

Harms and Benefits of Mammography Screening

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Abstract

Mammography is one of the most technically challenging areas of radiography, required high spatial resolution, excellent soft tissue contrast and low radiation dose. Mammography screening for breast cancer is worldwide available. Early detection of breast cancer through screening can lower breast cancer mortality rate and reduce the burden of this disease in the population, the benefits and harms of mammography screening have been debated in the past years. This review discuss the benefits and harms of mammography screening in light of findings from randomized trials and more recent observational studies performed in the era of modern diagnosis. The main benefit for mammography screening is reduces the risk of dying from breast cancer. Reduction vary from 15 to 20% in randomized trials to more recent estimates of 13 to 17% in analyses of observational studies. UK data of 2007 shows that for 1,000 women invited to biennial mammography screening for 20years to 50years age, 2-3 women's are prevented from breast cancer. Main harm of mammography screening is the over diagnosis of breast cancer. 15 women's over diagnosis for every 1000 women invited to biennial screening for 20 years from 50 years age. In an era of limiting health care services, screening services need to scrutinized and compared with each other regard to effectiveness, cost effectiveness and harms.

Introduction

The verb “to screen” means “to sift by passing through a screen” (1) and “to sift” is derived from an old Dutch word i.e ‘zeef’ a ‘utensil having a circular frame with a finely meshed bottom, which separate the coarser from the finer particles of any loose material’. The definition of screening vary among different setting, cultures and time periods (2, 3). Definition of screening include a diseases precursor or identification of disease among presumptively healthy individuals. Mainly there are two different approaches of cancer screening i. prevention of disease by finding and removing premalignant precursors of cancer ii. Early detection of cancer here goal is to treat the cancer in an early curable stage (4). In 1968, the WHO give 10 principles that should be fulfilled before implementing screening (table 1) (5). Principle 4 and 7 regard knowledge about biological development of cancer. Aim of screening for breast cancer with mammography is to detect breast cancer at an early stage. We anticipate a continuous, linear growth pattern of tumors for beneficial early screening and that breast cancer has not spread at the time when tumors are detectable at mammogram. So, if assumption of tumor growth are not correct that means if tumor is heterogenic then screening mammography is not an adequate tool for breast cancer reduction (6).

In 20th century US started idea of early detection with educational mass campaigns where a message of ‘don’t delay’ for seeking medical help for different cancer signs and symptoms was central (7). However, none of these early campaigns effect the mortality of breast cancer (8). In 1963 1st randomized trial of mammography screening was launched within the health insurance plan in New York (8). Many trials were performed before widespread use of anti-estrogens and modern chemotherapy with exception of the Canadian National Breast Screening Study and the age trial (10, 11).

Table 1:- 10 Principles of World Health Organization for screening.

1. Condition sought should be an important health problems.
2. There should be accepted treatment for patients with recognized disease.
3. Facilities related to diagnosis and treatment should be available.
4. There should be early symptomatic stage or recognizable latent.
5. There should be examination or suitable test.
6. Test should be acceptable to the population.
7. Natural history of the condition including development from latent to declared disease, should be adequately understood.
8. There should be agreed policy on whom to treat as patients.
9. Cost of the case finding should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be in continuing process and not a “once and for all”.

There has been a continuous discussion of mammography screening, which started in full in 2000 after a Cochrane review of the randomized trials indicate effect of screening (12). The effect of screening mammography outside the experimental setting, with improvement in awareness, diagnostics, and treatment has been discussed (13, 14).

Mammography debate has not only been about the benefits of screening mammography, but more recently also harms. Awareness of over diagnosis in mammography screening has emerged in last 10 years. Over diagnosis is defined as the detection of tumors at screening that might never have progressed to become symptomatic or life-threatening in the absence of screening. Over diagnosis is inherent to screening. Over diagnosis only have harmful effects rather than any benefit. Aim is to presenting the benefits and harms per 1000 women invited to mammography screening who started screening at age of 50 years and were screened every second year until 69 years, this age group has been shown to achieve most of the benefit with less harm (15, 16).

Screening Mammography

Rate of attendance

Most of the western countries recommend mammography screening. In Switzerland 'the Swiss medical board' independent panel of experts reviewed evidence on mammography screening and concluded that harms dominant the benefits and recommended against mammography screening that is screening programs will not be implemented in areas where these programs doesn't exist and ongoing programs should be phased out (17). For screening the age range differs in different countries from 40-75 years (4, 17). Recommended interval between two intervals varies from 1-3 years (18). Most of the countries have attendance rate more than 70%- and 50-69-years age group have highest rate of attendance.

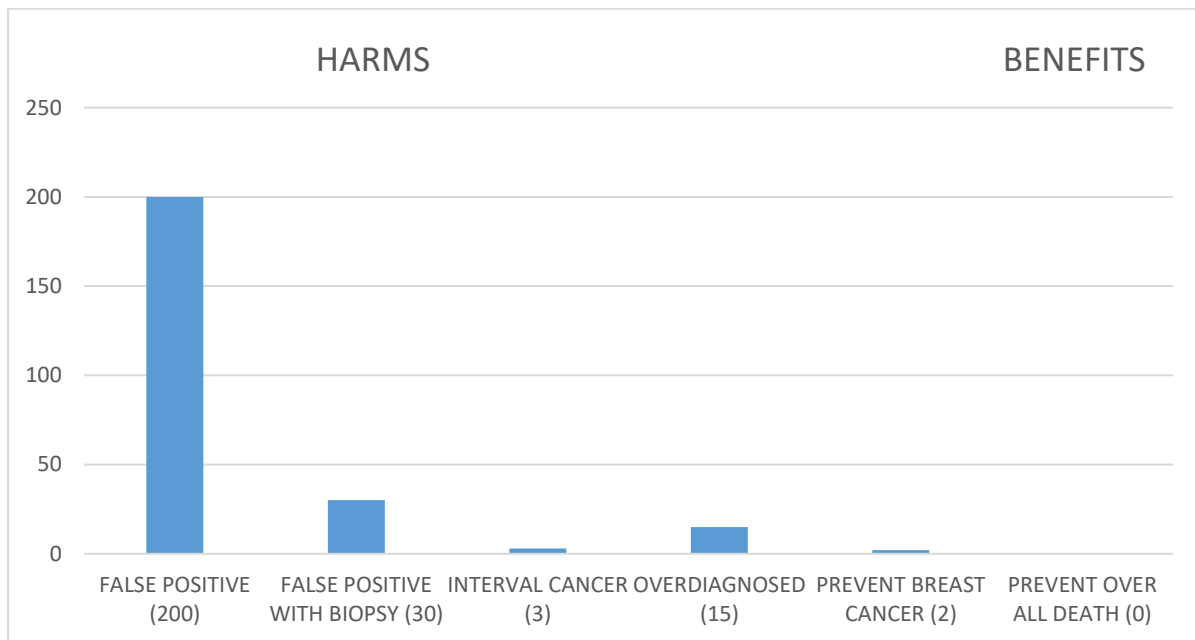
False positive tests

With diagnostic test sensitivity and specificity of screening are not perfect, different levels of sensitivity and specificity for detecting breast cancer have been published (20, 21). The risk of false positive mammogram for women undergoing age 50-69 years in Europe is about 20%, risk of experiencing biopsy due to this test is 3% (21). In UK 2.3% of women with this test had a lumpectomy, representing 76 out of 100,000 women screened in single screening round (22). Risk in US is higher, where 30% is the false positive rate of last 10 years, 50% of women's experience false positive tests at least once (23, 24). Apart from monetary cost there are some other challenges with false positive test like impaired psychological well-being and health behavior changes among women with false positive test. Only 64% of those recalled after 6 months due to false positive test they are declared cancer free, after 1 year around 90% were declared cancer free and after 2 years all declared cancer free (25). Research shows that false positive test negatively influence women's psychological well-being immediately after test and a recent study shows that women with false positive findings experience psychological harm after screening for last 3 years (26).

False negative tests

Interval cancers are detected after normal screening and before next scheduled mammogram. These cancers are overlooked at the last mammogram or during the growing stage of cancer which become apparent in screening (29). During re-interpretation of interval cancer, 35% were overlooked (30) and 65% were not visible in the latest mammogram but appeared in the interval between screening mammograms. Breast cancer detected in women's who participate

in screening 28-33% are interval cancer (20), this proportion seems stable in different screening rounds (29). Demand of digital mammography is increasing and detection rate of invasive cancer and DCIS (ductal carcinoma in situ) are higher. Amount of over diagnosis might increase with increasing detection rates with digital mammography (29). 1,000 women invited for screening mammography every second year for age from 20 years to 50 years, 200 will experience a false positive mammogram, 30 undergo biopsy due to false positive mammogram and 3 diagnosed with interval cancer (33) (graph 1).



Graph 1. Summary of benefits and harms when 1,000 women are screened every second years for 20 years starting at age of 50.

- Number of women with false positive and false positive with biopsy is on the basis of a review (32).
- Number of women's with interval cancer reported in National Health Service breast screening programme (33).
- Number of over diagnosis and prevented breast cancer death are based on the over diagnosis and reduction in mortality from breast cancer.

Over diagnosis

Mammography screening automatically includes increased breast cancer incidence (36) because of early detection of cancers that would otherwise have been diagnosed later in life and due to diagnosis of cancers that could not be identified clinically in remaining life time. Over diagnosis can occur because the tumor lacks potential to progress to clinical stage or over regresses (37) or women's dies from other cause before breast cancer surfaces clinically. Over diagnosis represents a substantial ethical dilemma and burdens patient and health care system. There are different treatments for the breast cancer like radiotherapy, surgery, chemotherapy and antiestrogen. With radiotherapy risk of death from cardiovascular disease is increased (38).

Breast cancer Mortality

According to the randomized trial done for breast cancer screening the reduction in mortality from breast cancer ranges between 15-25% (9, 22, 36) for women aged 50-69 years. For 25% estimate reduction, non-screening mammogram is compared with screening mammogram thus the Canadian trial was not included as they compared physical breast examination to combined physical breast examination and annual mammography (10, 36). For 15% estimate reduction methodological limitations in some trials was accounted (9) without this adjustment 20% reduction was found (9,22,25). No randomized trial show any effect on cancer mortality or all-cause mortality (9). 6660,000 number of women enrolled in randomized trial, 20% reduction in breast cancer mortality, 2% reduction in all-causes mortality should have been detectable. Absence of reduction in all-cause mortality shows that women die of other disease without screening.

Study design

There are different methods for investigation of effect of mammogram in a non-experimental setting. Cohort studies, case control studies, trend studies show different estimates of mortality reduction.

Cohort studies

This is a non-experimental design to investigate effect of mammography screening. Women invited and women non-invited to screening mammogram have similar baseline risk for breast cancer, breast cancer death and breast cancer treatment. Only few studies exist that show estimate effect of mammography screening on breast cancer mortality differ from 10-25% reduction. Pooled estimate of these trial show 13-17% reduction in breast cancer mortality (35).

Case-control studies

This studies sometimes called case-referent studies. In these cases women who die of breast cancer and controls are women who are alive stratified by whether they have undergone screening mammography or not. Validity of these studies is low because as of healthy screenee and self-selection bias, as women with breast cancer are not eligible to mammography screening or to be continued to be screened and women who participate in mammography screening may differ with regard to risk of death from those who do not participate (55). When randomized trial was analyzed as a case-control study 58% reduction was found in mortality from breast cancer, observed reduction in the trial was only 4%.

Trend studies

Studies of population-based breast cancer mortality over time in different ages and geographic areas. This data is easy to retrieve, but yearly mortality rate is not reflective of time of diagnosis, deaths from cancer diagnosed before invitation influences the mortality rate some years after screening is implemented. After a gap of 7 years follow up in the health insurance plan study the mortality reduction was no longer apparent that means screening has no longer effect if no longer offered. Most studies shows that breast cancer mortality has declined in most European countries since early mid-1990s. Decline in mortality is higher among younger women than the eligible age range of screening and for some countries reduction is observed for women

older than the eligible age group (59). Result could be that heightened awareness and improved therapy rather than screening mammography are responsible for the reduction (53,59,60).

Tumor stage

Benefit of mammography screening could be that the breast cancer detected at screening are smaller so less advanced than those detected clinically. Smaller tumors are more likely to resect by lumpectomy and less adjuvant therapy is needed. In National Health Service breast screening program in the UK, 30% of DCIS and 24% of invasive breast cancer was treated by mastectomy and early detection does not mean less aggressive treatment (61). Therefore, screening mammography does not seem to reduce the burden of receiving more aggressive treatment.

Causes of death

Number of women saved from breast cancer death might be outweighed by death from other causes due to harm of the treatment. According to UK data from 2007 for mortality from breast cancer in women aged 55-74years (34) and the reduction of 23-17% in breast cancer mortality based on meta-analysis of observational studies (35). From 1,000 women invited to screening mammography every second year for 20 years from age 50 2-3 women are prevented from death due to breast cancer.

Conclusion

Correct information should be given to women for the benefits and harms of mammography screening. Communicating information on benefits and harms of mammography screening is present in graph 1 among 1,000 women start screening at the age of 50 and screened for 20 years, 2-3 will prevent dying from breast cancer and 200 will have at least one false positive test, 30 undergo biopsy and 3 will be diagnosed with an interval cancer, and in 15 breast cancer will be over diagnosed.

With limited resources for health care and preventive services we need to examine our efforts in prevention and screening. One overarching goal of screening is the reduction of incidence or mortality disease. We do recommend some screening services like mammography while others are debated or discouraged like prostate-specific antigen screening.

Abbreviation

DCIS: - Ductal carcinoma in situ.

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