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# Current Evidence Supporting Fertility and Pregnancy Among Young Survivors of Breast Cancer

Karen Meneses and Aimee Chism Holland

**ABSTRACT**

Approximately 6% of invasive breast cancer is diagnosed in women younger than age 40 of age childbearing potential. Cancer-directed therapies can cause hormonal and anatomical changes that negatively affect the reproductive potential of young survivors of breast cancer. Recent national guidelines on fertility preservation are widely available. However, gaps in care exist in the interdisciplinary evidence-based management of young survivors of breast cancer with fertility and parenting concerns after cancer treatment.

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In the United States, breast cancer is the most common cancer to affect women and the second leading cause of cancer-related deaths in women in the United States (American Cancer Society [ACS], 2013). About 6% of invasive breast cancer is diagnosed in women with childbearing potential younger than age 40 (ACS, 2013). Thus, the possible loss of reproductive potential due to toxicities from cancer therapy has a profound impact on quality of life and can increase psychosocial distress among young survivors of breast cancer (Howard-Anderson, Ganz, Bower, & Stanton, 2012).

Trends in our management of the fertility-related concerns of young survivors of breast cancer have changed dramatically during the past 20 years. Recently, fertility discussions were infrequently or rarely provided by oncology specialists and other care providers (Dow, 1990). Young women had to actively seek reproductive counseling (Dow, 1994). With the wider availability of accepted assisted reproductive technology (ART), young women are being referred for reproductive counseling earlier after a breast cancer diagnosis. In addition, key professional and advocacy organizations have issued recent statements or updated guidelines to support discussions of fertility preservation.

Young survivors of breast cancer demand and deserve the most current evidence-based information about fertility preservation to achieve their goals of becoming pregnant and having children after breast cancer. Yet gaps remain in two key areas: the broader interdisciplinary dissemination of national fertility guidelines and research focusing on young women with breast cancer. The purpose of this review article is to provide the evidence for (a) the effects of cancer treatment on gonadal function in young women with breast cancer, (b) national fertility guidelines and the role of breast cancer advocacy, (c) implications for nursing practice, and (d) future implications in interdisciplinary care of young women with breast cancer with concerns related to fertility and pregnancy.

## Effects of Cancer Treatment on Gonadal Function

The incidence of ovarian failure with breast cancer treatment is related to type of chemotherapy regimen, age at diagnosis, and tamoxifen use. Chemotherapy regimens containing alkylating agents such as cyclophosphamide deplete of ovarian reserves and induce temporary or permanent amenorrhea. The incidence of chemotherapy induced amenorrhea among younger women ranges from 15% to 75% when cyclophosphamide is part of the regimen (Jung et al., 2010; Lambertini, Anserini, Levaggi, Poggio, & DeMastro, 2013; Pagani et al., 2011) compared to 9% in regimens that omit cyclophosphamide (Lambertini et al., 2013).

Age has an additive effect to chemotherapy resulting in an increase in the risk of amenorrhea and infertility. Women are born with a finite number of oocytes that decreases over time as women age into menopause. Women younger than age 35 treated with cyclophosphamide have approximately a 10% incidence of amenorrhea; women older than age 40 treated with cyclophosphamide have about a 75% incidence of amenorrhea (Lambertini et al., 2013).

Tamoxifen is often used as endocrine therapy after chemotherapy in premenopausal young women whose tumors are estrogen receptor positive. The duration of tamoxifen therapy generally lasts for 5 years. Although tamoxifen is associated with a low risk of amenorrhea, pregnancy attempts are contraindicated during this time period. At the completion of tamoxifen, young women will be 5 years older and will have a higher risk of permanent amenorrhea related to advancing age.

Young survivors of breast cancer who experience amenorrhea during and immediately after chemotherapy can resume normal menses (Petrek et al., 2006). Generally, women younger than age 35 at the time of chemotherapy will resume menses between 6 and 12 months after the end of chemotherapy. It takes longer for survivors of breast cancer between ages of 35 and 40 to resume menses than younger women. Survivors of breast cancer who are older than age 40 have the highest risk of developing permanent amenorrhea after chemotherapy. Moreover, despite resumption of menses, fertility can be compromised because chemotherapy increases the depletion of ovarian reserve.

## Fertility Preservation Guidelines and Breast Cancer Advocacy

The first comprehensive fertility preservation guidelines were issued by the American Society of Clinical Oncology (ASCO) in 2006 (Lee et al., 2006). In growing response to vocal concerns of many young cancer survivors, including those with breast cancer, ASCO convened a panel of oncologists, scientists, and advocates who met to examine the evidence and available research on fertility and cancer. The 2006 ASCO Fertility Preservation Guidelines highlighted the need for the following: having frank discussions of fertility preservation, starting prompt referral to reproductive specialists, addressing fertility preservation as early as possible and prior to the start of cancer treatment, documenting fertility discussions, answering basic questions, referring for psychosocial distress, and encouraging participation in clinical studies and registries where appropriate.

**Clinical practice guidelines for preserving fertility in cancer patients were updated in 2013 by The American Society of Clinical Oncology.**

Seven years later, ASCO convened another panel to examine updated evidence on fertility preservation and issued an update in 2013 (Loren et al., 2013). The revised guideline reconfirmed the 2006 recommendations, but two significant changes were added. First, the panel recognized oocyte cryopreservation was no longer experimental but a recognized standard fertility preservation practice. Second, the panel replaced the term *oncologist* with *health care provider* in recognition that nononcology physicians, nurses, social workers, psychologists, and nonphysician providers have an extremely vital role in the interdisciplinary approach to addressing and managing fertility concerns of young cancer survivors.

### Advocacy for Fertility Education and Support

Young survivors of breast cancer led the call for stronger advocacy regarding fertility education and support for survivors. Through their dedicated efforts, fertility information and support have been widely disseminated through the websites and social media of national and grassroots breast cancer advocacy groups (Gorman, Usita, Madlensky, & Pierce, 2011; Meneses, McNees, Azuero, & Jukkala, 2010). The advocacy groups with dedicated information about fertility preservation education and support include but are not limited to the following organizations: Fertile Hope, the Young Survival Coalition, Living Beyond Breast Cancer, and The Susan G. Komen for the Cure. The websites of these organizations contain excellent, reliable, literate, and evidence-based options and information regarding fertility preservation.

Regional and local advocacy organizations dedicated to the needs of young survivors of breast cancer often provide available resources, education, and networking for young survivors of breast cancer who are not able to attend or access national programs. Regional and local advocacy groups can also provide resources for spouses and families of young survivors. One such organization that has a family-centered approach