

Oncofertility

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When we talk about cancer, the world collapses and we are forced to postpone some personal projects. The focus of the attention is often directed towards treatment options and their effectiveness and it is easy to forget those other issues that are also important to preserving the patient's quality of life, namely the preservation and protection of fertility.

The rate of detection of cancer during the fertile ages is increasing and, with that, the need for professionals to be attentive and inform patients of the consequences that the treatments may have in the survival phase. Crucially, the **risk of infertility associated with the treatments** as well as the existing and appropriate options for their situation to preserve and protect their fertility, if it is their wish and their clinical acuity allows for the delay. It is important to clarify doubts, as well as refer the patient to fertility specialists as soon as possible. Effort is required by health professionals, as a team, to try to support the cancer patient to achieve their life projects, as these were forced to be postponed. To do that they need to be spoken about openly. Although it is a more suitable subject for the oncologist, the cancer nurses, in the first approach to the patient, should be able to talk about this topic and understand what the patient's expectations are and whether the issue of fertility preservation was addressed by the doctor. Fertility is not only influenced by treatments but is also dependent on multiple factors unique to each patient/couple (age, smoking, BMI, hereditary conditions, etc.) or to the disease itself. Therefore, counselling must be individualised, considering these factors, and without forgetting the psychosocial component.

The treatments used in the context of oncological disease (surgery, radiotherapy, and systemic therapy) can influence fertility through **direct gonadotoxicity**, in which there is direct damage to the ovary or the seminiferous epithelium in the testis, or **indirect gonadotoxicity**. This occurs when there is impact to the level of functioning of the hypothalamic-pituitary-gonadal axis, mainly through the effect on endocrine function, or by changes in uterine function in women, and erectile or ejaculatory functions in men. This can be caused by pelvic irradiation or by some types of surgery of the reproductive system.

Surgery, radiotherapy, chemotherapy, hormone therapy, biological therapies, immunotherapy; all these types of treatment have an impact on fertility, as they can induce amenorrhea or azoospermia.

Radioactive iodine treatment alone does not cause infertility (male or female), nor does it cause problems during pregnancy. However, as a precaution, pregnancy should be avoided for 1 year after treatment.

Fertility preservation techniques

The techniques for **preserving fertility in women** are the following:

- Cryopreservation of oocytes or embryos: stimulation of the ovaries is required and results in the postponement of the start of treatment by more than 2 weeks.
- Cryopreservation of ovarian tissue: this technique, which is still considered experimental, is the only one that does not require ovarian stimulation or follicular puncture. The bonus therefore is that there is minimal postponement of the treatment of the oncological disease (less than 2 weeks). However, as the age limit for this is 36 years, it is not a technique that is suitable for all patients (considered by ESMO Guidelines).
- In-vitro oocyte maturation: collection of immature oocytes (without resorting to ovarian stimulation and, therefore, without risk of plasma oestrogen elevation) for later in-vitro maturation before or after vitrification. It is an alternative technique whose effectiveness is difficult to quantify.

The techniques for **protecting fertility in women** consist of:

- Ovarian transposition and gonadal shielding during RT.
- Conservative gynaecological surgery: women with early-stage cervical cancer and lesions ≤ 2 cm, who wish to preserve their fertility or women with early stage ovarian cancer.
- Temporary suppression of ovarian function should be considered as a standard option for preserving ovarian function in premenopausal breast cancer patients undergoing (neo)adjuvant systemic cytotoxic therapy.

In the case of **men, fertility preservation** techniques are sperm cryopreservation, which has good success rates and is the standard treatment, or testicular tissue cryopreservation (experimental). This is indicated for patients who are unable to obtain a blood sample, adequate sperm or boys who have not yet reached puberty.

The techniques for **protecting fertility in men** are:

- Conservative surgery: using a partial orchidectomy.
- Medical gonadoprotection: hormone suppression treatments are not protective against cancer in men.
- Gonadal shielding during RT: reduces exposure of the germinal epithelium to radiation and protects reproductive function.

Pregnancy after cancer

The optimal interval between the end of systemic treatment and the planning of a pregnancy remains unknown. A multidisciplinary team is needed to assess the optimal time for pregnancy, and the follow-up strategy to be adopted.

When counselling young women about pregnancy after cancer treatment, consideration should be given to individual patient and disease characteristics, including age, previous parity, risk of recurrence, and expected residual fertility after treatment.

The fertility markers (ovarian reserve) are as follows:

- Serum measurement of anti-Mullerian hormone and follicle stimulating hormone (FSH),
- Antral follicle count (ultrasound performed in the early follicular phase),
- Number of successful pregnancies.

In general, pregnancy should be avoided within 6 months of any systemic treatment (chemotherapy, hormone therapy, monoclonal antibodies or TKIs) due to the teratogenic risk (DNA damage and chromosomal abnormalities in oocytes).

Oncofertility is a delicate area, full of ethical dilemmas and is one that needs particular attention, in the search for an ethically correct approach for patients.

Ethics applied to the preservation of fertility has to be pragmatic and cannot be reduced to a single ethical principle or system – the intentions, actions and consequences are all ethically relevant.

Health professionals should discuss with the patient/couple (or, in the case of children, with their parents or legal representatives) the risk of infertility and the possibilities of preserving fertility, considering the individual risk and the options for the preservation. Timely action is essential and fertility-preserving treatments need to be completed before starting treatments which are potentially harmful to gonadal function. It is also important to consider the future financial impact to the patient.

This blog article was written based mainly on ESMO Guidelines.

Lambertini, M., Peccatori, F. A., Demeestere, I., Amant, F., Wyns, C., Stukenborg, J. B., Paluch-Shimon, S., Halaska, M. J., Uzan, C., Meissner, J., von Wolff, M., Anderson, R. A., & Jordan, K. (2020). Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines. *Annals of Oncology*, *31*(12), 1664–1678. <https://doi.org/10.1016/j.annonc.2020.09.006>

Oktay, K., Harvey, B. E., Partridge, A. H., Quinn, G. P., Reinecke, J., Taylor, H. S., Hamish Wallace, W., Wang, E. T., & Loren, A. W. (2018). Fertility preservation in patients with cancer: ASCO clinical practice guideline update. *Journal of Clinical Oncology*, *36*(19), 1994–2001. <https://doi.org/10.1200/JCO.2018.78.1914>

Santos, T. A., Melo, C., Silva, C., & Augusto, I. (2016). Recomendações para a preservação do potencial reprodutivo no doente oncológico. *Revista Portuguesa de Oncologia Vol 2 (N1): 5-24, November*. https://www.sponcologia.pt/fotos/editor2/articulo_recomendaciones.pdf