# The Breast Cancer Overdiagnosis Conundrum: An Oncologist's Viewpoint

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Controversy about the appropriate age to begin and the frequency of mammography screening for breast cancer has been ongoing. The U.S. Preventive Services Task Force (USPSTF) has recommended that screening begin at an older age and at longer intervals than had been previously recommended (1). The change was prompted by evaluation of reports that screening mammography as currently practiced in the United States is associated with needless work-ups and attendant complications, resulting in the Task Force's conclusion that the harms outweigh the benefits for women aged 40 to 49 years and that screening could be reduced to every other year for women aged 50 to 59 years.

Research studies have found progression to invasive breast cancer in 14% to 53% of cases of ductal carcinoma in situ (DCIS) treated with biopsy alone, depending on length of follow-up (2). Screened populations have also been shown to have a higher incidence of breast cancer than unscreened populations, suggesting that some cases of screened cancer will never develop into clinically significant conditions during the patient's lifetime.

The term "overdiagnosis" has been applied to this phenomenon (3). Estimates of overdiagnosis range from 1% to 30%, depending on the population and type of analysis (4). We believe that the term "overdiagnosis" in the context of breast cancer places this problem in an inappropriate light, suggesting that these patients do not have cancer. The question is not whether we should find early, more easily treatable cases of breast cancer but rather how to treat early-stage cancer found on mammography.

The medical and research communities are now attempting to determine appropriate treatments for both DCIS and invasive cancer by using pathologic, biochemical, and genetic studies performed on biopsy specimens. All of these approaches require tissue from the patient's tumor to determine a treatment plan. Although these approaches hold much promise, we cannot yet confidently say that delaying treatment of breast cancer by not finding it early will make no difference in outcome.

Gerlinger and colleagues (5) recently demonstrated the genetic characteristics of tumor evolution. They showed the genetic heterogeneity of tumors and the evolution of genetic change in the tumor over time. When does that evolution occur, and what triggers it? Can the evolution from DCIS to invasive disease be pinpointed in a way that will allow us to choose whether to treat DCIS on the basis of the genetic evaluation of a lesion? Will a test be developed that will better tell us the aggressiveness of an invasive cancer? When during the natural history of these lesions do we need to find and treat them to ensure the best outcomes for our patients? For the individual patient, the question is not whether to have a mammogram that might "overdiagnose" breast cancer but how to treat early-diagnosed noninvasive or invasive breast cancer once we have found it.

It has been clearly demonstrated that screening mammography does just what it is supposed to do: It has reduced death from breast cancer in populations that have routine screening (4). It finds tumors when they are smaller and have spread less extensively (4, 6, 7). It has also led to a stage shift over time to noninvasive or less invasive cancer, reducing the need for chemotherapy and sometimes even radiotherapy for tumors that may not become invasive (6). On the other hand, frequent mammography may result in high recall rates and benign biopsy results, with the attendant discomfort, anxiety, and possible complications of these procedures in patients who prove to have no substantial lesions (1).

Cancer detected on mammography is generally less aggressive than patient-detected breast cancer and might safely be diagnosed with less-intensive screening and still be treated successfully (8, 9). However, there are no studies of watchful waiting or active surveillance for breast cancer as there are for prostate cancer. The conundrum is that to save lives and reduce treatment-related toxicity, tumors need to be found at an early, more treatable stage. Recommending reduced mammographic screening tells our patients that, because we are not sure how much treatment their precancerous or cancerous lesions may require, we would rather just not find them until they are at a point where we are sure of the appropriate treatment.

Surgery, radiation, chemotherapy, and hormone therapy all carry substantial toxicities. Just as in the treatment of Hodgkin disease, we need to maximize the effectiveness of treatment of breast cancer while minimizing toxicity. Although studies of tumor biology may eventually supplant staging as a way to determine treatment, all of the current analytic techniques require tissue from a diagnosed lesion.

We know now that mammography finds invasive and noninvasive tumors at an earlier stage, when they require less treatment, which results in less toxicity, a point not adequately considered in the USPSTF recommendations, which use mortality as the sole end point (1, 10). At the same time, we believe that the USPSTF has overstated the negative effect on patients of false-positive mammograms and recalls, given the stakes that these patients may face.

"Overdiagnosis" is not the way to couch this problem. Early diagnosis allows for effective and less toxic treatment with reduced population mortality. In fact, if we don't continue to find and do research on cases of early breast

 

cancer, we will never learn how to tell which cases have a good prognosis, and need less treatment, from cases with a bad prognosis that need more treatment.

At a time when, as a society, we cannot provide adequate health care for a major portion of our population, one can rightly ask whether the current frequency of breast cancer screening is cost-effective. In the ideal world, we will develop cheaper, more accurate, noninvasive diagnostic tests that not only find the lesions but also divine how aggressive they are and what type of treatment they need. However, until these advances occur, we need to diagnose breast cancer at the earliest possible time for the individual patient to have the best outcome with the least toxic treatment.

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