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The effects of cancer treatments on uterine function

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A R T I C L E I N F O

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A B S T R A C T

Advancements in cancer treatments and associated increased survival rates have led to a growing number of girls and women facing reproductive health challenges as a result of their oncologic treatments. Radiation and chemotherapy have been demonstrated to have adverse effects on fertility. Ovarian damage as a result of radiation and chemotherapy has been the subject of extensive study. Less well understood are the uterine changes mediated by these treatment modalities. Uterine damage from radiation therapy is related to dose, regimen, and patient age. Certain chemotherapies have demonstrated similar effects. Women with uterine damage have a lower likelihood of conceiving and a higher risk of pregnancy complications, including early pregnancy loss, preterm labor, and low birth weight infants. Surgical, medical, and genetic therapies are being evaluated to protect the uterus from treatment-related injury. Pre- and post-treatment consultation with oncofertility specialists is critical in assessing a patient's risk of uterine injury from a proposed cancer treatment plan as well as understanding treatment-induced injury to optimize fertility preservation.

1. Introduction

As the emergence of new treatments for pediatric, adolescent, and young adult (AYA) cancers continues to improve patients' prognoses, a growing number of survivors will experience the adverse effects of these therapies through their reproductive years and beyond. These trends underlie an increasing need for both patients and providers to incorporate reproductive potential as a critical metric of quality of life when developing comprehensive treatment plans. The effects of radiation and chemotherapy on the ovary have been well studied and characterized. However, the impact of these treatments on the uterus is less well documented. The field of fertility preservation should now more overtly include issues related to uterine preservation. A better understanding of the long-term effects of these treatments on future myometrial and endometrial function in young patients will enable providers to offer more appropriate pre-treatment fertility preservation counseling and prepare cancer survivors for potential future implications.

The integrity of the uterus and endometrium is essential to establishing and maintaining a healthy pregnancy. The onset of puberty marks the beginning of changes in uterine size, shape, and vasculature, which prepare the body for future pregnancies [1–6]. Due to the dynamic nature of the uterus during puberty, it may be more vulnerable to insult during the perimenarcheal years [7]. The uterine

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myometrium, endometrium, and vasculature are vulnerable to radiation-induced injury, which can ultimately impact the ability to sustain a pregnancy. Studies consistently demonstrate that the extent of radiation-induced uterine injury depends on treatment dose, regimen, and patient age, although the available data are limited [8,9]. Emerging evidence also suggests that the uterus may be a site of chemotherapy-induced damage [10,11]. Certain chemotherapeutic agents may induce endometrial changes via cell cycle disruption or DNA damage from free radical production [12]. One case-control study found an 82 % reduction in uterine volume in survivors who had undergone total body irradiation (TBI) at a dose greater than 10 Gy, and a 67 % reduction in those who received busulfan without radiation [13]. The impact of many chemotherapeutic agents on the uterus remains unknown and requires further exploration.

2. Uterine changes after cancer therapy

Up to 80 % of women under 40 years of age have an accelerated decline in fertility after cancer treatment [14]. The impact of these oncologic treatments on the uterus in terms of both achieving and maintaining pregnancy is less well understood. Based on retrospective clinical data, the uterus is often permanently damaged by radiation, though the effect depends on the age of the woman during treatment [9]. The mechanisms for uterine damage are becoming more widely appreciated.

Radiation reduces uterine length and volume, as demonstrated through studies examining women with radiation exposure using multiple controls, including women with primary ovarian insufficiency (POI) without radiation and women who received chemotherapy alone [9,13,15]. Girls who undergo radiation before menarche are particularly likely to experience decreased uterine volume compared to their peers [7]. This reduction may result from disrupted hormonal signaling, as many of these patients have concurrent radiation-induced gonadal failure. Additionally, pre-pubertal radiation may directly limit uterine growth due to intrinsic changes to the uterus itself. Unlike idiopathic POI, where high-dose therapy can improve uterine volume, this therapy appears ineffective in recovering pre-menarcheal uterine volume lost due to radiotherapy [16].

In post-pubertal, nulligravida women, uterine volume decreases following radiotherapy, whereas this effect is not observed in women with a history of pregnancy [15]. Radiotherapy has been shown to similarly damage uterine blood flow, impairing growth and vascularization of the endometrium and compromising normal myometrial and endometrial function. Studies indicate that 70 % of women with a history of radiation exhibit reduced uterine blood flow compared to those without prior radiation exposure [15]. Animal models further reveal that radiotherapy can cause endothelial dysfunction in the uterine artery [12,17,18].

Women treated with radiotherapy often exhibit an inability to develop an endometrial lining in response to exogenous estradiol, alongside a loss of distinct uterine zonal anatomy on MRI. These findings are likely due to reduced blood flow and fibrotic or necrotic changes within the endometrium and myometrium. Decreased endometrial thickness appears to result from a combination of free radical damage, fibrosis, and atrophy [6,19]. After radiotherapy, the myometrium becomes less elastic due to increased fibrosis, affecting the uterine musculature and vascular support. Consistent with these changes, MRI findings show decreased signal intensity in the myometrium [12]. These alterations, which occur soon after the onset of treatment and persist beyond its completion, limit uterine size and elasticity [6,12,19]. Overall, changes in uterine length, volume, function, blood flow, and contractility following radiation continue to be explored for their long-term impacts on post-treatment function and fertility.

Multiple histologic changes are associated with radiation-induced uterine damage. Atrophic myometrium is notable for the prominence of fibrosis in the submucosal area, while edema is more commonly seen at the serosal surface [19]. Additionally, the endometrium becomes thin and atrophic, and the vasculature exhibits significant alterations characterized by small, thickened blood vessels. Radiation has been linked to the development of lipid-containing foamy histiocytes, which are commonly associated with toxic and inflammatory exposures [12]. Furthermore, discrete areas of ulceration and coagulative necrosis, enclosed by fibrin, are frequently identified within the uterus following radiation [17,18,20]. Despite these observations, the full spectrum of histologic changes resulting from radiotherapy is not yet fully understood, highlighting the need for further research to better evaluate and characterize their clinical significance. Recent studies by Griffith et al., utilizing a mouse model, suggest radiation causes direct DNA damage and apoptosis within uterine cells. This cell death appears to be mediated by the P53 Upregulated Modulator of Apoptosis (PUMA). PUMA expression is significantly elevated in irradiated samples compared to non-irradiated controls in *in vitro* studies. However, contrasting evidence from recent *in vivo* studies indicated that gene expression related to uterine receptivity remains unchanged after radiation [21].

3. Impacts on future fertility and pregnancy

A study of over 3500 childhood cancer survivors found that, after adjusting for sociodemographic and behavioral risk factors, the relative risk of clinical infertility in survivors was 1.48 times greater compared to siblings [8]. The Children's Oncology Group's 2023 *Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* recommend at least an annual evaluation that includes pubertal progression, menstrual and pregnancy history, and sexual function assessment [22]. Determining the relative contributions of ovarian versus uterine damage to infertility remains challenging [23]. Studies on uterine damage following gonadotoxic chemotherapy are inconclusive, but women who have undergone chemotherapy have lower pregnancy rates and an increased risk of low birth weight (LBW)/small for gestational age (SGA) infants, preterm birth, and lower Apgar scores [13,23]. The underlying mechanism remains poorly understood.

Women who have had pelvic radiation also have lower pregnancy rates and more pregnancy-related complications, including early pregnancy loss, preterm delivery, fetal malposition, and LBW/SGA infants [18,21,23]. While no universal consensus exists on the acceptable dose of TBI or direct uterine radiation, adverse pregnancy outcomes are generally not observed when TBI doses remain below 0.5–2.5 Gy [24]. However, doses exceeding 10 Gy directed at the uterus have been shown to induce irreversible damage, with some providers advising patients exposed to more than 25 Gy to avoid pregnancy altogether [8,24].

In a comparative study, patients who received TBI for bone marrow transplantation had significantly higher rates of early pregnancy loss, preterm delivery, and LBW infants compared to those treated with high-dose chemotherapy for aplastic anemia and hematologic malignancies [6,19]. Additionally, sustained pregnancy with implanted embryos is less likely in patients after radiotherapy [25]. Recent studies in mouse models suggest that while early pregnancy milestones may proceed normally after radiation, increased early pregnancy loss occurs due to impaired endometrial stromal decidualization [21]. This impairment results from apoptotic injury, oxidative damage to the stroma, hypoxic vascular injury, and epigenetic alterations [21]. In a comparative study, patients who received TBI for bone marrow transplantation experienced significantly higher rates of early pregnancy loss, preterm delivery, and LBW infants compared to those treated with high-dose chemotherapy alone for aplastic anemia and hematologic malignancies [6,19]. Similarly, sustained pregnancy following embryo implantation is less likely in patients who have undergone pelvic radiotherapy [25].

4. Evaluation of uterine function

Compared to women who have not received radiation, those exposed to uterine irradiation show decreased uterine volume and length, decreased uterine arterial flow, and an inability to develop an endometrial lining in response to exogenous estradiol, as seen in ultrasound studies [7,9,15,26]. While sample sizes are small, studies consistently show that the length of the uterus in women who receive radiation during childhood is shorter than both healthy controls and women with POI who have not received radiation. Whole abdominal radiotherapy in childhood has been suggested to reduce the length of the uterus to an average uterine length of 4.3 cm, compared to an average of 7.1 cm uterine length in the control group of patients who had not received radiation therapy [27]. While there is some variation between individuals, this is a marked reduction in length with an almost 2.8 cm decrease in average uterine length for patients previously treated with whole abdominal radiotherapy [9,27]. The total dose of radiation received by the uterus during treatment most strongly correlates with uterine damage, impaired fertility, and adverse pregnancy outcomes [28]. Reduced uterine volume, blood flow, and length were not seen to increase in response to exogenous hormone supplementation (15, 27).

Although there is insufficient data to establish numerical criteria for diagnosis, it is evident that these properties can be significantly impacted by radiation, making ultrasound assessments valuable in identifying potential damage. In addition to decreased size, uterine arterial flow is impaired in patients who have undergone radiation therapy. Increased uterine artery pulsatile indices, associated with poorer outcomes with assisted reproductive technologies, have been observed in adults who received radiation therapy as children [29]. Uterine blood flow in patients treated with TBI is particularly impaired, with several studies indicating increases in uterine artery pulsatile indices by as much as 30.3 % [29]. In similar studies, 70 % of women who had been irradiated demonstrated no detectable blood flow in the uterine artery [9,28]. Lastly, while less commonly reported, detection of the endometrium may also be difficult in these patients, at least partially due to significant thinning [30]. This further underscores the importance of imaging modalities like ultrasound in evaluating radiation-induced uterine damage.

While ultrasonography has been the primary tool for assessing radiation-related uterine changes, pelvic magnetic resonance imaging (MRI) has shown promising diagnostic efficacy. Pelvic MRI has been increasingly utilized to evaluate uterine size, morphology, and blood flow, and has successfully detected radiation-induced changes in childhood and AYA cancer survivors. Consistent with ultrasound findings, MRI observations in pre-menopausal women who received radiation reveal reduced uterine musculature, decreased uterine volume, diminished endometrial thickness, and a loss of normal uterine zonal anatomy. Anatomic and histological examinations after hysterectomy have further confirmed these MRI findings, showing endometrial and myometrial atrophy and abnormal blood vessels. Additionally, evidence of fibrosis within the uterus has been observed and correlated with MRI results [6,19].

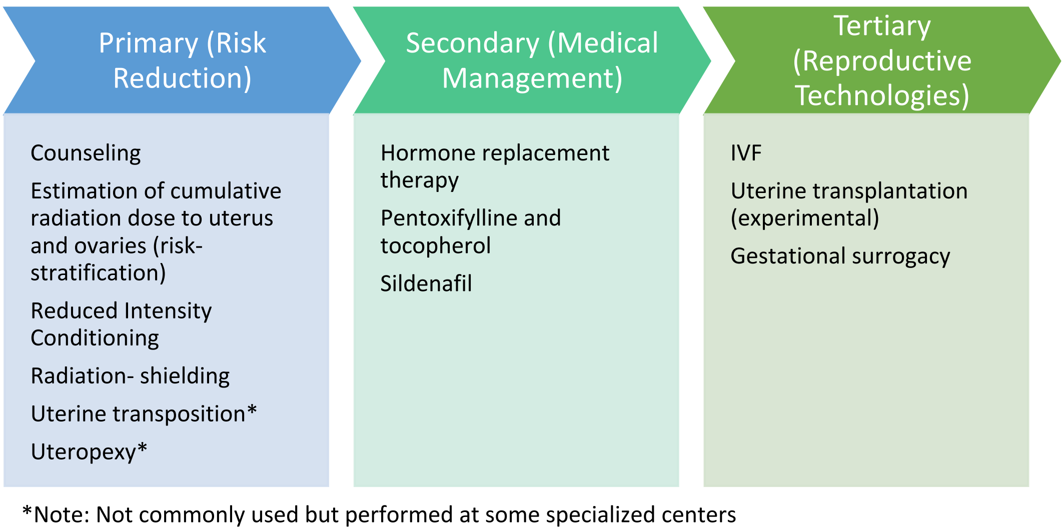

Fig. 1. Management considerations for therapy-related uterine dysfunction.

5. Management of therapy-related uterine dysfunction

As increasing numbers of women and girls survive cancers that necessitate pelvic or TBI, the need for conversations about fertility prior to treatment has intensified. Awareness of the impact of radiation on both ovarian function and uterine injury is necessary to provide patients with the information to make decisions about treatment as it relates to their future fertility. A new focus on the prevention of uterine exposure to radiation has included the development of more refined radiation shielding techniques, a narrowing of effective dose ranges, and evolving surgical techniques like uterine transposition [9]. Changes to conditioning protocols, including reduced intensity conditioning (RIC) regimens or ovarian shielding during TBI, have been found to be protective to ovarian function and may therefore have some protective effect for the uterus as well [31] (Fig. 1). However, ovarian shielding is not always feasible as it may obstruct the treatment area of interest. Ovarian suppression during treatment has the potential to mitigate some chemotherapy or radiation related damage but this has not demonstrated a protective effect for the uterus [32].

Small studies investigating uteropexy as a method to preserve uterine health and function suggest that it may provide some protection for the endometrium [33]. The goal of this procedure is to retain the native blood supply to the uterus while repositioning it outside the typical pelvic radiation field, similar to an ovarian transposition aimed at preserving ovarian function. However, further studies are needed to ascertain the safety and efficacy of uteropexy, particularly for young and pubescent cancer patients.

Hormone replacement therapies (HRT) are commonly used post-radiation to promote overall health, as estrogen has protective effects on cardiac and bone health. Notably, HRT may increase uterine size – as uterine response to hormone replacement may well depend upon age at the time of cancer treatment - and enhance endometrial development. Other strategies aimed at improving uterine function after chemotherapy and radiation have shown potential benefits for fertility. For instance, a combination of pentoxyfylline and tocopherol has been found in small studies to increase uterine thickness and improve endometrial function in women with abnormally thin endometrial linings, and to decrease radiation-induced fibropathy, thereby increasing the incidence of spontaneous pregnancy [34,35]. Although the data are limited, one study reported an increase in endometrial thickness and pregnancy rates of up to 40 % [36]. In addition, sildenafil has been studied in cases of infertility due to abnormally thin endometrium. While improvements were noted in endometrial thickness, myometrial volume, and uterine blood flow, there was no significant impact on fertility rates [37]. Ongoing research continues to assess the effectiveness of high-dose estradiol treatment in achieving adequate endometrial lining formation, an emerging area of interest in oncofertility.

Despite these promising findings, data on the efficacy of the medical management of successful pregnancies for patients with decreased uterine function who received chemotherapy or radiation remain limited. Much of the current knowledge is extrapolated from general infertility research rather than specific studies in the oncofertility context. However, recent studies have suggested that blocking PUMA can help restore the decidual response in irradiated mice, normalize uterine artery function, and improve pregnancy outcomes [6,19]. Understanding the role of PUMA in this process is critical, as it could become a target for future therapeutics and further lines of investigation into the underlying mechanisms [12].

Some post-pubertal women attempt to preserve fertility prior to chemotherapy and radiation through ovarian stimulation and oocyte retrieval for freezing and post-treatment in-vitro fertilization (IVF); however, prepubertal girls currently do not have access to this option. Recent developments in ovarian tissue freezing and in vitro maturation of oocytes have shown promise in fertility preservation before puberty [38–40]. While studies on ovarian tissue transplantation are ongoing, the full extent of its benefit for pre-menarcheal patients remains unclear, as many early test subjects are only recently starting to consider fertility [41]. Nonetheless, early results are promising, and numerous studies are underway to evaluate the impact of ovarian transplant on post-cancer treatment ovarian and uterine function and fertility.

For women who are able to cryopreserve eggs or embryos, gestational surrogacy presents a viable option, as a gestational carrier may have a higher likelihood of a successful pregnancy compared to a woman previously exposed to pelvic radiation. For those unable to undergo IVF before or after cancer therapy, egg or embryo donation may be a feasible alternative in those patients with lower radiation dose exposure [41,42]. However, studies show more embryo transfers required to achieve pregnancy, lower pregnancy rates and an increased risk of early pregnancy loss with oocyte donation following both chemotherapy and pelvic radiation [10,11]. Uterine transplantation, while an innovative and promising advancement, remains controversial due to the complexity of the procedure, compromised vasculature, and the increased risk of cancer recurrence associated with immunosuppression [17,43].

6. Conclusion

Elucidating the ramifications of oncologic therapies on the uterus is paramount for enhancing the long-term quality of life among pediatric, adolescent, and young adult cancer survivors. As cancer survival rates rise, it is crucial to address the enduring sequelae of these treatments on survivors' reproductive health. This review highlights the uterus's vulnerability to radiotherapy and chemotherapy, emphasizing critical risk factors such as patient age at treatment and cumulative radiation dose. Empirical evidence demonstrates that high doses of radiation, particularly during pivotal developmental stages, can inflict irreversible damage to the uterus. Such damage results in reduced uterine volume, compromised vascularity, and increased fibrosis, all of which impair fertility and negatively impact pregnancy outcomes. While the toxic effects of chemotherapy on the uterus are less extensively documented, existing evidence suggests a potential deleterious impact that merits further investigation. Advances in diagnostic modalities such as ultrasonography and MRI have enhanced our ability to detect and characterize these uterine injuries more effectively. Simultaneously, ongoing research into preventative strategies and therapeutic interventions—including hormone replacement therapy and surgical techniques—provides optimism for mitigating these adverse effects. Ultimately, a comprehensive multidisciplinary approach that integrates fertility preservation discussions and individualized treatment planning is indispensable for safeguarding the reproductive health of cancer survivors. By prioritizing these efforts, we can help ensure that cancer survivorship does not come at the cost of future reproductive potential and well-being.

CRediT authorship contribution statement

Emma Greenberg: Writing – original draft, Data curation, Writing – review & editing, Visualization. **Katya Strage:** Writing – review & editing, Visualization, Writing – original draft, Methodology, Data curation. **Noelle Ozimek:** Visualization, Writing – review & editing. **Kamilah Abdur-Rashid:** Writing – review & editing, Visualization. **Guluzar Turan:** Visualization, Methodology, Project administration, Writing – review & editing. **Sarah Milgrom:** Writing – review & editing, Methodology, Visualization, Conceptualization. **Leslie Appiah:** Conceptualization, Writing – review & editing, Methodology, Visualization.

Research agenda

There is no research data other than the references used in the article.

Practice points

- Female cancer survivorship
- Fertility preservation
- Uterine injury
- Counseling
- Patient care

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References

[1] Marshall WA, Tanner JM. Variations in pattern of pubertal changes in girls. Arch Dis Child Jun 1969;44(235):291–303. https://doi.org/10.1136/adc.44.235.291.
[2] Holm K, Laursen EM, Brocks V, Müller J. Pubertal maturation of the internal genitalia: an ultrasound evaluation of 166 healthy girls. Ultrasound Obstet Gynecol Sep 1995;6(3):175–81. https://doi.org/10.1046/j.1469-0705.1995.06030175.x.
[3] Laursen EM, Holm K, Brocks V, Jarden M, Müller J. Doppler assessment of flow velocity in the uterine artery during pubertal maturation. Ultrasound Obstet Gynecol Nov 1996;8(5):341–5. https://doi.org/10.1046/j.1469-0705.1996.08050341.x.
[4] Cheuiche AV, Moro C, Lucena IRS, de Paula LCP, Silveiro SP. Accuracy of Doppler assessment of the uterine arteries for the diagnosis of pubertal onset in girls: a scoping review. Sci Rep Apr 8 2023;13(1):5791. https://doi.org/10.1038/s41598-023-32880-2.
[5] Colvin CW, Abdullatif H. Anatomy of female puberty: the clinical relevance of developmental changes in the reproductive system. Clin Anat Jan 2013;26(1):115–29. https://doi.org/10.1002/ca.22164.
[6] Addley HC, Vargas HA, Moyle PL, Crawford R, Sala E. Pelvic imaging following chemotherapy and radiation therapy for gynecologic malignancies. Radiographics Nov 2010;30(7):1843–56. https://doi.org/10.1148/rg.307105063.
[7] Larsen EC, Schmiegelow K, Rechnitzer C, Loft A, Müller J, Andersen AN. Radiotherapy at a young age reduces uterine volume of childhood cancer survivors. Acta Obstet Gynecol Scand Jan 2004;83(1):96–102. https://doi.org/10.1111/j.1600-0412.2004.00332.x.
[8] Barton SE, Najita JS, Ginsburg ES, et al. Infertility, infertility treatment, and achievement of pregnancy in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol Aug 2013;14(9):873–81. https://doi.org/10.1016/s1470-2045(13)70251-1.
[9] Teh WT, Stern C, Chander S, Hickey M. The impact of uterine radiation on subsequent fertility and pregnancy outcomes. BioMed Res Int 2014;2014:482968. https://doi.org/10.1155/2014/482968*.
[10] Sauer MV, Paulson RJ, Ary BA, Lobo RA. Three hundred cycles of oocyte donation at the University of Southern California: assessing the effect of age and infertility diagnosis on pregnancy and implantation rates. J Assist Reprod Genet Feb 1994;11(2):92–6. https://doi.org/10.1007/BF02215994.
[11] Munoz E, Fernandez I, Martinez M, et al. Oocyte donation outcome after oncological treatment in cancer survivors. Fertil Steril Jan 2015;103(1):205–13. https://doi.org/10.1016/j.fertnstert.2014.09.027.
[12] Garg D, Johnstone EB, Lomo L, et al. Looking beyond the ovary for oncofertility care in women: uterine injury as a potential target for fertility-preserving treatments. J Assist Reprod Genet Jun 2020;37(6):1467–76. https://doi.org/10.1007/s10815-020-01792-9*.
[13] Beneventi F, Locatelli E, Giorgiani G, et al. Gonadal and uterine function in female survivors treated by chemotherapy, radiotherapy, and/or bone marrow transplantation for childhood malignant and non-malignant diseases. BJOG Jun 2014;121(7):856–65. https://doi.org/10.1111/1471-0528.12715*. discussion 865.
[14] de Roo SF, Rashedi AS, Beerendonk CCM, et al. Global oncofertility index-data gap slows progress. Biol Reprod Jun 1 2017;96(6):1124–8. https://doi.org/10.1093/biolre/iox051.
[15] Holm K, Nysom K, Brocks V, Hertz H, Jacobsen N, Müller J. Ultrasound B-mode changes in the uterus and ovaries and Doppler changes in the uterus after total body irradiation and allogeneic bone marrow transplantation in childhood. Bone Marrow Transplant Feb 1999;23(3):259–63. https://doi.org/10.1038/sj.bmt.1701569.
[16] Craciunas L, Zdoukopoulos N, Vinayagam S, Mohiyiddeen L. Hormone therapy for uterine and endometrial development in women with premature ovarian insufficiency. Cochrane Database Syst Rev Oct 6 2022;10(10):Cd008209. https://doi.org/10.1002/14651858.CD008209.pub2.
[17] Hawkins MM. Pregnancy outcome and offspring after childhood cancer. BMJ Oct 22 1994;309(6961):1034. https://doi.org/10.1136/bmj.309.6961.1034.

[18] Black KZ, Nichols HB, Eng E, Rowley DL. Prevalence of preterm, low birthweight, and small for gestational age delivery after breast cancer diagnosis: a population-based study. Breast Cancer Res Jan 31 2017;19(1):11. https://doi.org/10.1186/s13058-017-0803-z*.
[19] Arrivé L, Chang YC, Hricak H, Brescia RJ, Auffermann W, Quivey JM. Radiation-induced uterine changes: MR imaging. Radiology Jan 1989;170(1 Pt 1):55–8. https://doi.org/10.1148/radiology.170.1.2909120.
[20] Kim EK, Yoon G, Kim HS. Chemotherapy-induced endometrial pathology: mimicry of malignancy and viral endometritis. Am J Transl Res 2016;8(5):2459–67.
[21] Griffiths MJ, Marshall SA, Cousins FL, et al. Radiotherapy exposure directly damages the uterus and causes pregnancy loss. JCI Insight Mar 22 2023;8(6). https://doi.org/10.1172/jci.insight.163704*.
[22] Prasad M, Bhatia S, Arora RS. The children's Oncology group long-term follow-up Guidelines for survivors of childhood, adolescent and young adult cancers version 6. Indian Pediatr Apr 15 2024;61(4):380–2.
[23] Chiarelli AM, Marrett LD, Darlington GA. Pregnancy outcomes in females after treatment for childhood cancer. Epidemiology Mar 2000;11(2):161–6. https://doi.org/10.1097/00001648-200003000-00013*.
[24] Signorello LB, Cohen SS, Bosetti C, et al. Female survivors of childhood cancer: preterm birth and low birth weight among their children. J Natl Cancer Inst Oct 18 2006;98(20):1453–61. https://doi.org/10.1093/jnci/djj394.
[25] Meernik C, Poole C, Engel SM, Rauh-Hain JA, Luke B, Nichols HB. Outcomes after assisted reproductive technology in women with cancer: a systematic review and meta-analysis. Hum Reprod Jan 5 2023;38(1):30–45. https://doi.org/10.1093/humrep/deac235*.
[26] Critchley HO, Wallace WH. Impact of cancer treatment on uterine function. J Natl Cancer Inst Monogr 2005;(34):64–8. https://doi.org/10.1093/jncimonographs/lgi022*.
[27] Critchley HO, Wallace WH, Shalet SM, Mamtora H, Higginson J, Anderson DC. Abdominal irradiation in childhood; the potential for pregnancy. Br J Obstet Gynaecol May 1992;99(5):392–4. https://doi.org/10.1111/j.1471-0528.1992.tb13755.x.
[28] Sudour H, Chastagner P, Claude L, et al. Fertility and pregnancy outcome after abdominal irradiation that included or excluded the pelvis in childhood tumor survivors. Int J Radiat Oncol Biol Phys Mar 1 2010;76(3):867–73. https://doi.org/10.1016/j.ijrobp.2009.04.012*.
[29] Beneventi F, Locatelli E, Giorgiani G, et al. Adolescent and adult uterine volume and uterine artery Doppler blood flow among subjects treated with bone marrow transplantation or chemotherapy in pediatric age: a case-control study. Fertil Steril Feb 2015;103(2):455–61. https://doi.org/10.1016/j.fertnstert.2014.10.043.
[30] Buonomo B, Orecchia R, Tomao F, Pup LD, Garcia-Faura A, Peccatori FA. Uterine irradiation as a determinant of infertility and pregnancy losses in young cancer survivors. ecancermedicalscience 2020;14:1032. https://doi.org/10.3332/ecancer.2020.1032*.
[31] Bender JD, Oquendo-Del Toro H, Benoit J, et al. Reduced-intensity conditioning mitigates risk for primary ovarian insufficiency but does not decrease risk for infertility in pediatric and young adult survivors of hematopoietic stem cell transplantation. Transplant Cell Ther Feb 2023;29(2):130.e1–8. https://doi.org/10.1016/j.jtct.2022.10.018.
[32] Arecco L, Ruelle T, Martelli V, et al. How to protect ovarian function before and during chemotherapy? J Clin Med Sep 16 2021;10(18). https://doi.org/10.3390/jcm10184192.
[33] Turkgeldi L, Cutner A, Turkgeldi E, et al. Laparoscopic ovarian transposition and ovariopexy for fertility preservation in patients treated with pelvic radiotherapy with or without chemotherapy. Facts Views Vis Obgyn Sep 2019;11(3):235–42.
[34] Lédée-Bataille N, Olivennes F, Lefaix JL, Chaouat G, Frydman R, Delanian S. Combined treatment by pentoxifylline and tocopherol for recipient women with a thin endometrium enrolled in an oocyte donation programme. Hum Reprod May 2002;17(5):1249–53. https://doi.org/10.1093/humrep/17.5.1249.
[35] Delanian S, Lefaix JL. The radiation-induced fibroatrophic process: therapeutic perspective via the antioxidant pathway. Radiother Oncol Nov 2004;73(2):119–31. https://doi.org/10.1016/j.radonc.2004.08.021.
[36] Acharya S, Yasmin E, Balen AH. The use of a combination of pentoxifylline and tocopherol in women with a thin endometrium undergoing assisted conception therapies–a report of 20 cases. Hum Fertil Dec 2009;12(4):198–203. https://doi.org/10.3109/14647270903377178.
[37] Marin L, Andrisani A, Bordin L, et al. Sildenafil supplementation for women undergoing infertility treatments: a systematic review and meta-analysis of randomized controlled trials. J Clin Med Sep 24 2021;10(19). https://doi.org/10.3390/jcm10194346.
[38] Sirait B, Jusuf AA, Wiweko B, Handayani N, Aubry DA, Muharam R. Potential use of immature oocyte to improve fertility preservation outcome: a narrative review. J Hum Reprod Sci Jan-Mar 2022;15(1):3–11. https://doi.org/10.4103/jhrs.jhrs_112_21.
[39] Abir R, Ben-Aharon I, Garor R, et al. Cryopreservation of in vitro matured oocytes in addition to ovarian tissue freezing for fertility preservation in paediatric female cancer patients before and after cancer therapy. Hum Reprod 2016;31(4):750–62. https://doi.org/10.1093/humrep/dew007.
[40] Resetkova N, Hayashi M, Kolp LA, Christianson MS. Fertility preservation for prepubertal girls: update and current challenges. Curr Obstet Gynecol Rep 2013;2(4):218–25. https://doi.org/10.1007/s13669-013-0060-9.
[41] Gupta D, Singh S, Shukla S, Shrivastava S. Oncofertility: treatment options from bench to bedside. Cancer Pathog Ther Oct 2023;1(4):284–9. https://doi.org/10.1016/j.cpt.2023.05.001.
[42] Moravek MB, Confino R, Smith KN, et al. Long-term outcomes in cancer patients who did or did not pursue fertility preservation. Fertil Steril Feb 2018;109(2):349–55. https://doi.org/10.1016/j.fertnstert.2017.10.029.
[43] Johannesson L, Richards E, Reddy V, et al. The first 5 Years of uterus transplant in the us: a report from the United States uterus transplant consortium. JAMA Surg Sep 1 2022;157(9):790–7. https://doi.org/10.1001/jamasurg.2022.2612.