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Review Article

Breast cancer screening a literature review

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ABSTRACT

This article is looking at literature on breast cancer screening. Being the most common cancer worldwide and a leading cause of death, screening asymptotic women leads to early detection hence early treatment and with advances in treatments, breast cancer has better survival outcomes.

Keywords: Breast cancer, Screening, Mammogram, Barriers

INTRODUCTION

Breast cancer-the most common cancer worldwide and a leading cause of cancer death among women-disproportionately affects individuals in low- and middle-income countries. Breast cancer 5-year survival rates in high-income countries exceeds 90%, compared with 66% in India and 40% in South Africa. Early detection improves survival and reduces mortality therefore WHO had launched a new global breast cancer initiative (GBCI) framework which provides road map to save 2.5 million lives from breast cancer by 2040 which is a reduction by 2.5% of breast cancer deaths per year. GBCI employs three main strategies: health promotion for early detection, timely diagnosis, and comprehensive breast cancer treatment. Countries need to focus on early detection programs so at least 60% of breast cancer is detected at an early-stage disease, diagnosing breast cancer within 60 days of initial presentation, and starting treatment within 3 months of initial presentation improves outcomes and managing breast cancer so at least 80% of patients complete their recommended treatment. Mammography is the mainstay of breast screening.

LITERATURE SEARCH

Incidence of new breast cancer cases and deaths in 2020 were abstracted from GLOBOCAN database. Incidence was age standardized and mortality rate was calculated per 100,000 females by country, world reason and level of human development. Predicted cases and deaths were calculated based on the global projections for 2040.

Regarding breast cancer screening, the main study was the viewpoint of IRAC (International agency for research on cancer) working group where experts from 16 countries gathered to assess both effects and adverse effects of different screening methods on breast cancer prevention. Experts assessed all the scientific literature including randomized controlled trials openly. The working group and subgroups members were selected according to area of expertise and lack of conflict of interest. Each study was assessed fully and debated and then was summarized and reviewed by a group member who was not associated with the study. The next step was the working group reached a consensus on preliminary evaluations which was made in the subgroups.

For women 50 to 69 years of age who were invited to screen with mammography, on average there was a 23% reduction on the risk of breast cancer death. Data were more limited for women 40 to 49 years, and the reduction in breast cancer death for these women was less pronounced. The IARC concluded a net benefit for invitation to organized mammographic screening programs for women 50 to 69 years of age. However, the

evidence of efficacy for women in other age groups was inadequate.[16]

DISCUSSION

Geographic and regional variations

Breast cancer is indeed the most diagnosed malignancy accounting to 1 out of 8 cancer diagnosis worldwide according to a study from International Agency for Research on Cancer (IARC) 2022. In 2020, there were about 2.3 million new cases of breast cancer globally and about 685000 deaths from the disease, with large geographical and world regional variations. IRAC Estimated numbers of death 2020 of breast cancer of women of all ages in different countries.[1]

Incidence rates are highest in countries which had undergone economic transition, however, transitioning countries have disproportionally higher share of breast cancer deaths. By 2040, the same study predicts the burden from breast cancer will increase to over 3 million new cases and 1 million deaths every year because of population growth and aging alone.[1]

In the UK, breast cancer is the most common cancer counting to 15% of all cancers alone. There are around 55,900 new cases every year. That's more than 150 per day (2016-2018).

Since 1990's incidence has increased by 18% and projections suggest there could be around 69,900 new cases per year by 2028 -2040. The most common location of invasive cancer is upper outer quadrant of the breast in the UK. Mortality wise, there are around 11,500 breast cancer deaths in the UK every year, that's 32 every day (2017 -2019). Breast cancer is the 4th most common cause of deaths of cancer death in the UK accounting to 7% of all cancer deaths (2017-2019). Each year about half of cancer death (48 %) are in people aged 75 years old and over (2017-2019). Since the early 1970's breast cancer mortality rates have decreased by 41% in the UK, Over the last decade, mortality rates have decreased by 18%. In the UK, Breast cancer mortality rates are projected to fall by 13% between 2023-2025 and 2038-2040.[2]

Looking at Arab world's available data from 2010, 2013 and 2020, breast cancer is thought to be the most common malignancy diagnosed in Arab women estimating between 14-42 % of all tumors in some reports and between 17.7 and 19 % of all new cancers in others, depending on individual countries and type of reports viewed[3]. Although the incidence of new cases and the burden of the new disease seem to be lower than that in the western world and the global average in general, the incidence has been rising over the past few decades in a similar fashion to the global trend.[3]

The increase might be attributed to advances in screening, medical care, and diagnosis. However, this can also be partially attributed to actual demographic and lifestyle changes. The median age at the time of diagnosis of women with breast cancer in the Arab world is almost a decade younger than in industrialized countries such as Europe and USA. It's estimated in some reports to be around 48-52 years compared to around 63 years old with somewhat between one half and two thirds of diagnosed individuals below that age of 50 compared to only 23% below the aged of 50 in the United States.[3] This could be due to younger population structure and under representation of older Arab women.[3]

Screening uptake

Breast cancer screening uptake varies globally due to several factors, including healthcare infrastructure, cultural beliefs, awareness campaigns, and access to screening facilities. Here is a general overview of breast cancer screening uptake across different regions.

In high-income countries with well-established healthcare systems, breast cancer screening uptake tends to be relatively high. These countries often have organized national screening programs and guidelines in place, which contribute to higher participation rates. For example, countries like the United States, Canada, Australia, and several European countries have mammography screening programs that target specific age groups of women.

In middle-income countries, uptake of breast cancer screening varies. Some countries have implemented national screening programs, while others may have limited resources and infrastructure for widespread screening. Cultural beliefs and misconceptions about breast cancer and screening can also influence participation rates. Efforts are being made to increase awareness, access to screening services in these countries.

Breast cancer screening uptake is generally low in low-income countries. Limited resources, inadequate healthcare infrastructure and a lack of awareness and education about breast cancer contribute to low participation rates. Screening programs are often not widely available or accessible to the general population in these regions.

Significant global disparities exist in breast cancer screening uptake between different regions and within countries themselves. Urban areas tend to have better access to screening facilities compared to rural areas. Additionally, disparities based on socioeconomic status, education level, and ethnicity can affect screening rates even within the same country.[4]

Who is at risk of breast cancer? And strategies to increase survival

Approximately half of breast cancer develop in women who have no identifiable breast cancer risk factor other

that gender (female) and age (over 40 years). Moreover, other risk factors include obesity, harmful use of alcohol, family history of breast cancer, history of exposure to radiation, reproductive history (age of menarche and age of first pregnancy), tobacco use and postmenopausal hormone therapy (WHO).

Female gender is the most significant breast cancer risk. Can happen at any age after puberty. About 0.5 to 1% of breast cancers occur in men and the treatment follows the same guidance as females (WHO).

Certain inherited gene mutations increase breast cancer risk massively, the most dominant are mutations in genes BRCA1 and BRCA2. Women's carriers of these genes might consider risk reduction surgical removals of both breasts. This option needs to be carefully evaluated and should not be hasted.

Treatment of breast cancer can be highly effective, achieving excellent survival rates when the disease is identified early. Saying that, survival rates vary significantly geographically. Five years survival rates vary from 90% or more in high income countries to 60% in India and 40% in South Africa. Age standardized breast cancer mortality had dropped by 40% in high income countries between 1980's and 2020 (GBCI/ WHO). The drop is mainly due to effective treatments, a strong health system that support referrals from primary care and early detection. Due to the significance and impact of breast cancer, WHO had established GBCI in 2021 with objectives to reduced breast cancer mortality by 2.5% per year. Which translates into reducing by 2.5 million breast cancer death globally between 2020 and 2040 among women under 70 years old. The three main steps towards achieving this objective are: health promotion for early detection, timely diagnosis, and comprehensive breast cancer treatment.

Early detection

Early detection of breast cancer plays a crucial role in improving breast cancer management and treatment. It leads to improved treatment outcomes, reduced treatments intensity, also improves breast and body image, improves quality of life, and an increase in survival rates.

A variety of imaging techniques have developed over the years to assess breast suspicious lesions. However, Mammography remains the primary imaging for asymptomatic screening of breast cancer in average risk women[5].The important question is whether mammographic screening decreases breast cancer mortality. Nine randomized controlled trials, including more than 650,000 women, have been conducted and reported mortality data. All used mammography with or without clinical breast examination (CBE). Results of systematic reviews of the trials comparing mammographic screening with no screening show a benefit among women ages 40 to 69. A 2014 long-term follow-up study raised questions of overdiagnosis and a possible decreased impact of mammography as treatment for breast cancer becomes more effective.[6]

A 2012 meta-analysis of randomized trials found a 20% relative risk reduction for breast cancer mortality in women invited to screening compared with controls. It should be noted that most of these trials were performed decades earlier, at a time when treatment for breast cancer was less effective than with current protocols.[7]

A 2009 systematic review of screening mammography including eight studies of fair or better quality concluded that, with at least 11 years of follow-up, the pooled relative risk for breast cancer mortality was 0.85 (95% CI 0.75-0.96) for women 39 to 49 years of age, 0.86 (0.75-0.99) for women 50 to 59 years of age, and 0.68 (0.54-0.87) for women 60 to 69 years of age.[8]

The strongest evidence for an effective screening test is identified when randomized trials demonstrate a decrease in all-cause, as well as disease-specific, mortality. All-cause mortality is rarely documented because the required sample size for such a study is so large. In an analysis of four randomized trials in Sweden, breast cancer screening was associated with a slightly reduced all-cause mortality, although the association was of borderline statistical significance. The four trials followed 247,010 women for a median of 15.8 years; age-adjusted relative risk for total mortality was 0.98 (95% CI 0.96-1.00).[9]

There are several caveats to the findings from these trials: first the available data from most randomized trials of screening predate the current treatment protocols for breast cancer. Secondly, it is uncertain how much of the 30 percent reduction in breast cancer mortality since 1990 is due to screening and how much treatment advances. The randomized trials of screening also predate advances in breast imaging in that most were done using screen-film techniques. Secondly, it is unclear whether the results of careful randomized controlled trials can be replicated in the community setting.[10] Third, one review raised concern that breast cancer mortality outcomes in trials that did not blind assessment of the cause of death may have produced biased results in favor of screening.[11]

In the absence of more recent randomized trials, these questions have been evaluated by modeling and observational studies, including the following:

Using seven different statistical models, estimates of the proportion of total reduction in overall United States breast cancer mortality attributable to mammographic screening ranged from 28 to 65% (median 46%), with adjuvant treatment accounting for the rest. These results, based on studies when breast cancer mortality had dropped 20 percent, suggest that breast cancer mortality in the United States has dropped about 10 percent because

of screening, a more modest reduction than that found in randomized trials.[12]

A cohort study from Norway reviewed a 10-year period (1995 to 2005) of adjusted mortality data for women who were or were not invited for screening. Fewer breast cancer deaths occurred in women invited for screening, and it was estimated that 27 deaths from breast cancer were avoided for every 10,000 women who were screened every other year for 10 screening rounds.[13]

A case-control study of women in the Netherlands found that women aged 49 to 75 years who died of breast cancer were less likely to have had a mammogram compared with controls matched for age and invitation for mammography (odds ratio 0.51, 95% CI 0.40-0.66).[14] An earlier case control study in six community health plans in the United States did not show a statistical difference in screening rates for women who died of breast cancer compared with control patients matched for age and breast cancer risk, although there was a trend towards screening benefit among higher-risk women.[15] However, study limitations make it difficult to draw firm conclusions from this report.

In 2014, the international agency for research on cancer (IARC), with representatives from 16 countries, evaluated evidence from 20 cohort and 20 case-control studies regarding breast cancer screening. For women 50 to 69 years of age who were invited to screen with mammography, on average there was a 23 % reduction on the risk of breast cancer death. Data were more limited for women 40 to 49 years, and the reduction in breast cancer death for these women was less pronounced. The IARC concluded a net benefit for invitation to organized mammographic screening programs for women 50 to 69 years of age. However, the evidence of efficacy for women in other age groups was inadequate.[16]

In sum, systematic reviews of randomized controlled trials of mammography screening in women ages 40 to 69 years found a long-term 15 to 20 percent decrease in breast cancer mortality.[12]

Can screening be harmful?

The most important harms from mammography screening are false-positive results and overdiagnosis.

False positive tests: Positive results of screening that requires more work up. In the United States, for example, about 10 % of screening mammograms require further evaluation; the lesion turns out to be benign in more than 90% of cases.[17]

Over a 10-year period of annual mammography screening in the United States, about half of women will experience at least one false-positive mammogram. There are short-term negative psychological consequences of experiencing a false-positive mammogram that may last days to weeks, but there is no evidence of long-term, persistent adverse psychological consequences after a false-positive mammogram.[18]

The cumulative risk of false positive varies over time due to various patient and radiologist factors.[19] Factors contributing are young age, prior breast biopsy, family history of breast cancer, current estrogen use, 3 years between screenings, no comparison to prior mammograms, and radiologist random effect (tendency to call mammograms abnormal). Risk reduces with time in women with low risk profile. Understanding one's risk can help anxiety in cases of false positive results. Also reading mammograms and having a one stop clinic to assess abnormal breast finding can help reduce anxiety related to false positive results.[20]

Overdiagnosis: It is the detection of a disease by screening that would not have caused morbidity or mortality if it had not been found.[21] Estimates of the rate of overdiagnosis with mammographic screening are due to different definitions and methods, systematic review and meta-analysis of randomized trials estimated that 19% of breast cancers detected by screening represented over diagnosis.[22]

An ideal screening test is that detects tumors that have risk of progression and will need treatments and identify those with low risk of a disease and do not need treatment. Such screening does not exist. So, there is a chance of a percentage of patients receiving treatments without reduction in mortality. However, it was found in USA surveillance, epidemiology and end results program SEER Data from 1975 to 2012 that screening had reduced the rate of finding large tumors (2 cm or more) in women 40 years or older.[23]

False negative results: No screening test is perfect; some screening test results are negative but in fact the breast harbors a disease either due to the presence of mammographically subtle lesions or radiologist's reporting factors.[24,25] One in eight breast cancer cases are missing due to these factors.[26] Therefore, women who experience concerning breast symptoms despite recent negative screening results need to seek medical assessment in regarding to their concerns. Clinicians and radiologists must be familiar with various presentations of malignancy and various presentations that may lead to misdiagnosis.

Different considerations between the benefits and harms of routine screening have led to different guidelines regarding recommended starting ages and screening intervals.

Barriers to screening and how to overcome them

Lack of awareness and knowledge: Many individuals may not be aware of the importance of breast cancer screening or may lack knowledge about the recommended screening

guidelines. To overcome this barrier, public education campaigns should be developed to raise awareness about breast cancer, the benefits of screening, and the recommended screening methods. Healthcare providers can play a significant role in educating their patients about the importance of screening during routine check-ups.[27]

Socioeconomic factors, such as low income and limited access to healthcare services. To address this, efforts should be made to improve access to affordable or free screening services, particularly for underserved populations. This can involve implementing mobile mammography units, partnering with community clinics, and offering subsidies or vouchers for screening services. Unfortunately, during Covid 19 pandemic those factors have worsened compliance with breast cancer screening especially in poorer areas and within ethnic minorities.[28]

Fear, anxiety, and misconceptions about breast cancer screening procedures, such as mammograms, can discourage individuals from participating in screening programs. Healthcare providers can play a critical role in addressing these fears by providing clear information about procedure, its purpose, and potential benefits. Focusing on science behind screening is more informative and helps to reduce anxiety.[29] Sharing success stories of individuals who have undergone screening and early detection can also help alleviate anxiety.

Cultural beliefs, language barriers, and lack of culturally appropriate information can hinder participation in breast cancer screening. Efforts should be made to develop educational materials and programs that are culturally sensitive and available in multiple languages. Engaging community leaders, organizations, and healthcare providers from diverse backgrounds can help ensure that information reaches and resonates with various communities.[30]

Geographical factors, such as living in remote or rural areas, can limit access to screening facilities. To address this barrier, mobile mammography units can be deployed to reach underserved areas. Telemedicine and telehealth solutions can also be utilized to provide remote screening consultations and guidance, making it more convenient for individuals who face geographical challenges.[28]

Time constraints and busy lifestyles: Many individuals have time constraints and busy schedules as barriers to participating in breast cancer screening. To overcome this, efforts should be made to provide flexible screening options, including extended hours, weekend appointments, and workplace-based screening programs. Collaboration between employers and healthcare providers can help facilitate access to screening during working hours.[31]

Follow-up and treatment barriers: If an abnormality is detected during screening, follow-up tests and timely access to treatment are crucial. Barriers to follow-up care, such as long waiting times, lack of transportation, and financial constraints, should be addressed. Streamlining the referral process, providing transportation assistance, and ensuring affordable treatment options can help overcome these barriers.[32]

Empowering and engaging healthcare providers: Healthcare providers play a key role in promoting breast cancer screening. Continuing education and training programs can ensure that healthcare professionals are knowledgeable about the latest screening guidelines and techniques. They should be equipped with communication skills to engage patients in conversations about screening and address their concerns effectively.[33]

Overcoming barriers to breast cancer screening requires a comprehensive approach that involves public education, healthcare system improvements, community engagement, and policy changes. By addressing these barriers, we can increase participation in breast cancer screening programs, promote early detection, and ultimately reduce the burden of breast cancer.

CONCLUSION

Despite global efforts to reduce breast cancer impact, there is a scope for improvement worldwide. Breast cancer treatments are effective especially in early stages hence early detection is a key. Health systems need to implement strong well-structured screening programs and improve access to them to save lives. Governments need to improve the journey from breast cancer science to policymaking to reduced health inequalities. Countries need to work on providing effective breast cancer treatments and follow up too.

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