



Oncofertility: the oncologist point of view

Giovanni Codacci-Pisanelli, MD, PhD
Assistant Professor in Medical Oncology
Fertility and Procreation Unit
European Institute of Oncology (IEO)
Milan, Italy

Giovanni.Codacci-Pisanelli@uniroma1.it

For many years the focus of oncologists was on the most effective cancer treatment, with little attention being paid to patient needs, for the sake of “cure”. But with increasing prognosis, other aspects began to take scene. Quality of life during treatment, and quality (not only quantity!) of life after treatment became major topics.

Long term toxicities that for a long time had been neglected now required treatment and, even more so, prevention. Among these, the reproductive damage caused by anticancer agents. But again, for a long time this attention was limited to males. Gamete collection and conservation was easy and rapid: sperm banking and retrieval for cancer patients is a reality since a long time.

The attitude towards women was different: oocyte collection is more cumbersome and requires at least two weeks of ovarian stimulation... All these aspects appeared as absolute contraindications to fertility preservation. Furthermore pregnancy was considered dangerous, especially for women with breast cancer, and last but not least it was assumed that it was unethical to preserve fertility of a woman with a poor prognosis, that would then leave an orphan child (this apparently did not apply to men!). This situation has been analysed in papers originating from different Countries and cultural areas in the world [Shimizu et al 2013, Adams et al 2013, Forman et al 2010, Quinn et al 2009].

But as the Nobel laureate Bob Dylan would say: “times they are a’changin”. The issue of subsequent infertility is especially relevant for women undergoing chemotherapy [Partridge et al 2004], particularly for those that have not yet completed their reproductive plans; with the rapid increase of age at first pregnancy it is more and more common to be confronted with women that have not yet had their first child and that need chemotherapy for cancer (breast cancer and haematological malignancies are the most frequent situations). Oncologists are now more careful about fertility issues [Biglia et al 2015] even if the attitude toward fertility preservation must in many cases be improved: several recent articles published in different parts of the world underscore that fertility issues are often not properly discussed with patients and that many oncologists are still sceptical about the safety of these procedures [Abe et al 2016, Vu et al 2017, Fournier et al 2016, King et al 2012, Adams et al 2013, Woodruff et al 2016].

To improve this situation specific programmes have been introduced to help clinicians (and patients) to make an informed choice on this subject [Kelvin et al 2016].

On the other hand it is now firmly established that pregnancy does not affect the prognosis of breast cancer patients [Azim et al 2013] [Goldrat et al 2015, Peccatori et al 2009] even in women whose tumours expressed oestrogen receptors.

Technical progresses have made things easier: the possibility of effectively conserving non-fertilised oocytes not only swept away most ethical concerns related to preservation of fertilised oocytes, but also emancipated women from the need of a partner to preserve their fertility. At the same time the possibility of a random start of hormone stimulation allowed gynaecologists to collect oocytes with no need to synchronize treatment with the woman's menstrual cycle [Sonmezer et al 2011].

Finally, the coadministration of tamoxifen [Meirow et al 2014] or of aromatase inhibitors blunts the oestrogen peak and makes ovarian stimulation feasible even in women that have not yet been operated for breast carcinoma [Oktay et al 2005] [Azim et al 2007].

Several oncological associations issued guidelines on fertility preservation [Cardoso et al 2012, Loren et al 2013, Practice Committee of American Society for Reproductive Medicine et al 2013, Peccatori et al 2013].

But a real problem remains: time.

Very often oncologists refer women for fertility preservation just the day before chemotherapy, too late to do anything [Lee et al 2010].

Time, on the other hand, is the main cause of ovarian damage in women. The progressive exhaustion of oocyte reserve and the increased susceptibility of older women to chemotherapy-induced ovarian damage lead to uneasy decisions. Waiting five years to complete the standard endocrine treatment of young breast cancer patients will lead to an age when the probability of having a child are low. For this reason a trial [International Breast Cancer Study Group et al 2014] is evaluating the outcome of women that interrupt hormonal treatment for the time necessary to give birth and then resume treatment to complete the standard five years of tamoxifen.

Prevention is more effective than cure, so it is now possible to protect fertility of women undergoing adjuvant chemotherapy for breast cancer by the administration of LHRH analogues [Del Mastro et al 2011].

New promising techniques are being evaluated [Rodriguez-Wallberg et al 2011], including ovarian preservation that has already become standard in some Countries [Meirow et al 2016].

Female fertility is something precious, fragile and vanishing. It seems that oncologists now realise how important it is to preserve it, but too often they do not act at the proper time. Hopefully, once again, "times, they are a'changin".

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