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Early detection of second breast cancers halves women's risk of death

A group of international researchers has found the first reliable evidence that early detection of subsequent breast tumours in women who have already had the disease can halve the women's chances of death from breast cancer.

According to the research published online today (Wednesday 18 March) in the cancer journal, *Annals of Oncology* [1], if the second breast cancer was picked up at its early, asymptomatic stage, then the women's chances of survival were improved by between 27-47% compared to women whose second breast cancer was detected at a later stage when symptoms had started to appear.

Until now, the impact of early detection of second breast cancers was unclear. Attempts to investigate it have been complicated by the fact that it is not possible to run randomised controlled trials because women who have already had one breast cancer are at higher risk of a relapse or a second breast cancer and, therefore, are generally advised to have regular breast checks as part of their follow-up care. What studies there have been have not made adjustments for the main factors that could bias the findings from a non-randomised study and often have looked at breast cancers occurring in either the same breast (ipsilateral relapse) or the other breast (contralateral) but not either breast.

The current study looked at 1,044 women who had attended one clinical centre in Florence (Italy) between 1980-2005 and who had developed a second breast cancer. In that time 455 women had ipsilateral breast cancers (IBC) diagnosed and 589 women had contralateral breast cancers (CBC) diagnosed. Of these second cancers, 699 (67%) were asymptomatic and 345 (33%) were symptomatic.

The researchers found that mammography was more sensitive than clinical examination for detecting second cancers (86% versus 57%). However, 13.8% of cases were only detected by clinical examination. Asymptomatic cancers were smaller than symptomatic for both IBC and CBC; early stage cancers were more frequent in asymptomatic (58.1%) than in symptomatic (22.6%) women; and fewer women with asymptomatic than symptomatic CBC had node metastases (an indicator that the cancer may have spread).

In the analysis of the results, the researchers (from Italy, Australia and the UK) adjusted to allow for lead-time bias (bias caused by an earlier detection of the cancer) and length-time bias (bias caused by the fact that some breast cancers develop more slowly than others and, therefore, are more likely to be detected at the asymptomatic stage and are less likely to cause death).

Associate Professor Nehmat Houssami, a breast physician and principle research fellow at the University of Sydney's School of Public Health, Australia, who led the study, said: "Intuitively, it makes sense to consider that early detection of second breast cancers will improve prognosis, since breast cancer survivors have a long-term risk of developing further disease or relapse in either breast. However, due to a paucity of evidence about this until now, current recommendations on surveillance of breast cancer survivors vary substantially between countries and organisations.

"Our study provides new evidence on several aspects of early detection of second breast cancers. We set out to estimate the effect of early, asymptomatic detection while adjusting for the two main biases known to be associated with non-randomised studies of the impact of early detection – lead time and length bias – so we believe that the estimates we report are more valid than previously reported estimates, while acknowledging the limitation that the evidence is not from a randomised controlled trial.

“In addition, we have estimated this for early detection of either ipsilateral or contralateral breast cancer, while other studies have focused on one or the other. So our estimates may be more useful for clinicians discussing this aspect of breast cancer follow-up with their patients.”

She continued: “To our knowledge, this is the only study to have taken length-time bias into account when quantifying the impact of early, asymptomatic detection of breast cancer. This is important because slow-growing or indolent cancers have a much smaller probability of proving fatal, and this group of women will tend to be over-represented in the early-detected cancers, biasing the effect of screening to make it appear more beneficial.”

In their paper, the researchers write: “Recommendations on follow-up after treatment of early breast cancer should consider our findings, which suggest that early detection of second breast cancer events improves prognosis in this ever-increasing group of women.”

Prof Houssami said: “Periodic surveillance of women with BC is currently under scrutiny in some countries and questions have been raised as to the value of sustained follow-up of breast cancer survivors in some health settings. So I think this work provides a timely reminder of the potential benefit of early detection of second breast cancers and supports ongoing surveillance in this group of women.”

She said that their finding that nearly 14% of second breast cancers were only detected by clinical examination and that mammograms had a sensitivity of 86% was also important. “There are health settings where new imaging (ultrasound or MRI) is advocated for screening because of the belief that mammography is not sufficient and misses too many cancers in breast cancer survivors. Our data suggest that mammography, with clinical examination, is sensitive and effective (with the caveat that the Florence centre where the study originated has established experience in mammography of at least 40 years). We feel that additional screening imaging should only be used selectively, for example, in women with extremely dense breasts, or when investigating questionable findings from the mammogram or clinical examination.”

Prof Houssami concluded: “The next step is to determine how to maximise early detection in this specific setting while ensuring feasibility and efficiency. One possibility currently under exploration would be to estimate the risk of a symptomatic tumour and the stage of the symptomatic tumour by time since the last mammogram. There are many questions about the optimal process and model of surveillance, such as frequency for surveillance and who should be performing longer-term surveillance in breast cancer patients, that we have not addressed in this study. These issues require further research.”

(ends)

Notes:

[1] Early detection of second breast cancers improves prognosis in breast cancer survivors. *Annals of Oncology*. doi:10.1093/annonc/mdp037

A pdf of the full research paper can be downloaded at:

http://www.oxfordjournals.org/our_journals/annonc/press_releases/freepdf/mdp037.pdf

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