

# Fertility concerns and preservation strategies in young women with breast cancer

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Prospective study of fertility concerns and preservation strategies in young women with breast cancer was a prospective survey of attitudes regarding fertility among younger women (age 40 and under) with breast cancer in the US (1). The study examined whether or not fertility was discussed when the patient was diagnosed, whether or not the patient had fertility concerns when treatment began, what steps could be taken to preserve fertility, and what effect fertility concerns actually had on treatment decisions.

The concept of survivorship, or helping individuals diagnosed cancer to lead full lives, has gained widespread acceptance. In Europe and the US, guidelines have been issued predicated on the recognition that fertility preservation (FP) should be considered for all patients with cancer who are of reproductive age and who will be undergoing anti-cancer drug therapy (2-4). Other reports, however, have suggested that breast cancer specialists' knowledge and their attitudes towards actively FP were related to their efforts to provide information to patients (5). These studies also surmised that there are differences in the information and options offered to patients depending on the physician. This study by Ruddy *et al.* reported that 68% patients discussed fertility issues with their physicians before starting therapy. Previous studies from Europe and the US have found that patients are not adequately informed of the effects of drug therapy on reproductive function, including early menopause, or of the FP (6-11). Those previous studies noted differences in whether or not FP was explained depending on aspects such as the patient's age at diagnosis, whether or not the patient had children, the patient's educational level, the type of drug therapy, and the stage of cancer. Several problems for oncologists

are not known a reproductive specialist to confer with and time constraints upon clinical practice (5). Issues that need to be dealt with are creation of an information network for oncologists and reproductive specialists and establishment of a system for collaboration.

That said, there were very few prospective studies on the current state of patients' attitudes. This study by Ruddy *et al.* found that half of all patients were concerned about becoming infertile after treatment and that greater concern about fertility was associated with younger age, nonwhite race, not having children, and receipt of chemotherapy. According to the study, concerns about fertility were significantly affected by social background. These findings do not necessarily apply everywhere around the world. Aspects such as the average marrying age, the role of women in society, and childrearing conditions differ considerably in depending on the country and region. However, the incontrovertible fact is that numerous patients need to be fully informed about a treatment's effects on their fertility before that treatment begins.

A more significant finding reported by Ruddy *et al.* is that there were instances where the strategy for treatment of breast cancer was changed because of its potential effects on fertility. In many of those instances, standard postoperative drug therapy was originally intended to limit recurrence as much as possible but this regimen was modified or its duration was shortened. Such a decision must be made prudently since it has the potential to worsen a patient's prognosis. A patient must be fully informed of a treatment's effects on her fertility and other options, including preservation of fertility, in order to choose a treatment. However, there appears to be little available evidence of

this at the current point in time. Effects on fertility differ depending on the patient's age, ovarian reserve, and type of medication, so many uncertainties remain with regard to whether a patient will be able to have children after undergoing drug therapy. Thus, research is beginning to look at indices to predict ovarian reserve prior to treatment and after drug therapy. Anti-Mullerian hormone (AMH) is one such index. Patients with chemotherapy-related amenorrhea are reported to have low levels of AMH prior to treatment (12,13). If research into these factors progresses, then the subsequent findings will help with patient discussions of fertility prior to treatment and allow planning of a treatment strategy in light of survivorship after treatment.

Medical reproductive technology is being used to grant the wishes of younger patients with cancer who are undergoing anti-cancer drug therapy but who want to have children. Embryos or oocytes are being preserved before the start of drug therapy, and the cryopreservation of ovarian tissue has recently been attempted (14). This technique could preserve reproductive function if guidelines on the standard treatment for breast cancer are followed. This technique would prove extremely useful in terms of both treating breast cancer and preserving reproductive function to the maximum extent. However, this technique still has a number of issues, such as the fact that its effects on breast cancer prognosis are not known, it results in a low rate of successful conception, and it is highly expensive. The study on ovarian tissue cryopreservation by Fabbri *et al.* used a small subject sample. A major issue with ovarian tissue cryopreservation is that no studies have reported the prognosis when patients with breast cancer use reproductive medicine. FP often involves inducing oocyte stimulation in order to harvest numerous eggs from the patient and it increases levels of estrogen in the blood compared to those during a normal menstrual cycle, so a hormone-sensitive tumor may recur or become more aggressive. Over the past few years, studies have begun to attempt to limit the rise in estrogen levels to the extent possible by inducing oocyte stimulation using aromatase inhibitors (15,16).

The dearth of evidence has hampered the informing of patients with breast cancer about fertility and the selection of a suitable treatment in accordance with the patient's wishes. However, a study on the decision to undergo counseling with regard to early menopause when treatment starts and treatment's effects on reproductive function has reported that counseling should not be limited to patients who actually have their reproductive function preserved (17).

Instead, the study reported that all women of childbearing age with breast cancer who underwent counseling had a higher QOL after treatment. Moreover, another study indicated that an explanation needs to be provided by an oncologist as well as a reproductive specialist so that a patient can select a treatment without regrets (7). Patients lack adequate knowledge of issues with their reproductive function at the start of treatment, but providing information at the appropriate time both allows the patient to select a treatment without regrets (18) and it significantly alleviates subsequent distress and symptoms due to menopause (19). Prospective studies like that by Ruddy *et al.* need to be assembled and current conditions and needs must be prospectively studied, as the study by Ruddy *et al.* did, in accordance with social backgrounds in different places. Based on these findings, fertility counseling systems and FP strategies tailored to those places must be crafted by medical personnel in multiple disciplines such as oncologists and reproductive specialists.

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