Systematic Review

Mammographic screening for breast cancer: an ounce of prevention worth a pound of harm?

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Introduction

Although breast cancer screening by means of mammography was implemented almost 20 years ago it is still a subject of much controversy. Recent systematic reviews suggest a significant reduction in breast cancer related mortality due to screening. There are however reasons for skepticism. The incidence of advanced breast cancer has not decreased. Apart from the dubious benefits of screening, a myriad of adverse effects has been reported. Overdiagnosis results in unnecessary mastectomies, chemotherapy and radiotherapy which all cause undue physical harm and squander of resources and specialist care. False-positive mammograms cause unnecessary psychological distress. In scientific literature, particularly by interested parties, these drawbacks tend to be underexposed. From an ethical point of view there are firm objections to breast cancer screening in its current mode. To live up to the principle of beneficence the principle of non-maleficence should not be neglected. Recent evidence suggests an alternative way of screening in which adverse effects are diminished. This paper looks to explore whether mammographic screening is still the best approach in view of the above points and to contrive the answer to a question that affects hundreds of thousands of women: ‘Should mammographic screening be reconsidered?’

Screening for hundreds of thousands of women

Every year hundreds of thousands of women in the Netherlands receive an invitation to participate in the population screening program for breast cancer. Since 1996, women between the ages of 50 to 69 years of age have the opportunity to be screened for malignancies in the breast. In 1998, women 70 to 75 years of age were added to the population that is invited to be screened every other year\cite{1}. Participating women are subjected to mammography. The mammograms are subsequently examined by two independent radiologists. Outcomes are measured against the BI-RADS (Breast Imaging Reporting and Data System) classification. The main goal of this biennial screening is early detection of breast cancer, which is the most common form of malignancy in women\cite{2}. Early detection, before the cancer has metastasized, can make the difference between a curative therapy or a palliative treatment\cite{3}. Between 1990 and 2012 the breast cancer screening program has been evaluated by a national team of scientists from the Erasmus MC and the Radboud University Medical Centre. This National Evaluation Team for Breast cancer screening (NETB) estimated the number of deaths prevented annually by the breast cancer screening program to be 775\cite{4}. Notwithstanding this report and other studies from Dutch soil that affirm the benefit of mammographic screening\cite{5,6}, disagreement on this topic persists in the scientific community. Contradictory research results, mostly of foreign origin, and polemic within the scientific realm concerning the benefits and drawbacks of mammographic screening, result in conflicting media coverage\cite{7,8}. There has been a measurable decline in participation since 2007 which is potentially the consequence of this. It lies in the interest of all Dutch women that a clear answer is contrived to the question: ‘Should the population screening for breast cancer be reconsidered due to recent scientific insights or not? Do the benefits still outweigh the risks?’

Reduction in breast cancer related mortality

The most important pillar that supports the national breast cancer screening program is the axiom that breast cancer screening reduces breast cancer related mortality. There is no doubt that the 5-year survival of breast cancer patients has increased and mortality has decreased significantly since the onset of the breast cancer screening\cite{2}. Needless to say, improved treatment contributed vastly to these developments. The exact numbers that can be attributed to screening is hard to quantify. In recent years a number of studies have been published that sum up the results of all relevant randomised controlled trials that have been conducted. These systematic reviews suggest a 15% to 20% reduction in relative risk of breast cancer related mortality for women participating in the breast cancer screening compared to women not participating\cite{9,10}. These reviews originated in the United States and the United Kingdom respectively, both countries with a similar breast cancer screening program. This makes the results from these studies applicable for the Dutch population. With this in mind, these figures seem to be a major justification for continuation of the breast cancer screening program.
There are however some matters that raise doubts about this apparent success. First of all, remarks can be made about the U.S. Preventive Services Task Force review and the Independent UK Panel on Breast Cancer Screening review concerning methodology. It appears that in some of the trials that were included in these systematic reviews the randomisation process, when subjected to the criteria of the Cochrane Handbook, should have been considered suboptimal[11,12]. When data is analysed from solely the trials with an optimal randomisation process little remains of the beneficial effect of mammographic screening on breast cancer related mortality[11]. Second is the fact that the current course of epidemiology is not consequent with a successful screening program. In countries with an established breast cancer screening, at best only a marginal decrease in advanced breast cancer has been observed[13,14]. This fact undermines the efficacy of breast cancer screening, for a decrease in advanced cancer has always been regarded as an early indication of success[15]. An example of this is the decreased incidence of cervical cancer after the implementation of the pap smear[2].

The drawbacks of mammographic screening

As stated earlier it is unclear the extent in which mammographic screening reduces breast cancer related mortality. Doubts raised by this obscurity are reinforced by the adverse effects that screening has. Screening on a large scale by means of mammograms in most cases detects benign abnormalities. Additionally malignancies are discovered that would not have caused harm to the individuals within their lifetime[11,14,16]. For example, carcinoma in situ which in many cases does not metastasise, is found more often by screening than on the basis of clinical symptoms[17]. In women 39 to 74 years of age this over-diagnosis accounts for 30% of screen detected breast cancers[11,14,18]. In women 40 to 59 years of age, 22% of screen detected cancers is due to overdiagnosis[19]. Healthy women are being labelled and treated as if they were breast cancer patients. These women are subjected to surgery, chemotherapy and radiotherapy while they never would have been diagnosed with breast cancer had they not participated in mammographic screening. Besides the psychological distress these women are exposed to, for instance anxiety and depression, they experience all kinds of side effects due to therapy. Lymphedema, fatigue, sexual dysfunction, vasomotor symptoms and cognitive complaints are among the most common[20]. At the same time there is an increasing amount of false positive mammograms. The estimated risk of a mammogram being erroneously labelled positive for women regularly attending biennial screening accumulates to 16%[6]. A false positive mammogram is associated with anxiety, insomnia and a negative impact on sexuality and relations with friends and family[21]. Complaints due to a false positive mammogram can persist long after cancer has been excluded[22]. Apart from unnecessary harm these false positive mammograms and overdiagnosis result in squander of funds and specialist care. Scientists and authors who have an interest in large scale mammographic screening tend to ignore, play down or disclaim these drawbacks[23,24]. Lastly there is a theoretical risk of creating a false sense of security. In the case of an aggressive tumour the interval between two mammograms is long enough for the tumour to metastasise[16].

These interval tumours are usually of a more fatal nature than screen detected tumours[25]. A large scale mammographic screening potentially creates a certain sense of safety causing participating women to underestimate the chance of interval cancer. A possible consequence of this could be that participating women are less attentive of abnormalities in the breast.

Proportionality and subsidiarity

The continuation or discontinuation of the breast cancer screening program in the current modus, by means of mammography, is not only a question of medical science but also one of medical ethics. The idea of preventive screening, to avert morbidity and mortality, is derived from the ethical principal of ‘beneficence’. An important underlying idea behind screening however is also that the population should not be needlessly exposed to risks[26]. This idea originates in the ethical principal of ‘non maleficence’. Screening of healthy individuals results in short as well as long term psychological damage due to false positive mammograms[21,22]. In addition, abnormalities are being detected and treated which would, in the absence of screening, not have resulted in illness[10,11,14]. This results in harm due to all kinds of unnecessary treatment such as surgery, chemotherapy and radiotherapy[20]. The ultimate question in this matter is: Is the amount of harm caused by mammographic screening proportionate with the reduction in mortality; Is the breast cancer screening program in accordance with the ethical principle of proportionality?

Assuming a reduction in breast cancer related mortality of 15%, it can be stated that for every 2000 women that participate in mammographic screening during 10 years one life is saved[9,11]. Taking in account an overdiagnosis of 30%, in this group 10 women receive a redundant cancer diagnosis and are unnecessarily treated[11,14,18]. Allowing for a false positive recall rate accumulating to 16% in 25 years, hundreds of these women will have a false positive mammogram[6,11]. Apart from the principle of proportionality, medical ethics reckons with the principle of subsidiarity. It implies that when an intervention is needed, the least harmful option has to be employed. A recent Canadian study in which annual mammographic screening was compared with annual physical examination by trained nurses placed subsidiarity of screening by means of mammography in an entirely different context. After a 25 year follow-up, breast cancer related mortality was observed to be equivalent whereas in the mammography group a 22% breast cancer excess was found due to overdiagnosis[19]. These results support the conclusion of an earlier article form Canadian soil that stated that mammography makes no contribution to the benefit of screening by annual clinical breast examination[27]. An explanation for these observations might be found in the fact that mammography can detect cancer in a non-palpable stage. As mentioned earlier however, some tumours do not cause morbidity and mortality within the patient’s lifetime. It might be assumed that the bulk of these tumours are non-palpable. In the Canadian National Breast Screening Study half of screen detected non-palpable cancers were over-diagnosed. Physical breast examination self-evidently does not detect non-palpable tumours and the fact that cancer is detected only when it has grown to a palpable size apparently does not lead to an increased mortality[19].
Systematic Review

To prevent or to cure?
Recent scientific observations indicate that the breast cancer screening program by means of mammography requires a thorough reconsideration. The actual absolute reduction in breast cancer that can be attributed to screening is still subject to uncertainty. The most solid evidence, coming from the systematic reviews of the US Preventive Services Task Force, the Independent UK Panel on Breast Cancer Screening and the Cochrane Collaboration, presents percentages of approximately 15%-20%. There are however reasons to pose a skeptical attitude towards these figures. In addition to a decrease in advanced breast cancer in the overall population, one would expect to find decrease in incidence of advanced breast cancer when screening is implemented. This however is not the case. Apart from a lack of solid evidence to confirm the efficacy of breast cancer screening, an abundance of adverse effects has been observed due to mammography. Overdiagnosis results in unnecessary mastectomies, lumpectomies, chemotherapy and radiotherapy which all cause undue physical harm and squander of resources and specialist care. False-positive mammograms cause unnecessary psychological distress. In scientific literature, particularly by interested parties, these drawbacks tend to be underexposed. Finally there is the calming effect and a false reassurance that could possibly arise from large scale screening whereas in reality it offers no protection from aggressive tumours. The benefits women could possibly gain from participation in mammographic screening are in no way commensurate with the risks they are exposed to. The ethical principle of 'non maleficence' being trampled in order to save a limited number of lives, and that is not in accordance with the underlying ideas of preventive screening.

Conclusion
Breast cancer is a prominent cause of morbidity and mortality in women and therefore awareness of- and research on this topic is of great importance. The recently published twenty five year follow-up of the Canadian National Breast Screening Study might offer an alternative way of conducting breast cancer screening. Physical examination by trained nurses instead of mammography could turn out to be equally effective and prevent the better part of adverse effects. Although this finding indicates a possible way to get rid of overdiagnosis and undue harm, most investigations into the efficacy of breast cancer screening have compared mammography to no screening at all. Inquiry should be made specifically into the effect of mammography compared to the effect of physical breast examination on long term breast cancer mortality. A frequently quoted statement of Founding Father Benjamin Franklin is that ‘An ounce of prevention is worth a pound of cure.’ Prevention by means of mammography however has so far not yielded satisfactory results. As long as this stays unaltered, directing all efforts on the treatment of breast cancer seems an advisable approach. Recent successes such as hormonal therapy and immunotherapy are indications of the progress that ,with resources now being spent on screening, could be achieved in the field of pharmacotherapy.

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