Radiotherapy in Young Patients Linked to Worse Breast Cancer Survival

BY WARREN FROELICH

Adolescent and young females treated with radiotherapy for childhood cancers are more than twice as likely to die from secondary breast cancer compared to women with primary breast cancer, according to researchers from the UC Davis Comprehensive Cancer Center.

In their study, women treated with radiotherapy who typically have a better prognosis for primary breast cancer—including those with hormone receptor-positive tumors, tumors without lymph node involvement, stage I disease, and women of Asian or Pacific Island ethnicity—experienced worse survival after diagnosis with a secondary breast cancer.

The results were somewhat unexpected, the researchers said, since conditions generally considered “good risk factors” for primary breast cancers were now associated with poor survival in this study of secondary breast cancers.

“We found that the negative impact of secondary breast cancer among women previously treated with radiation was particularly strong in subgroups of patients that have superior survival after primary breast cancer,” said Candace A.M. Sauder, MD, MEd, a surgical oncology specialist and Assistant Professor of Surgery at UC Davis, and first author of the study published in the September 1, 2020 issue of Cancer Epidemiology, Biomarkers & Prevention (2020; doi: 10.1158/1055-9965.EPI-20-0260).

“Once patients develop a secondary breast cancer, our job as their physicians is to treat them as appropriately as possible,” she added in an interview. “The data in this study suggests that likely means more aggressively than if it is a primary breast cancer, because we know that the patient’s survival is significantly decreased in this scenario, even more than when they developed their primary cancer.”

The researchers acknowledged some study limitations, including lack of comorbidity data and genetic information, including BRCA mutation status, which can influence treatment decisions and may affect second primary cancer outcomes.

“Despite these limitations, the study includes a large number of patients from population-based registries, increasing the generalizability of our results,” the researchers wrote in their paper.

Adolescents and young adults (AYA) have the highest absolute excess risk for secondary cancers of any age group, including most commonly breast cancer. Radiotherapy is an integral component of therapy against common AYA and childhood cancers, such as Hodgkin’s lymphoma, sarcoma, and breast cancer.

But even though radiation therapy is a centerpiece in a multidisciplinary approach to treat these AYA cancers, multiple studies have found an increased risk among premenopausal women for secondary breast malignancies.

Study Details

To shed light on this issue, the UC Davis team sought to evaluate the characteristics and breast-cancer specific survival (BCSS) of premenopausal secondary breast cancer after radiotherapy in AYA and childhood cancer survivors. Using data from the large population-based California Cancer Registry, Sauder and colleagues examined demographic and clinical characteristics and BCSS in premenopausal patients with secondary breast malignancies as compared to those with primary cancer.

Their study included 107,731 female patients aged 12-30 years, diagnosed with primary breast cancer from January 1, 1988 to December 31, 2014, compared with 1,147 patients with secondary breast cancer who were treated with radiotherapy for their primary tumor from ages 12-39 years.

Characteristics of the cohorts included age at diagnosis, race/ethnicity, stage, tumor grade, histology, tumor size, lymph node involvement, estrogen receptor, progesterone receptor, HER2 tumor expression status, and sequence of primary cancer.

The results, as described in the research, showed that the secondary breast cancer cohort was more likely to be Hispanic or Black, be 33-45 years of age, have earlier stage tumors, be higher grade, have no lymph node involvement, and be hormone receptor-negative. All women showed worse BCSS for large tumor size, lymph node involvement, and hormone receptor-negative status.

Women with second primary breast cancer in this cohort had roughly twice the risk of breast cancer-specific death compared with women with primary breast cancer. Associations were most profound in younger women, as well as those with earlier stage, lymph-node negative, and hormone receptor-positive disease, and in Hispanics and Asian-Pacific Islanders, who experienced a two-fold increased risk of breast cancer-related death compared to those with primary breast cancer.

Again, the results seem somewhat confounding since the “historic principles,” based on primary breast cancer data, "no longer hold the same benefit in this situation” Sauder said.

“It is unknown if there is a necessarily genetic component for the poor mortality outcomes for Hispanic and Asian/Pacific Islanders,” she added. “But there is something that is inately different in the secondary breast cancer setting than with the primary.

“Whether that is due to tumor genetics, treatments still available for usage since many cannot be repeated once used for the primary tumor, or patient factors—I do not know, but this is an area that continues to need to be studied.”

Sauder and colleagues also noted that HER2 negativity was only associated with worse BCSS in women with primary cancer and the impact of secondary breast cancer on BCSS was similar across HER2 status, “suggesting that regardless of phenotype of the tumor, breast cancers arising in patients treated prior with radiotherapy are more aggressive.”

The bottom line, she said, is that oncologists need to consider more aggressive treatments for patients who were previously considered low-risk populations.

“Traditionally, breast cancers were all treated the same, but over the last 30-plus years breast cancer has been shown to be multiple diseases, needing variations in treatment,” Sauder said. “Likely, secondary breast cancers also need to be treated differently instead of following the algorithm for primary cancers.”

Warren Froelich is a contributing writer.