinary task force composed of 26 healthcare professionals. The initial development—including all task force meetings and drafting of the first reference proposals—took place between autumn 2017 and autumn 2018. A first update, based on a renewed literature review and additional consensus meetings, was carried out in 2020. The present manuscript reflects the latest revision, following another comprehensive bibliography review and a final presentation to the AFSOS J2R in December 2024. The task force brought together expertise from radiation oncology, medical oncology, gynecology, pediatric oncology, pediatric gynecology and endocrinology, pediatric surgery, sexology, and general medicine. Scientific coordination was ensured by 2 radiation oncologists, supported by 2 methodologists and 1 administrative coordinator. An external review was carried out by an additional multidisciplinary national panel of 21 experts to validate the recommendations.

The development process followed a structured 4-step methodology.

- (1) Comprehensive literature review and synthesis phase (autumn 2017–spring 2018; updated in 2020 and 2024)

The comprehensive literature review was conducted in the PubMed database, under the guidance of a professional documentalist. The full search query and filtering strategy are presented in [Appendix 1](#). Search criteria were: radiation-induced gynecological toxicities, neoplasia, fertility with particular attention to definitions, risk factors, pathophysiology, prevention, and therapeutic strategies. Editorials, letters, case reports, and articles published in languages other than English, or French were excluded. Data extraction was carried out independently by 2 members of the task force to ensure rigor and reproducibility. A synthesis of data from the literature was compiled to enable the drafting of reference proposals.

- (2) Drafting phase of the initial version:

A series of virtual meetings and written exchanges allowed the task force to draft the recommendations. These were organized pragmatically and supported by decision-making algorithms and concise evidence summaries. The most notable bibliographic references have been listed.

- (3) Proofreading phase:

The preliminary version of the guidelines was then submitted for external review during the AFSOS National Guidelines Network Day, allowing the review panel to assess, refine, and validate the recommendations by consensus.

- (4) Finalization phase:

Feedback from the multidisciplinary review panel was integrated to refine the final version, which was made publicly available on the AFSOS website in December 2024 (<https://www.afsos.org/fiche-referentiel/toxicites-gynecologiques-radio-induites-cancer/>).

These guidelines are intended to support clinicians in daily practice, without replacing clinical judgment. They are non-regulatory in nature and must be adapted to individual patient profiles and evolving scientific evidence. To ensure ongoing relevance, the recommendations will be reviewed and updated at least every 3 years, in accordance with newly emerging data and clinical advancements. In the absence of high-level evidence on several aspects of this topic, certain recommendations rely primarily on expert consensus. These were established through multidisciplinary discussion and validated by consensus within the task force and external review committee.

Recommendations

Epidemiology

The epidemiology of radiation-induced gynecological toxicities remains insufficiently characterized in the literature. Reported incidence rates vary widely, a discrepancy largely attributable to the lack of standardized grading systems, inconsistent definitions of toxicity, and variable reporting practices across institutions. These adverse effects are observed following external beam radiotherapy or brachytherapy in the treatment of gynecologic malignancies—including cervical, endometrial, vaginal, and vulvar cancers—but they also arise in the context of pelvic irradiation for non-gynecologic tumors, such as those of the rectum, anal canal, bladder, or soft tissue sarcomas.

This variability in clinical contexts, coupled with the evolving nature of radiotherapy techniques, contributes to an underestimation of both the frequency and severity of such toxicities.^{3,6} Advanced modalities, like IMRT, while offering dosimetric advantages, complicate long-term comparisons due to the paucity of mature follow-up data.

Late-onset toxicities, in particular, remain underreported. This is often due to insufficient post-treatment surveillance and the difficulty in attributing delayed symptoms—such as vaginal stenosis, mucosal atrophy, or sexual dysfunction—to prior radiation exposure, especially in complex oncologic trajectories. However, these complications have tangible clinical consequences: they may compromise quality of life, affect intimate relationships, and impede follow-up care by making pelvic examinations painful or even unfeasible, thus delaying the diagnosis of recurrence.

Pathophysiology

Radiation-induced gynecological toxicities are typically categorized into 2 temporal patterns: acute effects, which emerge during or within the first 6 months after its completion, and late effects, which may arise months or even years later. This distinction reflects underlying differences in tissue response and biological mechanisms.

Acute toxicities generally affect rapidly proliferating tissues and appear within the first 6 months following irradiation. These manifestations—such as erythema, mucosal inflammation, or

transient discomfort—are usually reversible and are not considered predictive of late sequelae. They are thought to result predominantly from deterministic radiation effects, which are dose-dependent and follow a predictable threshold-response pattern.

By contrast, late toxicities involve slowly renewing tissues and are frequently irreversible. Their onset is often insidious, and their severity unpredictable. These effects are influenced by both deterministic and stochastic mechanisms, and they may be difficult to distinguish clinically from tumor recurrence, especially when they manifest as ulcerations, fibrosis, or fistulae.⁷

The anatomical diversity of the female pelvis results in organ-specific patterns of injury. The vulva often exhibits early erythema, which can progress to desquamation or, more rarely, acute radionecrosis. Chronic changes such as sclerotic atrophy, telangiectasia, and localized hair loss may persist. Because of the high risk of recurrence in this area, any ulceration warrants close clinical scrutiny.

The vaginal mucosa is particularly vulnerable. Initial epithelial loss may lead to progressive fibrosis, re-epithelialization, and narrowing of the vaginal canal. Vascular damage may result in mucosal ulceration, necrosis, or the formation of fistulae—rectovaginal, vesicovaginal, or urethrovaginal—which carry significant functional and psychological consequences.

The uterus, although less frequently symptomatic, may develop mucosal ulceration and necrosis, followed by fibrotic remodeling. Ovarian tissue is highly radiosensitive, and exposure can lead to significant follicular depletion and architectural disruption, often culminating in premature ovarian insufficiency.⁸ This risk increases with patient age at the time of treatment.

It is important to note that most pelvic organs have a mixed tissue architecture, with both serial and parallel functional sub-units. This complexity influences their radiobiological response and dictates the spatial distribution and severity of radiation injury.⁹

Assessment of Side Effects

The severity of radiation-induced gynecological toxicities is commonly evaluated using the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE), version 5 (Table).¹⁰ The risk of developing toxicities depends on a complex interplay of anatomical, technical, and patient-related factors.^{1,2,11-13} Among the most influential parameters are the volumes irradiated, the total and fractional radiation doses, vaginal dose and the technique employed. Tissue characteristics, such as trophicity, elasticity, and lubrication, are highly dependent on hormonal status and age. Post-menopausal patients, or those undergoing concurrent chemotherapy or targeted therapies, may

Table Classification of Radiation-Induced Gynecological Side Effects According to NCI-CTC AE V5 (National Cancer Institute Common Terminology Criteria for Adverse Events)

Side effect	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Vaginal dryness	Mild vaginal dryness not interfering with sexual function	Moderate vaginal dryness interfering with sexual function or causing frequent discomfort	Severe vaginal dryness resulting in dyspareunia or severe discomfort		Death
Vaginal stricture	Asymptomatic; mild vaginal shortening or narrowing	Vaginal narrowing and/or shortening not interfering with physical examination	Vaginal narrowing and/or shortening interfering with the use of tampons, sexual activity, or physical examination		Death
Vaginitis	Mild discomfort or pain, edema, or redness	Moderate discomfort or pain, edema, or redness; limiting instrumental ADL	Severe discomfort or pain, edema, or redness; limiting selfcare ADL; small areas of mucosal ulceration	Life-threatening consequences; widespread areas of mucosal ulceration; urgent intervention indicated	Death
Dyspareunia	Mild discomfort or pain associated with vaginal penetration; discomfort relieved with use of vaginal lubricants or estrogen	Moderate discomfort or pain associated with vaginal penetration; discomfort or pain partially relieved with use of vaginal lubricants or estrogen	Severe discomfort or pain associated with vaginal penetration; discomfort or pain unrelieved by vaginal lubricants or estrogen		Death
Edema: trunk/genital	Swelling, orange peel skin or altered anatomy on close examination; edema taking up the well	Modified anatomy, easily visible; removal of skin folds and furrows; deviation from normal anatomical contours easily visible	Lymphorrhea; affecting activities of daily living; significant deviation from normal anatomical contours	Progression related to a malignant tumor (ie, disabling lymphangiosarcoma)	Death

exhibit heightened vulnerability to mucosal injury. Surgical interventions prior to radiotherapy—especially extensive tumor or lymph node dissections—can predispose patients to edema and tissue fragility, further increasing susceptibility to late effects. Additional determinants include the size and anatomical location of the primary tumor, its extension into the vaginal canal, and the presence of comorbidities such as diabetes, obesity, or vascular disease. Lifestyle factors like smoking, and pre-existing gynecological symptoms, also contribute to individual radiosensitivity. Moreover, a history of prior irradiation and potential genetic predispositions may amplify the severity of late-onset complications.

In addition to clinical examination, validated screening tools such as the Female Sexual Function Index and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Cervical Cancer Module (EORTC QLQ-CX24) questionnaire can be used to systematically assess sexual dysfunction in women treated with pelvic radiotherapy. Combining these standardized patient-reported outcomes with physical evaluation of vaginal stenosis, mucosal atrophy, and hormonal status enables a more accurate diagnosis and facilitates timely initiation of tailored supportive care interventions.

The repercussions of these toxicities on quality of life are profound. Beyond their physical manifestations, they can disrupt sexual function, alter body image, and generate significant emotional distress.^{4,14} In more severe cases, hospitalization and advanced pain management—including opioid therapy—may be required. In rare but critical situations, toxicities can lead to treatment interruption, thereby compromising oncologic outcomes.

Best Practices in Supportive Oncology Care: A Three-Phase Management Approach

The optimal management of radiation-induced gynecological toxicities hinges on a proactive and continuous strategy encompassing the entire treatment timeline—before, during, and after radiotherapy (Figure 1). Each phase represents a critical window for intervention, combining preventive measures, symptom control, and long-term support to preserve quality of life and treatment adherence (Figure 2).

Before radiotherapy, patient education serves as the cornerstone of effective prevention. During the pre-treatment consultation, the radiation-oncologist should inform patients and their partners about the potential gynecological and sexual side effects of radiation, fostering an open and anticipatory dialogue. Hygienic recommendations—such as wearing breathable cotton underwear and avoiding irritant practices like vaginal douching—should be discussed. Nutritional and psychosocial support may also be proposed, especially in vulnerable individuals. For women aged <35 years, the preservation of fertility must be addressed through timely counseling and referral for ovarian transposition or gamete cryopreservation when appropriate.^{15,16} Patients should be reassured that radiotherapy does not render them radioactive, and that sexual activity remains possible, depending on their comfort.

Preventive care may also include the early initiation of topical treatments—such as vitamin E and zinc-based creams for external application, or hydrating vaginal suppositories (eg, hyaluronic acid-based)—aimed at maintaining mucosal integrity. Where necessary, support systems should be organized in advance, particularly for patients with social fragility or limited autonomy. Patients should also be advised to avoid high-impact

PATIENT-CENTERED CARE MODEL



Figure 1 Three-phase management approach for radiation-induced gynecological toxicities.

pelvic sports from the third or fourth week of treatment onward, and to exercise caution with aquatic activities in the presence of mucosal or cutaneous lesions. Finally, an early referral for onco-sexological consultation may prove beneficial, allowing patients and their partners to address anticipated changes in sexual health and intimacy within a supportive framework.¹⁴

In addition, primary prevention also includes radiotherapy planning optimization. Advances in external beam radiotherapy (ie, IMRT, Volumetric Modulated Arc Therapy (VMAT)) and image-guided adaptive brachytherapy (IGABT) have enabled more precise dose distributions and better sparing of organs at risk, including the vagina. Several studies, including EMBRACE I, have recently reported a high prevalence of vaginal toxicities following radiotherapy and brachytherapy for cervical cancer.^{17,18} In their integrative review, Chin and Damast¹⁹ emphasized the correlation between vaginal dose exposure and the severity of morbidity, underlining the need to systematically consider the vagina as an organ at risk. Importantly, there is now strong evidence of a dose-effect relationship for vaginal morbidity. In the EMBRACE II ongoing study, specific recommendations for vaginal dose constraints have been incorporated.²⁰ EMBRACE II primarily recommends limiting the dose to the recto-vaginal reference point to <65 Gy EQD2 (soft constraint), with an upper limit not to exceed 75 Gy EQD2. Additional secondary planning aims are also described, including the ratio of vaginal TRAK to total Total Reference Air Karma (TRAK), the lateral vaginal reference dose point at 5 mm from the applicator surface, the spatial extent of the 140% isodose, and the dose to the mid and lower vagina, all of which should be carefully monitored to reduce the risk of stenosis and functional impairment.

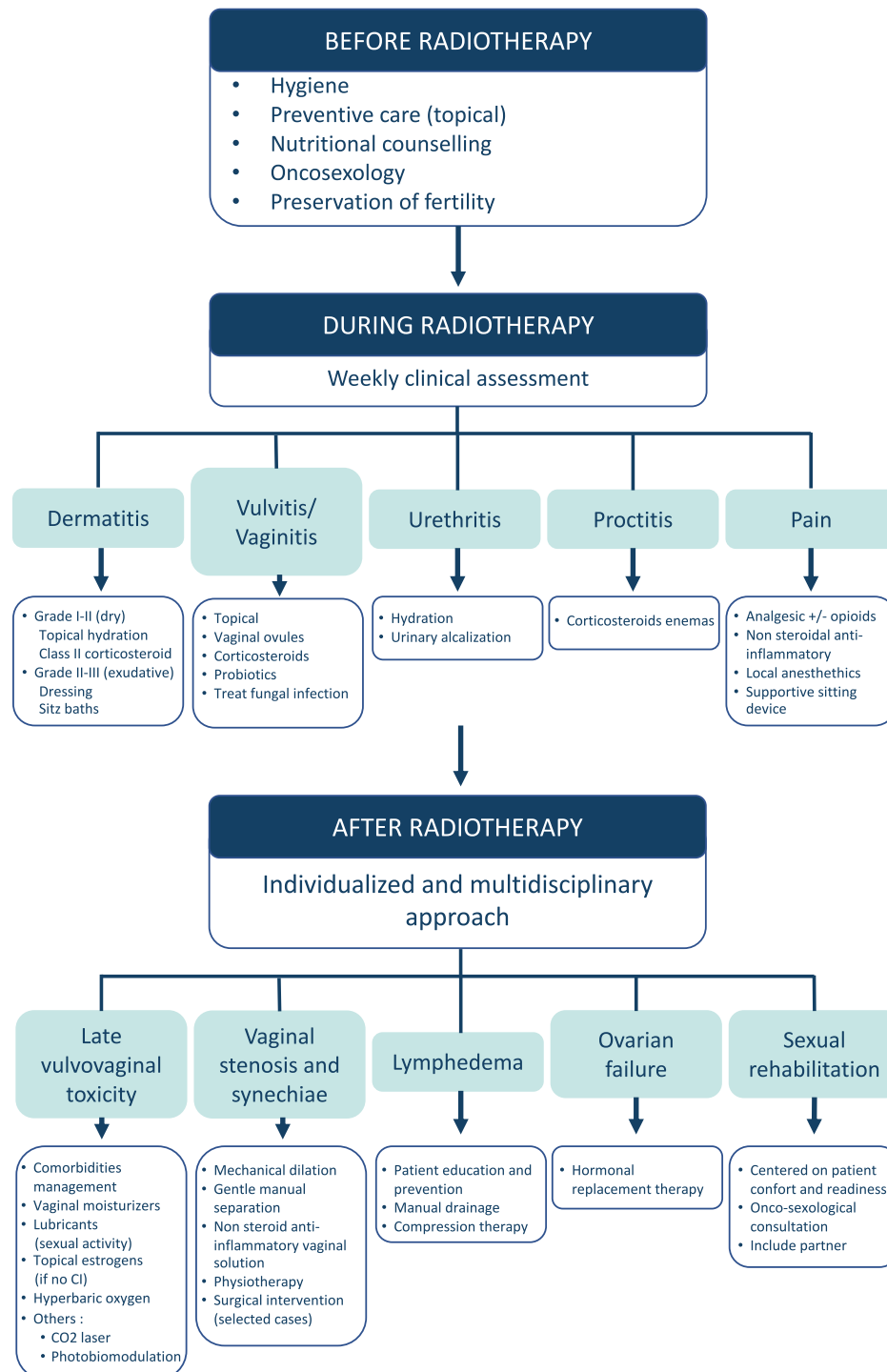


Figure 2 Patient-centered care model for supportive oncology care.

During radiotherapy, close monitoring is essential. Weekly clinical assessments enable early detection and timely management of acute toxicities. Mild-to-moderate dermatitis (grade 1-2) may respond to topical hydration and class II corticosteroid creams,²¹ while more severe exudative (grade 2-3) lesions may require advanced dressings, bicarbonate sitz baths, and analgesia. Figure 3 illustrates 2 clinical examples of acute radiation-induced vulvovaginitis, graded according to CTCAE criteria, highlighting the

variability of mucosal involvement observed during pelvic radiotherapy

Mucosal inflammation, including vulvitis and vaginitis, often warrants the continuation of preventive measures (topical and hyaluronic acid-based vaginal suppositories), sometimes complemented by local corticosteroids. Vaginal discomfort can be mitigated through the use of probiotics and the temporary suspension of sexual activity. If a fungal superinfection is suspected,

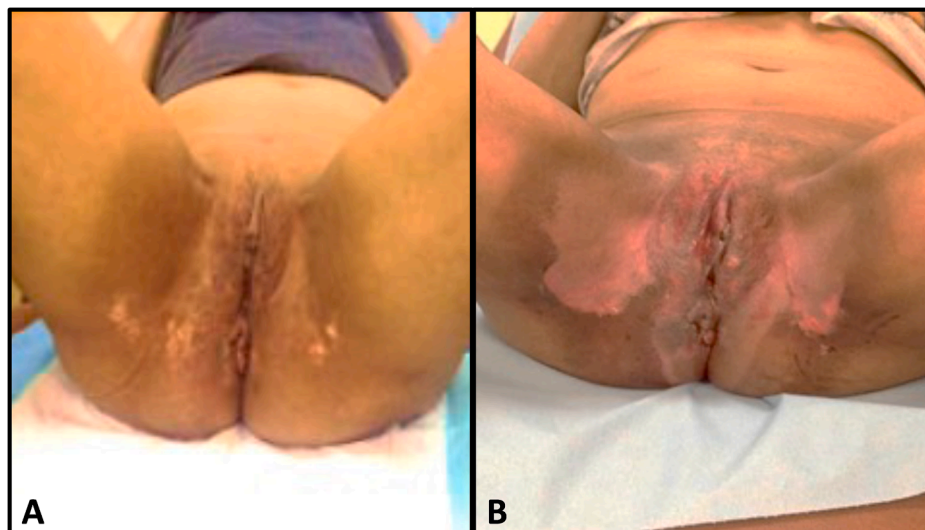


Figure 3 Clinical presentation of radiation-induced vulvovaginitis in patients undergoing pelvic radiotherapy. **A**, Moderate involvement characterized by localized erythema and superficial desquamation, consistent with CTCAE grade 2 toxicity. **B**, Severe involvement with marked erythema, edema, and exudative mucosal lesions, consistent with CTCAE grade 3 toxicity. CTCAE, Common Terminology Criteria for Adverse Events.

local antifungal treatment should be initiated. Symptoms of urethritis can be mitigated by encouraging adequate hydration and, when necessary, urinary alkalinization to reduce discomfort. In parallel, proctitis may be managed with topical corticosteroid enemas to alleviate rectal inflammation. Pain should be managed using a multimodal strategy, including non-steroidal anti-inflammatory drugs, opioids when necessary, local anesthetics, and supportive devices to reduce discomfort in sitting. Coordinating with home care services can ensure the continuity of supportive measures outside the hospital and help limit both the intensity and duration of acute symptoms.

After radiotherapy, follow-up must focus on the identification and management of late effects. A gynecological examination is recommended within 2 to 8 weeks following treatment completion, allowing early evaluation of mucosal healing and the emergence of sequelae. Sexual rehabilitation should be initiated promptly after radiotherapy, while always being approached gradually and respectfully, centered on patient comfort and readiness. Early patient education and timely introduction of preventive measures are essential to limit the risk of stenosis and fibrosis. Throughout this process, onco-sexological support plays a key role in helping patients and their partners navigate the complex interplay between physical healing and emotional intimacy.¹⁴ Preventing vaginal stenosis and dryness is a major objective: this can be achieved through regular sexual activity or, when not feasible, the use of vaginal dilators, fingers, or other sexual aids (eg, vibrators).²² Dilators are generally recommended to begin within 2 to 8 weeks post-treatment, used 2 to 3 times per week for at least 5 to 10 minutes, and maintained over the long term to preserve vaginal patency. Complementary techniques such as vulvar massage, perineal physiotherapy, and the use of vaginal moisturizers (including hyaluronic acid or polycarbophil-based products) may be offered.^{23,24} Topical estrogen therapy can be considered when not contraindicated. In selected cases, physical modalities like CO₂ laser treatment²⁵ or photobiomodulation²⁶ may provide additional benefit.

Management of Late Radiation-Induced Toxicities

The long-term consequences of pelvic radiotherapy on gynecological structures are diverse, often persistent, and frequently under-diagnosed. Their management requires an individualized and multidisciplinary approach, sensitive to the intimate and functional repercussions experienced by patients.

Late vulvovaginal toxicities, particularly dryness and inflammation, are among the most frequent sequelae and can severely compromise sexual health and emotional well-being. A comprehensive assessment should explore potential contributing factors, including active infections such as candidiasis, comorbidities like diabetes or neurological disorders, and medications known to impair mucosal function. Lifestyle factors, including smoking, should also be addressed. Beyond biological causes, it is essential to consider psychological dimensions such as fear, diminished desire, or relationship strain. Therapeutic management typically begins with the use of lubricants during sexual activity and regular application of vaginal moisturizers. When not contraindicated—particularly in the setting of hormone-sensitive malignancies—topical estrogens may be prescribed.^{23,24} In more resistant cases, hyperbaric oxygen²⁷ can be used, particularly for refractory mucosal necrosis or severe vaginal morbidity. In addition, emerging modalities such as CO₂ laser therapy,²⁵ or photobiomodulation,²⁶ are increasingly reported as promising strategies for the management of vulvovaginal toxicities. However, their use is still supported by limited evidence. Throughout treatment, the integration of onco-sexological support remains a key element in restoring intimacy and self-confidence.

Vaginal stenosis and synechiae represent another frequent and debilitating complication. These fibrotic changes can hinder gynecologic follow-up, impair sexual function, and delay the detection of local recurrence. Prevention and treatment require a long-term commitment to mechanical dilation—using vaginal dilators, fingers, or vibrators—and gentle manual separation of adhesions when feasible during gynecologic examinations.²² The use of non-steroidal anti-inflammatory (NSAID) vaginal solutions

may also contribute to reducing inflammation and maintaining canal patency. In cases of chronic radiodermatitis, therapeutic options are more limited but may include combinations of pentoxifylline and vitamin E,²⁸ physiotherapy, or, in selected cases, surgical intervention.

Lymphedema of the perineum and lower limbs is a complication that significantly impairs daily functioning and body image. While prophylactic manual lymphatic drainage is not currently recommended, patient education and early detection remain crucial. Once established, lymphedema is best managed through a combination of manual drainage and compression therapy, in accordance with existing protocols for limb lymphedema.²⁹

Ovarian failure is a common late effect in premenopausal women exposed to pelvic irradiation. In patients aged <35 years, fertility preservation must be discussed systematically before initiating treatment.^{15,16} Options such as ovarian transposition or cryopreservation should be offered when feasible. After treatment, attention must turn to the hormonal consequences of ovarian insufficiency, particularly in women experiencing premature menopause (Figure 4). Hormone replacement therapy (HRT) may be considered following a careful assessment of individual risk factors.^{30,31} For patients with an intact uterus, estrogen-progestin therapy is required, while estrogen-only regimens may be used post-hysterectomy. Different schemes may be prescribed, including sequential (cyclic) regimens with withdrawal bleeding or continuous combined regimens leading to amenorrhea. Estrogens can be administered orally or via transdermal formulations (eg, patch, gel, spray), the latter being preferred in women at higher thromboembolic or metabolic risk. The progestin component is usually given orally or through an intra-uterine device. In all cases, treatment should be initiated at the lowest effective dose (eg, estradiol 25 µg/day transdermal patch or 1 mg oral estradiol or 0.75 mg/day for transdermal gel), with progestins given at protective doses for the endometrium (eg, micronized progesterone 200 mg/day for 12–14 days/month in sequential regimens or 100 mg/day continuously). Dosage should be titrated according to symptoms and tolerance, and treatment reassessed annually. HRT remains contraindicated in cases of hormone-dependent cancers, and clinical monitoring is essential to evaluate cardiovascular, skeletal, and endocrine health.

For local vulvovaginal symptoms, low-dose estriol or estradiol vaginal inserts, or promestriene cream, may be prescribed when not contraindicated. In young women with premature menopause induced by pelvic irradiation, HRT is particularly important to

reduce long-term cardiovascular and bone health risks and should ideally be continued until the age of natural menopause.

For patients unable to receive hormonal therapy, alternative strategies may help alleviate vasomotor symptoms. Pharmacological agents such as selective serotonin or norepinephrine reuptake inhibitors, gabapentin, or clonidine may be considered. Behavioral approaches—although supported by limited evidence—such as relaxation techniques or hypnosis, may also provide benefit in selected individuals.

Pediatric Considerations

The management of radiation-induced gynecological toxicities in pediatric and adolescent patients requires a multidisciplinary, age-appropriate, and long-term approach. While acute side effects are generally similar to those seen in adults, specific precautions must be taken—such as avoiding vaginal irrigations in virginal or pre-pubescent patients. Fertility preservation is a key concern, often involving ovarian transposition and early referral to reproductive specialists to explore all available options.

In the longer term, transition to adult care must include structured education about gynecologic risks related to pelvic irradiation, and the importance of early obstetric follow-up in case of pregnancy. Gynecologic follow-up should ideally begin before puberty (around age 11 years) and continue throughout adolescence, involving pediatric gynecologists and endocrinologists, with an organized transfer to adult teams. Topics such as puberty onset, sexual health, contraception, and fertility should be addressed progressively and with sensitivity.

Particular attention must be paid to endocrine sequelae, especially radiation-induced ovarian insufficiency, and premature menopause. These complications are more likely to occur when the ovaries are exposed to doses above 4 Gy and are influenced by age, total radiation dose, and concurrent chemotherapy.^{32–34} Consequences may include impaired pubertal development, growth disturbances, bone loss, and increased cardiovascular risk. Anti-Müllerian hormone is the most relevant biomarker to assess follicular reserve,³⁵ and HRT should be considered when indicated, under joint supervision by pediatric endocrinologists and gynecologists.

Long-term complications may include vaginal stenosis, synechiae, and uterine abnormalities. In cases of high-dose pelvic irradiation or brachytherapy, regular gynecologic assessments—sometimes under general anesthesia in young children—are necessary to detect and manage adhesions or

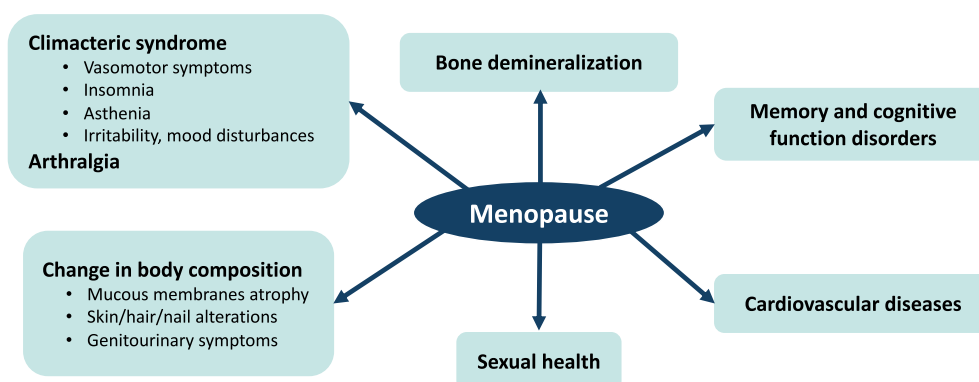


Figure 4 Hormonal consequences of radiation-induced menopause.

anatomical sequelae. Uterine exposure can result in hypotrophy, reduced elasticity, and vascular damage, leading to increased risks of miscarriage, fetal growth restriction, and uterine rupture.^{33,34,36,37}

These pregnancies should be managed in high-risk obstetrical centers. While no standardized treatment exists for uterine sequelae, hormonal therapies and experimental approaches (eg, pentoxifylline and vitamin E) have shown potential to improve endometrial parameters.

Throughout follow-up, Human Papilloma Virus vaccination and cervical cancer screening should follow general population guidelines, with no pediatric-specific contraindications. Onco-sexological support and pelvic floor rehabilitation may also be offered, as part of a comprehensive, patient-centered care pathway.

CONCLUSIONS

Radiation-induced gynecological toxicities represent a persistent and often underestimated burden in the management of pelvic malignancies. Despite their considerable impact on patients' quality of life, intimacy, and long-term well-being, these adverse effects remain insufficiently addressed in daily practice. Their underdiagnosis not only reflects a lack of awareness but also a structural absence of dedicated, evidence-based clinical frameworks.

In response to this gap, the guidelines developed by AFSOS aim to provide a structured and multidisciplinary approach to the prevention, identification, and management of these toxicities. By promoting early intervention, personalized follow-up, and integrated supportive care—including onco-sexology and fertility counseling—these recommendations seek to restore quality of life while preserving oncologic outcomes.

Symptom control must be regarded as an intrinsic component of cancer care rather than a secondary consideration. Standardizing practices across institutions and professionals will help reduce disparities, enhance patient support, and ultimately contribute to a more holistic and humane model of oncologic treatment.

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During the preparation of this work the authors used ChatGPT-4o to improve readability and language. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

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Appendix 1. Full search query and filtering strategy "radiotherapy"[MeSH Terms] AND ("fertility"[MeSH Terms] OR "vaginitis"[MeSH Terms] OR "urethritis"[MeSH Terms] OR "proctitis"[MeSH Terms] OR "menopause"[MeSH Terms] OR "lymphedema"[MeSH Terms]) AND "adverse effects" [Subheading] OR "wounds and injuries"[MeSH Terms] OR "radiation injuries"[MeSH Terms]) AND ("Pelvic neoplasms"[MeSH Terms] OR "Anus neoplasms"[MeSH Terms] OR "Rectal neoplasms"[MeSH Terms] OR "Vulvar neoplasms"[MeSH Terms] OR "Vaginal neoplasms"[MeSH Terms] OR "endometrial neoplasms"[MeSH Terms] OR "Uterine Cervical neoplasms"[MeSH Terms]) AND (y_10[Filter]) AND (clinicalstudy[Filter] OR clinicaltrial[Filter] OR clinicaltrialphasei[Filter] OR clinicaltrialphaseii[Filter] OR clinicaltrialphaseiii[Filter] OR clinicaltrialphaseiv[Filter] OR comparativestudy[Filter] OR consensus developmentconference[Filter] OR consensusdevelopmentconferencenih[Filter] OR controlledclinicaltrial[Filter] OR guideline[Filter] OR meta-analysis[Filter] OR observationalstudy[Filter] OR practiceguideline[Filter] OR pragmaticclinicaltrial[Filter] OR randomizedcontrolledtrial[Filter] OR review[Filter] OR systematicreview[Filter]) AND (humans[Filter]) AND (female[Filter]) AND (english[Filter])

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