

The Role of Radiotherapy and Chemotherapy in Treating Female Reproductive System Cancer (REVIEW)

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ABSTRACT

Chemotherapy and radiotherapy play vital roles in treatment some of female reproductive system cancers predominantly vaginal and cervical cancers. For cervical cancer, modalities can cause acute complications for instance genitourinary symptoms and gastrointestinal issues, alongside long-term effects comparable dyspareunia and vaginal atrophy that expressively affect sexual health. Combination of chemotherapy and radiotherapy is related with further severe late toxicities associated to radiotherapy only. In vaginal cancer, radiotherapy is mainly used in adjuvant setting to avert local revert post-surgery usually combined with chemotherapy to augment treatment efficacy expressly in advanced cases. Nevertheless, pelvic radiotherapy can cause vaginal morbidity comprising dryness, shortening and affecting sexual function. These treatments are important for successful survival consequences and organization disease-correlated symptoms.

Objective of this study to assess complications from radiotherapy and chemotherapy in some female reproductive system cancers in addition to appreciate impacts on female reproductive health after treatment.

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INTRODUCTION

Female reproductive system

Female reproductive system (Figure 1) contains numerous important organs, comprising ovaries, uterus, fallopian tubes, and cervix, besides vagina. On puberty, ovaries begin producing eggs and hormones starting menstrual cycle, through which eggs are released into uterus via fallopian tubes. If fertilization arises, egg develops in uterus; if not, follow the menstruation (1).

Health of reproductive system can be considerably impacted by treatment of cancer for instance radiotherapy and chemotherapy that may lead to infertility through reducing the level of hormone and damaging function of ovarian (2,3). Understanding structure and function of the female reproductive system is vital, particularly in context of protective fertility through cancer treatment (4).



Figure 1: Anatomy of female reproductive system (5)

Some type of cancer in female reproductive system

1- Cervical cancer

Cervical cancer is major malignancy assuming women, predominantly dominant between those aged 30 to 60, and is second greatest common cancer, donating to considerable number of cancer-associated deaths worldwide(6,7) . It is mainly associated with infection of human papillomavirus that can be transmitted during several means, comprising sexual contact (6). Disease is staged using International Federation of Gynecology and Obstetrics system that evaluates range of cancer progression (8). Treatment modalities comprise radiotherapy, and chemotherapy with radical simultaneous chemo radiation being standard for close by advanced cases and surgery, (7,9) . In spite of advancement in treatment, cervical cancer residues leading cause of cancer mortality between women, prominence need for actual prevention and early revealing strategies (6,7).

Two histopathological types of chiefly manifests of cervical cancer that include adenocarcinoma and squamous cell carcinoma, through squamous cell carcinoma being maximum widespread form. These types are categorized based on their cellular origin, with squamous cell carcinoma rising from squamous epithelial cells coating adenocarcinoma and cervix originating from glandular cells. Treatment styles for these types depend on numerous factors containing stage of disease and particular histopathological type with radical simultaneous chemoradiation being standard for far away advanced cases (7,8). Incidence of increase risk human papillomavirus types, mainly HPV-18 and HPV-16 is important risk factor accompanying with development of cervical cancer types (10).

2- Ovarian cancer

Ovarian cancer is record fatal gynecologic malignancy with five-year persistence rate of fewer than 50% and appraised 22,000 novel diagnoses yearly in United States, leading to around 14,000 deaths every year (11,12). Two main types characterize it include Type I tumors that low-grade and frequently diagnosed at early stage then Type II tumors that high-grade and usually existing at advanced stages because of ambiguous symptoms (11). Majority of individuals with advanced ovarian cancer involvement reappearance after initial treatment, prominence need for amended therapeutic strategies (12, 13). Current advancements in genetic and molecular understanding have begun to redesign approach to treatment, comprising reassessment of radiotherapy as viable option (11,12).

3- Vaginal cancer

Vaginal cancer is unusual malignancy, which can rise from vaginal epithelium, habitually concomitant with substantial morbidity because of treatment effects. Radiation therapy, generally used for gynecological cancers that lead to acute and chronic alterations in vagina comprising narrowing, mucosal atrophy and fibrosis that may cause reduced sexual function and painful intercourse and (14, 15). Treatment of cervical cancer that comprise radiation has been accompanying to incessant vaginal morbidity with several stayers reporting issues for instance vaginal stenosis and diminutive lubrication (14, 15).

Type of therapy

1- Radiotherapy

Radiotherapy is therapy modality, which operates rescind cancer cells and high energy radiation to target frequently employed in several cancer types comprising ovarian and cervical cancers. Methods for instance brachytherapy and external beam radiation are generally used with particular dosages besides fractionation programs tailored to individual needs, as realized in medication of locally advanced cervical cancer using doses of 45 Gy above 25 fractions and extra brachytherapy doses (7). Moreover, advancements in radiation technology, such as stereotactic body radiotherapy permit for accurate delivery of great doses to tumors however minimizing exposure to adjacent healthy tissue demonstrating efficiency in oligometastatic disease (16). Radiotherapy plays critical role in management of cancer donating to local control and enhanced existence outcomes (16,17).

Radiotherapy embrace several techniques tailored to treat cancer successfully. External beam radiotherapy is generally used in combination with brachytherapy that sends radiation directly to site of tumor, great local control while lessening damage to surrounding tissue (9). Advanced approaches like stereotactic body radiotherapy and intensity-modulated radiotherapy permit for exact targeting of tumors, improving dose escalation and decreasing toxicity (9, 13). Palliative radiotherapy is employed to relieve symptoms in advanced cases consuming regimens similar 8-10 Gy in single fraction and 20 Gy in 5 fractions (13). Choice type of radiotherapy depends on tumor location, disease stage and patient specific factor (17,18).

2- Chemotherapy

Chemotherapy denotes to use chemical agents to treat cancer with prevalent drugs comprising carboplatin, cisplatin and 5-fluorouracil between others. That administered only or in combination frequently directing to decrease tumor size before decisive treatments such as surgery or radiotherapy, strategy identified as neoadjuvant chemotherapy. Effectiveness of approach in cervical cancer residues debated that has not revealed significant development in inclusive endurance compared to radiotherapy only or concurrent chemo radiotherapy (CCRT) (9). Chemotherapy is related with substantial systemic toxicity, gastrointestinal, renal, hematological affect, and skin systems necessitating cautious monitoring of patients through treatment (9). Moreover, synchronous chemotherapy can improve effects of radiotherapy by synchronizing cancer cells and inhibiting damage repair to more susceptible phase of cell cycle (19).

The role of radiotherapy and chemotherapy in treating of some female reproductive system cancer

Chemotherapy and radiotherapy play important roles in curing cancers of female reproductive system that lead to intense late effects on reproductive health (20).

1- Cervical cancer

Radiotherapy usually comprising mixture of external beam radiotherapy plus brachytherapy is critical for maximizing loco-regional tumor control at cervical cancer however diminishing complication from radiation exposure to normal tissues (9). Concurrent chemoradiotherapy is become standard care for locally advanced cervical cancer representing significant upgrading in overall and progression free existence rates compared to radiotherapy only(9). Cisplatin is greatest usually used chemotherapeutic agent that combine with other drugs such as 5-fluorouracil (9). Nonetheless, role of neoadjuvant chemotherapy previous to decisive treatments residues controversial, as studies have revealed no overall existence benefit and potential delays in actual treatment (9,21).

2- Ovarian cancer

Radiotherapy is traditional use as adjuvant treatment for ovarian cancer, mainly for micrometastatic disease next surgery, but its role reduced with advent of platinum-based chemotherapy that remains cornerstone of treatment for advanced stages of disease (11). Modern advancements in radiotherapy procedures like and stereotactic body

radiotherapy and intensity-modulated radiotherapy have improved interest in its application, exclusively for oligometastatic cases where present of limited metastatic lesion (19, 11). Other studies show that radiotherapy can provide important local control and encompass chemotherapy-free intervals theoretically refining overall survival rates in selected patient (10,18). Conversely, combination of surgery and chemotherapy remains to be prioritized, as it effectually addresses high recurrence rates related with advanced ovarian cancer (18).

3- Vagina cancer

Radiotherapy plays substantial role in administration of vaginal cancer, mainly in adjuvant setting to avoid local relapse after surgery that combine with chemotherapy to improve treatment efficiency specifically in advanced cases. For instance, simultaneous chemo radiotherapy has been consumed in locally advanced cervical cancer that shares comparable treatment methods with vaginal cancer because of pathological and anatomical similarities (19). Pelvic radiotherapy can cause vaginal morbidity containing shortening and dryness that affect sexual function (22,23). While particular effects of chemotherapy on vaginal cancer are fewer detailed in provided papers, treatment strategy highlights importance of both modalities in refining survival consequences and managing symptoms related with disease (16).

Complication in radiotherapy and chemotherapy in treating some female reproductive system cancer

Complications emerge from radiotherapy and chemotherapy in treating some female reproductive system cancer include

1- In cervical cancer

Radiotherapy and chemotherapy can cause range of complications affecting numerous organ systems. Public acute side effects through treatment comprise gastrointestinal issues for instance diarrhea nausea and abdominal cramps, in addition to genitourinary symptoms comparable rise urinary frequency and dysuria (9). Long-term sequelae may include stenosis, vaginal atrophy and dyspareunia expressively impacting sexual health (9,15). Patients frequently involvement neurological symptoms comprising insomnia and pain with numerous accounting multiple adverse effects (6). Combination of chemotherapy and radiotherapy is related with more intense late toxicities compared to radiotherapy only mainly in postmenopausal women (15). These complications highpoint need for real management strategies to ameliorate quality of life for cervical cancer stayers (6,9).

2- In ovarian cancer

Complications are significant concerns. Radiotherapy historically underutilized because of high toxicity levels has realized advancements for and stereotactic body radiotherapy and instance intensity-modulated radiotherapy that purpose to decrease damage to surrounding healthy tissues and diminish side effects(11,12). Traditional radiotherapy approaches have been related with acute and late gastrointestinal toxicities that lead to reduced use (11). Chemotherapy predominantly with platinum-based agent usually results in persistent disease, with above 70% of patients experiencing recrudescence (12). Furthermore, chemotherapy can encourage ovarian damage that lead to diminished ovarian reserve or temporary amenorrhea that complicate treatment for women interest fertility preservation (24).

3- Vaginal cancer

Radiotherapy can lead to important acute and chronic complications that include acute reactions for instance moist desquamation, erythema and mucositis that usually resolution within 2 to 3 months post-treatment. Nonetheless, chronic changes may progress that include narrowing ,vaginal atrophy and loss of elasticity frequently resulting in painful intercourse and decrease lubrication because of fibrosis and vascular damage at vaginal tissue (32,25). Moreover, chemotherapy can exacerbate these effects augmenting mucosal responses then leading to additional complications for instance myelosuppression and chronic gastrointestinal reactions (17). Interplay of this treatment can cause complex array of signs that pointedly influence quality of life for individual undergoing therapy for vaginal cancer (15).

CONCLUSION

- 1- Complications from therapy expressively distress patient quality of life.
- 2- Advanced methods Radiotherapy is vital for management some female reproductive system cancers.
- 3- Decrease toxicity while refining treatment efficacy.
- 4- Combination treatments boost survival rates at advanced cervical cancer.
- 5- Requirement for actual management strategies to progress patient consequences.

REFERENCES

- [1] American University of Beirut Medical Center. (2015). Copyright 2015 American University of Beirut. All rights reserved.
- [2] American Cancer Society. (n.d.). Cancer.org. <https://www.cancer.org>, 1-800-227-2345.
- [3] Marci, R., Mallozzi, M., Benedetto, L. D., Schimberni, M., Mossa, S., Soave, I., Palomba, S., & Caserta, D. (2018). Radiations and female fertility. *Reproductive Biology and Endocrinology*, 16(112).
- [4] Griffiths, M. J., Winship, A. L., & Hutt, K. J. (2020). Do cancer therapies damage the uterus and compromise fertility? *Human Reproduction Update*, 26(2), 161–173. <https://doi.org/10.1093/humupd/dmz041>
- [5] Anatomy of Female Reproductive System. National Cancer Institute. (n.d.).
- [6] Palagudi, M., Para, S., Golla, N., Meduri, K. Ch., Duvvuri, S. P., Vityala, Y., Sajja, D. Ch., & Damineni, U. (2024). Adverse effects of cancer treatment in patients with cervical cancer. *Cureus*, 16(2), e54106. <https://doi.org/10.7759/cureus.54106>
- [7] Katke, A., Nanda, R., Thejaswini, B., Pasha, T., Giri, G. V., Babu, G., & Pawar, Y. (2021). Weekly vs. tri-weekly cisplatin-based chemoradiation in carcinoma cervix: A prospective randomized study of toxicity and compliance. *Reports of Practical Oncology and Radiotherapy*, 26(6), 948–954. <https://doi.org/10.5603/RPOR.a2021.0115>
- [8] Šarenac, T., & Mikov, M. (2019). Cervical cancer, different treatments and importance of bile acids as therapeutic agents in this disease. *Frontiers in Pharmacology*, 10(484).
- [9] Non-surgical management of cervical cancer. (n.d.). In *Chapter 15*.
- [10] Shen, J., Sun, H., Chu, J., Gong, X., & Liu, X. (2024). Cervicovaginal microbiota: A promising direction for prevention and treatment in cervical cancer. *Infectious Agents and Cancer*, 19(13). <https://doi.org/10.1186/s13027-024-00573-8>
- [11] Fields, E. C., McGuire, W. P., Lin, L., & Temkin, S. M. (2017). Radiation treatment in women with ovarian cancer: Past, present, and future. *Radiation Oncology, Frontiers in Oncology*, 7(177). <https://doi.org/10.3389/fonc.2017.00177>
- [12] Macchia, G., Titone, F., Restaino, S., Arcieri, M., Pellicchia, G., Andreetta, C., Driul, L., Vizzielli, G., & Pezzulla, D. (2023). Is it time to reassess the role of radiotherapy treatment in ovarian cancer? *Healthcare*, 11(2413). <https://doi.org/10.3390/healthcare11172413>
- [13] Moss, E., Taylor, A., Andreou, A., Ang, Ch., Arora, R., Attygalle, A., Banerjee, S., et al. (2024). British Gynaecological Cancer Society (BGCS) ovarian, tubal and primary peritoneal cancer guidelines: Recommendations for practice update 2024. *European Journal of Obstetrics and Gynecology*, 300, 69–123.

- [14] Jensen, P. T., & Froeding, L. P. (2015). Pelvic radiotherapy and sexual function in women. *Translational Andrology and Urology*, 4(2), 186–205.
- [15] Hofsjö, A., Bergmark, K., Blomgren, B., Jahren, H., & Bohm-Starke, N. (2018). Radiotherapy for cervical cancer – Impact on the vaginal epithelium and sexual function. *Acta Oncologica*, 57(3), 338–345. <https://doi.org/10.1080/0284186X.2017.1400684>
- [16] Macchia, G., Titone, F., Restaino, S., Arcieri, M., Pellecchia, G., Andreetta, C., Driul, L., Vizzielli, G., & Pezzulla, D. (2023). Is it time to reassess the role of radiotherapy treatment in ovarian cancer? *Healthcare*, 11(2413). <https://doi.org/10.3390/healthcare11172413>
- [17] Shen, J., Tao, Y., He, L., Guan, H., Zhen, H., Liu, Z., & Zhang, F. (2022). Clinical application of radiotherapy in patients with oligometastatic ovarian cancer: A sharp tool to prolong the interval of systemic treatment. *Discover Oncology*, 13(82). <https://doi.org/10.1007/s12672-022-00540-y>
- [18] Dang, Y-Z., Li, X., Ma, Y-X., Li, X-L., Yang, T., Lu, W-L., & Huang, S-G. (2019). 18F FDG PET/CT guided intensity modulated radiotherapy for 42 FIGO III/IV ovarian cancer: A retrospective study. *Oncology Letters*, 17, 149–158.
- [19] Rose, P. G., Bundy, B. N., Watkin, E. B., Thigpen, J. T., Deppe, G., et al. (1999). Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *The New England Journal of Medicine*, 340(15).
- [20] Salama, M., & Woodruff, T. K. (2017). Anticancer treatments and female fertility: Clinical concerns and role of oncologists in oncofertility practice. *Expert Review of Anticancer Therapy*, 17(8), 687–692. <https://doi.org/10.1080/14737140.2017.1335199>
- [21] Carvalho, H. d. A., & Mauro, G. P. (2023). History of radiotherapy in the treatment of uterine cervix cancer: An overview. *Revista da Associação Médica Brasileira*, 69(Suppl 1), e2023S126.
- [22] Hickey, M., Basu, P., Sassarini, J., Stegmann, M. E., Weiderpass, E., Chilowa, K. N., Cheng-Har, Y., Partridge, A. H., & Brennan, D. J. (2024). Managing menopause after cancer. *The Lancet*, 403, 984–96.
- [23] Jensen, P. T., & Froeding, L. P. (2015). Pelvic radiotherapy and sexual function in women. *Translational Andrology and Urology*, 4(2), 186–205.
- [24] Sellami, I., Beau, I., & Sonigo, C. (2023). Chemotherapy and female fertility. *Elsevier*. <https://doi.org/10.elsevier.com/open-access/userlicense/1.0>
- [25] Grigsby, F. W., Russell, A., Bruner, D., et al. (1995). Late injury of cancer therapy on the female reproductive tract. *International Journal of Radiation Oncology, Biology, Physics*, 31(5), 1281–1299.

دور العلاج الإشعاعي والعلاج الكيميائي في علاج سرطان الجهاز التناسلي الأنثوي

الخلاصة

يلعب العلاج الكيميائي والعلاج الإشعاعي دورًا حيويًا في علاج بعض سرطانات الجهاز التناسلي الأنثوي وخاصة سرطان المهبل وعنق الرحم. بالنسبة لسرطان عنق الرحم، يمكن أن تسبب هذه الطرق مضاعفات حادة مثل أعراض الجهاز البولي التناسلي ومشاكل الجهاز الهضمي، إلى جانب التأثيرات طويلة المدى مثل عسر الجماع وضمور المهبل التي تؤثر بشكل واضح على الصحة الجنسية. يرتبط الجمع بين العلاج الكيميائي والعلاج الإشعاعي بمزيد من السمية المتأخرة الشديدة المرتبطة بالعلاج الإشعاعي فقط. في سرطان المهبل، يستخدم العلاج الإشعاعي بشكل أساسي في وضع مساعد لتجنب الارتداد الموضعي بعد الجراحة، وعادة ما يتم دمج مع العلاج الكيميائي لزيادة فعالية العلاج بشكل واضح في الحالات المتقدمة ومع ذلك، يمكن أن يسبب العلاج الإشعاعي للحوض اعتلالات مهبلية تشمل الجفاف والتقصير والتأثير على الوظيفة الجنسية. هذه العلاجات مهمة لعواقب البقاء الناجحة وتنظيم الأعراض المرتبطة بالمرض.

الهدف من هذه الدراسة هو تقييم المضاعفات الناجمة عن العلاج الإشعاعي والعلاج الكيميائي في بعض سرطانات الجهاز التناسلي الأنثوي بالإضافة إلى تقدير التأثيرات على الصحة الإنجابية الأنثوية بعد العلاج.