Fertility Preservation in Women With Breast Cancer: Challenges and Opportunities

June 15, 2013
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Collaboration between oncologists and reproductive endocrinologists/infertility specialists not only will improve patient care, but it also will facilitate advances in the field through cooperative research and education.

This important and timely review by Dr. Munster effectively highlights the complexity of addressing fertility-related issues and fertility preservation in young women with breast cancer. Given the lack of long-term data, we are often left with more questions than answers about determining the appropriate management of these patients. Caring for women with estrogen receptor-positive tumors and BRCA mutations can add additional complexity. Women with hormone receptor-positive tumors face years of estrogen deprivation and/or endocrine therapy that is contraindicated during pregnancy. BRCA mutation carriers may also consider risk-reducing surgeries to decrease the risk of second breast cancers or to prevent ovarian cancers, thus further limiting fertility potential. In considering fertility issues in breast cancer patients, we must also contemplate the available data regarding the safety of pregnancy after breast cancer, the effects of breast cancer treatment on fertility, and how these effects impact women’s ability to cope with their diagnosis and their survivorship. This intersection of oncology and reproductive endocrinology will provide greater coordination of care and offer even more opportunities for our patients to pursue fertility options along with their cancer care.

Recent literature has explored the safety of pregnancy in breast cancer survivors; two meta-analyses have shown a survival benefit for women who conceive after cancer, even when controlling for the healthy mother effect.[1,2] The healthy mother effect is the idea that women who are healthy are more likely to conceive and give birth than those who are not; this effect can be a potential source of bias in studies of the impact of pregnancy on prognosis in women with a history of cancer.[3] Furthermore, a recent retrospective cohort study showed that women with estrogen receptor-positive cancers who became pregnant did not fare any worse than those who did not become pregnant.[4] These are retrospective in nature, since no prospective randomized trial can be done; therefore showing benefit may be interpreted as at least showing no significant increase in death. In several of these studies, it was shown that women who waited 2 and even more than 4 years after diagnosis had a decreased risk of dying when compared with women who did not have a subsequent pregnancy.[5,6] Thus, it appears that for some women, pregnancy is a viable and reasonable option, but each woman needs to discuss and understand her personal risk of recurrence when deciding whether or not to pursue pregnancy after a breast cancer diagnosis.

Pregnancy is often delayed because of the recommendation that women wait at least 2 years before attempting to conceive, and because of the need for adjuvant hormone therapy with tamoxifen for 5 years. In these cases, women who have elected not to pursue fertility preservation may have chemotherapy-induced ovarian dysfunction that is further compounded by older age. As such, current considerations to extend tamoxifen therapy to 10 years will place biologic parenthood out of reach for almost all but the youngest women.[7]

While there are many challenges and uncertainties, we know that cancer-related infertility is real and that many women are concerned about it.[8,9] Although women often do not see fertility preservation as a priority at the time of diagnosis, it may become increasingly important to them after they have been treated. It has been shown that cancer-related infertility causes significant distress, particularly if patients feel that their reproductive risks and concerns were not adequately addressed or discussed. We also know that many women lack adequate access to fertility preservation counseling and services, as a result of deficient knowledge and awareness on the part of both patients and providers, misconceptions about safety and timing, and providers’ personal biases about the appropriateness of such a referral.[10,11]

Although our current armamentarium for fertility preservation has limitations, we still have a lot to...
offer to our patients. Though imperfect, measurements of anti-Müllerian hormone (AMH) and antral follicle counts (AFC) by ultrasound can help us estimate a woman’s baseline ovarian reserve, which can help to guide fertility preservation counseling.[12,13] As Dr. Munster has detailed, advances in assisted reproductive technologies (ART) have resulted in acceptable pregnancy rates (which may be even better because cancer patients are not an infertility population) and reassuring safety profiles.[14,15] While ART remains the most viable option with the highest success rates, research evaluating other potential fertility preservation methods—such as ovarian tissue freezing, in vitro maturation, and the use of gametes derived from stem cells—is in progress; these new techniques could ultimately revolutionize how we preserve fertility in patients with cancer and expand our ability to reach a broader population of patients.[16,17]

In every challenge lies opportunity. While there is still much work to be done, we have tremendous room for improvement in utilizing the resources that we have; we must do a better job of referring women for a fertility preservation consultation and supporting them during the decision-making process. Patients who have fertility preservation consultations report less distress than those who did not, even if they elect not to preserve fertility.[18] Although we have directed tremendous time and effort toward improving fertility preservation techniques, we have neglected to consider the factors that influence whether or not a woman ultimately decides to opt for fertility preservation. Unlike most other medical decisions, young women with breast cancer have to make a complex, future-oriented decision under significant physical, emotional, and financial stress. This decision may be further complicated by uncertain feelings about biological parenthood, the knowledge that a successful pregnancy is not guaranteed, the expenses associated with the various fertility preservation methods, and the fact that these techniques may end up being unnecessary. Making a decision about fertility preservation is a process that is currently overlooked; future research should focus on interventions that could facilitate this process, such as the use of psychological counseling and decision aids.

At a minimum, we owe it to our patients to consider their individual circumstances, provide them with the best risk assessment we can with respect to the impact of their chemotherapy on fertility, and empower them with the knowledge to make an informed decision that is appropriate and consistent with their desires and values. Achieving this requires thoughtful coordination of care through a multidisciplinary collaboration of providers who are committed to these issues. Collaboration between oncologists and reproductive endocrinologists/infertility specialists not only will improve patient care, but it also will facilitate advances in the field through cooperative research and education.

**Financial Disclosure:** The authors have no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

**References:**

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