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Imaging in the evaluation and follow-up of early and advanced breast cancer: When, why, and how often?

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ABSTRACT

Imaging in the evaluation and follow-up of patients with early or advanced breast cancer is an important aspect of cancer care. The role of imaging in breast cancer depends on the goal and should only be performed to guide clinical decisions. Imaging is valuable if a finding will change the course of treatment and improve outcomes, whether this is disease-free survival, overall survival or quality-of-life. In the last decade, imaging is often overused in oncology and contributes to rising healthcare costs. In this context, we review the data that supports the appropriate use of imaging for breast cancer patients. We will discuss: 1) the optimal use of staging imaging in both early (Stage 0–II) and locally advanced (Stage III) breast cancer, 2) the role of surveillance imaging to detect recurrent disease in Stage 0–III breast cancer and 3) how patients with metastatic breast cancer should be followed with advanced imaging.

Introduction

Imaging in cancer patients is an important aspect of cancer care. In patients with a new diagnosis of early or locally advanced breast cancer, breast imaging is essential to properly stage patients and determine the best first steps in their care [1]. However, the utility of advanced imaging techniques to rule out occult metastatic disease is less certain. In patients with metastatic breast cancer (MBC), imaging is also extremely valuable in assessing patients' symptoms, extent of disease or their response to treatments – all of which affect clinical decisions [2]. While it is clear that imaging has an important role in the clinical practice of oncology, in this review, we will present the data both supporting and refuting the need for imaging in both early and advanced breast cancer patients, and discuss how overuse of imaging may cause harm.

The cost of cancer care has risen precipitously over the past few decades. In 2010, total spending on cancer care in the United States was approximately $125 billion. It has been estimated that as much as 30% of resources spent on health care in the United States (US) does not directly improve the health of patients [3]. Dollars spent on unnecessary care, including over-testing, contribute to health care costs and may reduce resources available for interventions that more directly improve outcomes. Imaging scans that are unnecessary to inform clinical decisions not only contribute to health care costs and waste resources, but also expose patients to unnecessary radiation [4], consume patients' time, and generate false positive results that can cause both patient and provider anxiety and prompt additional evaluations that are invasive and/or uninformative.

Imaging that is unlikely to inform medical decision-making is frequently offered to cancer patients [5]. Fear of malpractice, physician and patient preferences, duplication of care secondary to fragmented care and poor record keeping are all potential drivers that contribute to the overuse of imaging in cancer patients [6,7]. Imaging can also negatively impact the care of a patient. For example, staging CTs in a woman with clinical Stage I breast cancer may reveal an unanticipated finding for which additional workup is required. The vast majority of the time, the findings will ultimately be deemed benign, but can contribute to a delay in the start of definitive therapy for early breast cancer. Unnecessary scans that contribute to delays in care are problematic since treatment

Abbreviations: ASCO, American Society of Clinical Oncology; NCCN, National Comprehensive Cancer Network; ESMO, European Society of Medical Oncology; ESO, European School for Oncology; MBC, metastatic breast cancer; n.a., not applicable.

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delays impact breast cancer stage and outcomes [8–11]. Likewise, in metastatic breast cancer, restaging imaging if performed too early can prompt a change in therapy if the metastatic sites exhibit a flare effect and are misinterpreted as progressive disease – a phenomenon that is well described for many new immunotherapy treatments [12], but is also observed with endocrine therapy [13,14].

In this context, we will review the data for how imaging is best used after a new diagnosis of non-metastatic (early and locally-advanced) breast cancer, how and when to use surveillance imaging for non-metastatic breast cancer, and the optimal use of imaging in the metastatic setting.

Staging imaging after a new diagnosis of early (Stage 0–II) breast cancer

National and international guidelines (ASCO, NCCN, ESMO, ESO) discourage the use of staging imaging for asymptomatic patients newly diagnosed with Stage 0–II breast cancer, even if there is nodal involvement (Supplemental Table 1) [2,15–17]. In contrast, routine staging is recommended for patients who present with stage III disease.

In 2012, ASCO highlighted this issue as part of their "Choosing Wisely" initiative since many patients with Stage 0–II breast cancer receive advanced imaging at diagnosis [15]. Despite guideline recommendations, CT imaging, bone scan and PET imaging are routinely used to screen for distant metastases in practice and this use has increased over time [18,19]. At Washington University in St. Louis, 15% of Stage I patients (312/2044) and 46% of Stage II patients (570/1247) underwent staging with CT, bone scan or PET within 6 months of diagnosis [20]. Among Stage II patients treated at two academic cancer centers in Boston between January 2006 and December 2007, 58% underwent initial staging CTs [21]. This is not an isolated phenomenon at US academic centers: in Ontario, Canada imaging was performed in 79.6% (10,921/13,724) of Stage I patients and 92.7% (11,882/12,823) of Stage II patients with breast cancer within 3 months of diagnosis [19]. Although these examples may not reflect practice patterns in 2016, one small study among women with early breast cancer – disappointedly – showed no change in the use of advanced imaging after ASCO's Choosing Wisely initiative [22].

Why have the recommendations not made a more substantive difference?

First, the historical data have been somewhat challenging to interpret for several reasons: 1) the range of detection of occult metastases has been wide, and this has led to concerns of under-diagnosis especially with modern imaging techniques, and 2) physicians have argued that perhaps CT imaging does have a role in patients with early breast cancer, especially in those with more aggressive disease phenotypes like triple negative breast cancer (TNBC) or HER2-positive (HER2+) disease, and these nuances were not captured in older published experiences. Second, patients themselves often request staging scans and consider these part of "standard care".

Review of the historical data generally shows that use of advanced imaging modalities, including bone scans, computed tomography (CT), and positron emission tomography (PET), for staging asymptomatic women with early breast cancer has a low yield to detect occult metastatic disease [20,21,23–27]. For asymptomatic women with Stage I breast cancer, the chance of identifying occult metastatic disease with advanced imaging ranges from 0% to 5.1% [20,21,23,24,26,27]. For asymptomatic Stage II breast cancer, the incidence of occult metastatic disease detected by advanced imaging is 0–5.5% [20,23,24,26,27]. A review on this topic reported that the prevalence of metastatic disease in Stage II breast cancer may be as high as 34.2% [26], however, this result is from a study where newly diagnosed Stage IIB and III patients underwent both CT and PET imaging, and were analyzed together [28]. These patients were not asymptomatic and did not have biopsies to confirm that the radiographic findings were indeed metastatic breast cancer [28], and thus, these findings should not guide clinical practice recommendations.

To further address the criticisms associated with the historical series, we recently investigated this issue among patients presenting with either stage IIA or IIB breast cancer at two academic practices in Boston (Dana-Farber Cancer Institute and Beth Israel Deaconess Medical Center) between January 2006 and December 2007. We found that although providers are more likely to order CT imaging for patients with Stage II TNBC or HER2+ breast cancer subtypes, the yield of detecting distant metastatic disease in these subgroups is equivalent to those with hormone-receptor positive breast cancer [21]. Overall, the rate of detection of true occult metastatic disease on initial imaging was 2.1% for Stage II disease (2.2% for those with ER/PR-positive disease, 2.1% for TNBC, and 1.9% for HER2+). The rate of abnormal findings was high and up to 36% of patients who underwent CT imaging required additional imaging and 33% required interval imaging to follow an abnormal finding. Furthermore among women who received staging imaging at diagnosis and later developed metastatic disease, 85% (29/34) had no abnormal findings on their initial imaging that correlated with where they later developed metastatic disease.

In summary, there is overwhelming data indicating that there is no role for advanced imaging (liver ultrasounds, bone scans, CTs, or PET) to be performed in asymptomatic patients newly diagnosed with early (Stage 0–II) breast cancer. Advanced imaging can and should be performed in patients with early breast cancer who have focal signs or symptoms that are concerning for metastatic disease.

Staging imaging after a new diagnosis of locally-advanced (Stage III) breast cancer

All patients with locally-advanced breast cancer should undergo staging imaging and this is recommended by current guidelines (Supplemental Table 2) [15–17]. Based on the literature, advanced imaging with bone scan, CT or PET will detect occult metastases in 6.0–14% of Stage III patients who are asymptomatic at diagnosis [23,24,27]. There is value in evaluating patients with Stage III disease using advanced imaging at diagnosis since the chance identifying metastatic disease increases with tumor size and nodal involvement [26]. If a patient has an abnormality on imaging that is suspicious for metastatic disease, a biopsy should always be performed to confirm that this is indeed breast cancer and not a second malignancy or non-malignant finding (e.g. sarcoidosis, infection, etc).

Surveillance imaging of early or locally-advanced (Stage 0–III) breast cancer

In patients with non-metastatic breast cancer who have been treated for curative intent, the goals of follow-up care and surveillance are to manage the effects of their diagnosis and treatment, maximize adherence to adjuvant therapy, encourage a healthy lifestyle, and to identify any curable breast cancer recurrences or new primary breast cancers [2]. The goal of surveillance is not to detect asymptomatic metastatic cancer as there is no data that early detection of metastases in patients without

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