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Fertility Preservation Strategies in Cancer Patients: A Comprehensive Review

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Abstract

Introduction and purpose. Preserving fertility is crucial for cancer patients, aligning with advancements in oncology. As survival rates improve, addressing treatment-related late effects gains importance. Many young patients, aware of therapy toxicity, consider future conception chances, impacting treatment decisions. With a trend toward delayed childbirth and a growing population facing unplanned family planning disruptions, the demand for fertility preservation is expected to rise. This paper provides a brief review of available methods for preserving fertility in cancer patients.

State of knowledge. Freezing semen in liquid nitrogen vapor is a standard method for preserving reproductive potential in male cancer patients. Shielding during total-body radiation limits testicular volume reduction, indicating less damage to the germinal

epithelium. Hormone suppression treatments are not protective in male cancer patients. Oocyte and embryo cryopreservation are considered secure methods before anticancer treatments, with oocyte cryopreservation being preferred for post-pubertal women. Ovarian tissue cryopreservation remains an alternative method without preliminary treatment, suitable when time is insufficient for ovarian stimulation. Ovarian transposition beyond the intended radiation area, performed laparoscopically, can retain ovarian function. GnRH agonist administration before and during chemotherapy aims to minimize the likelihood of premature ovarian insufficiency.

Summary. Advancements in fertility preservation for cancer patients, ranging from traditional cryopreservation to innovative methods like ovarian tissue preservation, highlight a commitment to empowering individuals facing cancer diagnoses. Ongoing research expands possibilities, ensuring a diverse range of strategies that offer tangible and hopeful prospects at the intersection of cancer and reproductive health.

Keywords: cancer; fertility; pregnancy

Introduction

Preserving fertility in cancer patients has become a paramount concern in the realm of contemporary oncology. Along with developing effective treatment methods and improving survival rates in most malignancies, health care is faced with treatment-related late effects [1]. Thus, the need has increased to improve the quality of life and return patients to normal functioning after achieving long-term remissions. Aware of the toxicity of therapy, many young people at the time of diagnosis are faced with chances of conception in the future. This may significantly influence their choices and adherence to the proposed anticancer treatments [2]. Given the increasing tendency to postpone childbirth and the growing population of individuals who have not finalized their family planning when diagnosed, there is anticipated growth in the need for fertility preservation.

Gonadotoxicity of anticancer treatments

Both the proposed anticancer therapies, as well as the type of cancer, and the overall condition of the patient may induce treatment-related gonadal failure and infertility. of treatment-related azoospermia and infertility in male patients [3]. Factors that put patients at the highest risk of azoospermia in male and amenorrhoea in female include: conditioning radiotherapy (RT) and/or chemotherapy (ChT) for haematopoietic stem cell transplantation (HSCT), RT to a field including the testicles or ovaries, as well as ChT with alkylating agents (e.g., cyclophosphamide, procarbazine) [4].

1. Fertility preservation in male patients

1.1. Sperm cryopreservation

Sperm cryopreservation is a standard-of-care method to preserve reproductive potential in adult or adolescent male cancer patients. This strategy involves freezing semen samples mainly in liquid nitrogen vapor for later reuse in various assisted reproductive techniques (e.g., intrauterine insemination, in vitro fertilization, intracytoplasmic sperm injection) [5]. On the basis of numerous studies the efficacy has been estimated at the aggregate rate of around 49% [6]. It has also been noted that long-term storage of cryopreserved sperm does not come at the expense of deterioration of semen quality and, therefore, worse outcomes. As potential genetic abnormalities may occur in sperm after exposure to ChT or RT, sperm cryopreservation should be offered before treatment initiation [5].

1.2. Gonadal shielding during RT

Gonadal shielding during total-body RT has been shown to contribute to limiting the reduction in testicular volume, which indirectly indicates less damage to the germinal epithelium [7]. Therefore, it should be used whenever possible to minimize radiation exposure.

1.3. Medical gonadoprotection

Hormone suppression treatments such as a gonadotropin-releasing hormone (GnRH) agonist, with or without androgens, antiandrogens or progestins, are not protective in male cancer patients [8].

2. Fertility preservation in female patients

2.1. Oocyte and embryo cryopreservation

Cryopreserving oocytes and embryos prior to starting anticancer treatments is a secure and effective practice. While embryo cryopreservation is a well-established and reliable method, it necessitates the involvement of sperm and the availability of a partner or donor [9]. In contrast, oocyte cryopreservation can be performed independently, making it the preferred choice for the majority of post-pubertal women [10]. For oocyte and embryo cryopreservation, ~2 weeks of ovarian stimulation with gonadotropins is required, followed by follicle aspiration [11]. The success of generating a future pregnancy through oocyte and embryo cryopreservation is closely linked to the quantity of mature oocytes obtained following ovarian stimulation. This may be reduced in women with poor ovarian reserve due to age, previous diseases or ovarian surgery [12]. Recent findings indicated that the cumulative live birth rate ranged from 43.4% to 61.9%, with variations influenced by age and the quantity of cryopreserved oocytes [13]. The use of ovarian stimulation may result in side effects from the medication and potential complications during the oocyte retrieval process, such as bleeding from the ovary and the risk of pelvic infection [14]. These should be considered especially in relation to the overall picture of the patient and the conditions that may predispose to the occurrence of the complications. In estrogen-sensitive tumors, it is advisable to lower estradiol levels during ovarian stimulation. This can be accomplished through co-treatment with aromatase inhibitors (such as letrozole at a dosage of 2.5 mg twice daily) [15]. Combining ovarian stimulation with the cryopreservation of ovarian tissue could enhance the success rate for women undergoing highly gonadotoxic treatments.

2.2. Ovarian tissue cryopreservation

Cryopreserving ovarian tissue serves as an alternative method for preserving fertility prior to undergoing gonadotoxic treatments. Typically, laparoscopic procedures under general anesthesia are employed for the performance of ovarian cortex biopsies or unilateral ovariectomies [16]. No preliminary treatment is necessary, allowing the procedure to be completed promptly, and chemotherapy can commence the following day if needed [17]. At present, transplantation, whether performed orthotopically or heterotopically, is the sole clinically utilized method to restore ovarian function and fertility through the use of cryopreserved ovarian tissue [18]. The study results showed that ovarian function was restored in an average of 95% of patients undergoing the procedure [19]. Ovarian tissue cryopreservation is suitable in situations where the time frame before initiating anticancer treatments is insufficient for ovarian stimulation prior to oocyte or embryo cryopreservation [20]. In special cases the procedure can be performed following an initial, low-intensity ChT to mitigate the potential presence of neoplastic cells in the ovaries [21].

2.3. Ovarian transposition and gonadal shielding during RT

The practice of routinely employing ovarian transposition beyond the intended RT area is a common technique aimed at reducing the exposure of ovarian follicles to radiation [22]. While it is feasible to perform the procedure using either laparotomic or laparoscopic methods, the preference is generally for laparoscopy [23]. This choice is made to expedite recovery and prevent any delays in the administration of RT. One study has shown that patients who undergo surgery and radiation therapy typically experience a retention of ovarian function at a rate of around 63.6% [24]. Limited data exist regarding pregnancy rates, with observed variations ranging from 15% to 80% [25]. The use of lead blocks for gonadal shielding during RT decreases the anticipated radiation dose. [26]. However, it is necessary to maintain an appropriate margin to reduce the impact of inner organ movement.

2.4. Medical gonadoprotection

The objective of medical gonadoprotection during ChT is to minimize the likelihood of premature ovarian insufficiency (POI) and the consequential impacts on fertility and endocrine functions [27]. Hence, this approach could also be beneficial for individuals who

do not intend to conceive and are not concerned about preserving fertility. To induce temporary ovarian suppression during chemotherapy, a GnRH agonist is administered, commencing at least one week before the onset of systemic cytotoxic therapy and sustained throughout the treatment period [28]. It has been suggested that in a group of women diagnosed with estrogen receptor-positive breast cancer prolonged application of GnRH agonist up to 5 years post-diagnosis may serve as adjuvant endocrine therapy [29]. It is essential to note that for individuals concerned about preserving fertility using a GnRH agonist should not be viewed as a substitute for cryopreservation techniques.

Summary

The evolving landscape of fertility preservation methods in cancer patients reflects a commitment to enhancing the reproductive choices of individuals facing cancer diagnoses. From conventional cryopreservation techniques to innovative approaches like ovarian tissue preservation, these methods underscore the resilience of the human spirit and the collaborative efforts of medical science. As research continues to push boundaries, the integration of these diverse strategies ensures that fertility preservation remains a tangible and hopeful prospect for those navigating the complex intersection of cancer and reproductive health.

Author's contribution

Conceptualization: MR, PB; methodology: MR, PB; software: MR, PB, PR, JR; check: MR, PB, PR, JR; formal analysis: MR, PB, PR, JR; investigation: MR, PB, PR, JR, JR, BM, KM, WR; resources: MR, PB, PR, JR; data curation: MR, PB, PR, JR, JR, BM, KM, WR; writing - rough preparation: MR, PB, PR, JR, JR, BM, KM, WR; writing - review and editing: MR, PB, PR, JR, JR, BM, KM, WR; visualization: MR, PB; supervision: MR, PB; project administration: MR, PB. All authors have read and agreed to the published version of the manuscript.

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