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EDITORIAL – BREAST ONCOLOGY

Imaging Surveillance After Definitive Treatment for Breast Cancer

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With diagnosis of breast cancer at earlier stages and improvements in locoregional and systemic treatments, the proportion of survivors needing follow-up care has increased. Oncology societies in the United States and Europe recommend that breast cancer survivors undergo history and physical examinations and mammography on an annual basis.[1] Routine surveillance imaging to detect distant recurrence is not recommended except for evaluation of individuals with symptoms or clinical findings suspicious for a recurrence event. This is based on data from randomized trials reporting that routine imaging screening for distant metastases in asymptomatic patients after treatment does not affect survival or quality of life and that it increases costs.[2–4]

The American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) recommend screening for metastases in patients experiencing symptoms or clinical signs of disease and strongly urge avoidance of asymptomatic screening with bone scans or positron emission tomography (PET)/computed tomography (CT) scans.[5,6] Asymptomatic patients undergoing surveillance imaging contribute to the increased cost of care and use resources that might be allocated for other individuals. The potential risks of intense follow-up evaluation include excess radiation exposure, false-positive results that need further workup, and an increase in psychological distress and anxiety to patients.[1]

Despite the availability of guidelines recommending against surveillance imaging, it is reported that patients still undergo at least one advanced imaging method after curative treatment.[7] However, no studies have shown whether the lack of adherence to guidelines is due to overuse among asymptomatic patients or whether imaging is ordered based on clinical signs and symptoms.

In the current issue of *Annals of Surgical Oncology*, Schumacher and colleagues[8] used the National Cancer Database (NCDB) to assess the number of surveillance systemic imaging studies performed after breast cancer treatment and worked with local cancer registrars to determine whether imaging was obtained for evaluation of symptoms or performed for routine surveillance. They included women with stage 2 or 3 breast cancer diagnosed in 2006–2007 who were treated with curative intent and had 5-year follow-up evaluation. They randomly selected 10 patients (7 with stage 2 disease and 3 with stage 3 disease) from 1231 facilities accredited by the Commission on Cancer because this reflects the ratio of stage 2 to stage 3 patients nationally. Importantly, they trained facility registrars to review relevant patient records from their own institution and any outside facilities in which the patient received care.

The authors found that 48% ($n = 5220$) of women received one or more cancer-related advanced imaging scans during the follow-up period. However, once the intent of the scan was considered, the study showed that 30% ($n = 3254$) received one or more asymptomatic surveillance scans, and only 12% ($n = 1308$) had two or more surveillance scans. Most of the scans took place in the first year after treatment, and the factors significantly associated with ordering asymptomatic scans included stage 3 disease, triple-negative tumors, human epidermal growth factor receptor 2 (HER2)-positive tumors, receipt of chemotherapy, and treatment with mastectomy.

Although a rate of 30% of patients receiving asymptomatic surveillance is lower than reported in prior studies,[7,9] a shortcoming of this study was the lack of information about which type of physician ordered the

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screening. It has been shown that the type of physician (primary care vs. cancer specialists including medical oncology, radiation oncology, and surgery) a patient sees after breast cancer treatment may influence the type of surveillance received. Keating et al.[3] used Surveillance, Epidemiology, and End Results-Medicare data from a cohort of 44,511 breast cancer survivors and concluded that specialists, especially medical oncologists, order more tests in the follow-up period. However their study failed to differentiate the intent of testing, whether it was due to symptoms or just overuse. Similarly, in a retrospective review of 11,219 asymptomatic breast cancer survivors, Grunfeld et al.[2,9] showed a variation in adherence among oncologists and primary care physicians with respect to guidelines, and interestingly, one-fourth of the women had fewer than the recommended annual mammograms, and half had more imaging than recommended for surveillance of metastatic disease.

Potential physician barriers that may result in lack of adherence to published guidelines include lack of awareness, lack of agreement with guidelines, practice environment, and patient preferences.[10] Creation of a survivorship care plan can be a useful tool to counteract these barriers and educate patients and providers alike concerning recommendations.[11] Using these tools early in the follow-up period can be important such that patients know what to expect at their future follow-up visits, and providers can focus on addressing any change in clinical signs and symptoms.

Schumacher and colleagues[8] noted that surveillance imaging was more frequent for patients based on approximated subtype. They reported that the diagnosis for the cohort was determined during a period (2006–2007) when HER2 status was not routinely tested and HER2-targeted treatment was not routinely administered. With the advancement of HER2-targeted therapies and improvement in outcomes for this subtype, the rate of ordering unnecessary tests and the likelihood of distant breast cancer recurrence is likely to decrease.

In an era of continued debate about the optimal strategy for surveillance of breast cancer patients, we congratulate Schumacher and colleagues[8] on their work because this is the first study of this magnitude to examine a large national database in order to report the rate of follow-up imaging scans ordered and to define scan intent. With their analysis, we understand a bit more about who is being imaged, when they are likely to be imaged, what scans are being obtained, and why they were obtained. It suggests that compliance with current guidelines is higher than previously reported and informs us that women who do receive imaging are at a higher risk of recurrence. Physicians appear to be guided by tumor biology and treatment rendered when it comes to ordering tests for early detection of metastases. However, it raises the question whether this clinical practice pattern is warranted and effective for screening this subgroup of patients.

Currently, many more sophisticated tools are available to help us understand which patients are at highest risk of recurrence and who therefore might warrant surveillance imaging studies. Sparano et al.[12] recently reported on the identification and enumeration of circulating tumor cells (CTCs) in stage 2 and stage 3 high-risk patients with hormone receptor-positive, HER2-negative disease after systemic chemotherapy. They found that a single positive CTC result 5 years after diagnosis was prognostic for late recurrence. Circulating tumor DNA (ctDNA) also has been shown to predict recurrence in patients with early-stage breast cancer, with one study reporting a median lead time of 7.9 months.[13] The c-TRAK TN trial is using ctDNA screening for patients with triple-negative breast cancer who have completed standard-of-care systemic therapy (NCT03145961; PI Nick Turner, MD, PhD). Patients detected to have ctDNA will be randomized to observation or pembrolizumab treatment for 1 year. Similar to the findings of surveillance imaging studies, it is unclear how frequently these liquid biopsies should be obtained and from which patients. Should they be used to guide surveillance imaging strategies or to determine who should receive additional adjuvant therapy? To realize the full potential, we need to design clinical trials to address these important questions.

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