Overdiagnosis

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Overdiagnosis, defined as: “breast cancer detected at screening that would not have been diagnosed by usual care or become clinically evident in a woman’s lifetime” is often cited as a major risk of screening by those opposed to mammography. Hiqh quality screening mammography provides earlier detection and reduces mortality from breast cancer. Some have suggested that 0–50% of all breast cancer represent overdiagnosis from screening.

It is important to acknowledge the difference between invasive and in situ cancers when discussing overdiagnosis. There is no data that proves overdiagnosis of invasive cancer. However, the indolent nature of some DCIS allows the possibility of low levels of overdiagnosis. It is also important to acknowledge that critics of screening primarily object to possible overtreatments of DCIS rather than the simple act of diagnosis.

DCIS triggers operations, radiation therapy, and hormonal suppression recommendations that carry costs related to time, expense, self-image, and potential side effects. Usual care may not be optimal care. Some low grade in situ disease may remain non-invasive for a decade or more and not have an impact on quality of life or mortality. Adherence to the standard of care in such cases could be considered overtreatment. However, recent research suggests that identification and treatment of DCIS decreases the subsequent incidence of invasive cancer (1). Unfortunately, we cannot accurately predict, either by imaging or histology, the patient-specific timing or severity of progression, yet. We need to actively participate in refining standards to reduce overtreatment.

The most reliable way to calculate overdiagnosis is to examine randomized controlled trials, where a population is randomly divided into two groups; one group undergoes screening, and the other control group does not. If the number of cancers detected in each group is equivalent after long-term follow up there is no overdiagnosis. However, those patients participating in screening are likely to have their cancers detected earlier compared to the control group. Any excess number of cancers detected in the screened group, compared to the unscreened group, after long-term follow up represent the overdiagnosed cancers. Long-term follow up is critical in order for the non-screen detected cancers to become clinically apparent.

In the randomized Malmo trial, screening mammography detected approximately 10% more cancers than in the control group at 15 years of follow up (2). Two other randomized control trials (Two County and Gothenburg Trials) estimated even lower rates of overdiagnosis at 1% (3). Therefore, reliable estimates using large databases and long-term trends in women over 40 indicate that 1–10% of cancers diagnosed on screening mammography may represent overdiagnosis with only as much as 1% representing invasive cancer (4).

Some researchers have used population and epidemiologic data to estimate overdiagnosis by subtracting the expected incidence of cancer from the observed incidence. It is important to note that this approach is severely limited by the inability to identify which patients participated in screening. The SEER registry provides robust data regarding observed incidence that are not linked to screening information. Defining the expected incidence of breast cancer is critical for correct calculation of overdiagnosis. Overdiagnosis is minimal if the expected incidence is close to the observed incidence. For example, overdiagnosis is 5% if we were expecting 100 cancers but found 105 in the screening population. But overdiagnosis is 50% if we were expecting 70 cancers and found 105. This illustrates how critical the estimate of expected cancers can be to the calculation of overdiagnosis.

In 2012 Bleyer and Welch used a "best guess" (exact words in the published article) to calculate overdiagnosis. Interestingly, they used data from women *under* 40 years-old to estimate the number of expected cancers. Ultimately, the authors predicted that the annual increase in breast cancer was a mere 0.25% and estimated that 31% of all breast cancer represents overdiagnosis (5). However, there are flaws with this estimation. Breast cancer is uncommon in women under 40. It does not accurately reflect the incidence in women older than 40 who harbor the vast majority of cancers. In addition, as noted by Kopans in a careful analysis of the Bleyer and Welch article, the authors combined DCIS and invasive cancers for their estimates (6). Other data, using the population in question, are available and more reliable.

Helvie et al used data from the Connecticut tumor registry spanning four decades (1940–1982) and found the incidence of breast cancer increased 1.2% per year (7). Among women 40 and older in the SEER database, incidence increased 1.3% per year from 1977–1982. These annual percentage changes are 4-5 times higher than the estimate published by Bleyer and Welch. In the United Kingdom incidence has increased between 0.7 and 2.3% per year in women 40 and older. Using these estimates of expected incidence, overdiagnosis accounts for less than 10% of all cancers detected and the majority are DCIS.

Autopsy studies are another way to estimate overdiagnosis by counting the cancers that had not become "clinically apparent." On average, 1.3% of women had undetected invasive breast cancer and 8.9% had DCIS at autopsy (8). It is unlikely that overdiagnosis exceeds the incidence of undetected disease in autopsy studies.

The exact frequency at which overdiagnosis occurs is unknown and remains overemphasized by the critics of screening. The highest reliable estimates remain less than 10% with only 1% representing invasive disease (9). There are two ongoing challenges. We need to develop non-invasive imaging techniques that consistently distinguish which findings will impact patients and further reduce the low levels of overdiagnosis. Until that technology is available we need to collaborate to refine therapy paradigms to minimize overtreatment, the real downstream effect of diagnosis (10). In the meantime we should continue to screen because it reduces mortality and treatments for breast cancer through early detection.

References

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