Chapter

Breast Cancer Screening

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Abstract

Breast cancer is a common malignancy worldwide. It is considered top cancer in women and about 13% of women in the general population will develop breast cancer sometimes during their lives, with a gradual increase in incidence as survival increases. Primary prevention of breast cancer is directed toward promoting a healthy lifestyle and reversing modifiable risk factors; these factors include smoking cessation, physical activity, alcohol, and dietary modification. Imaging plays an important role in the diagnosis and management of breast cancer, it is also considered the most valuable tool in screening breast cancer. Mammogram is the most widely used method; it is recommended by many societies and committees as a useful method for early detection of breast cancer. False-positive and over-diagnosis constitute a problem in using screening mammogram. The implementation of a screening program faces many issues that may adversely affect its success such as personal factors, social factors, and accessibility issues. These issues should be identified as the initial step in program implementation. The role of Magnetic Resonance Imaging and Ultrasound is mainly in high-risk patients. The introduction of Artificial Intelligence in Mammogram may add beneficial effects in time and efforts improving its efforts.

Keywords: breast cancer, screening, mammogram, breast self-examination, breast ultrasound

1. Introduction

Breast cancer is a common malignancy worldwide. It is considered top cancer in women and about 13% of women in the general population will sometimes develop breast cancer during their lives, with gradual increase in incidence as survival increases [1]. That is the reason why Breast cancer prevention is the core of many researches and trials worldwide. The World health organization has recommended breast self-examination, mammography as an effective screening tool since 2007. As in conclusion, early detection of breast cancer (secondary prevention) remains the cornerstone for breast cancer control [2].

Educating the population about eliminating modifiable risk factors (e.g. smoking, obesity) remains essential in the primary prevention of breast cancer [3].

1.1 Age

As a rule of thumb, breast cancer shows an increase in incidence as the age increases, about 8 in 10 cases of breast cancer occurs in women aged 50 or above [4].

However, this may not be applicable for all countries, as a study done by Mutar et al. shows that 45% percent of breast cancer patients were younger than 50 years [5].

The disease is extremely rare before the 20s, and it is as highly prevalent as 20% at age of 80 [6]. It is important to mention that the age may be the only risk factor present in a woman who develops breast cancer [7].

1.2 Hormonal factors

It is proposed that the longer a woman is exposed to cycling reproductive hormones, the higher the risk of breast cancer disease [8].

1.2.1 Time of menarche and menopause

In a large meta-analysis study done in 2012 [9]. An apparent association was found between the early age of menarche and the late age of menopause and breast cancer development, with the first factor being a stronger independent factor for breast cancer development.

In addition to that, these two factors seem to play a more complex role; they favor the development of estrogen-receptor positive disease & lobular histological type of breast cancer.

1.2.2 Parity, breastfeeding and age of having a first child

Breast cancer is more common in nulliparous women and breastfeeding, in particular, appears to be a protective factor. Also, having the first child at an early age seems to be protective [6].

Increasing parity was associated with a pronounced decrease in the risk of breast cancer, with each extra birth granting about 10 percent reduction of breast cancer risk, and the disease is 13 times more common for each five years increment in the age of having the first child [10].

And just like the effect of menarche & menopause, these factors not merely affect the duration of hormonal exposure but also the hormonal receptor status of breast cancer; for example, breastfeeding is inversely associated with hormone receptor-negative breast cancers and parous women were shown to have a lower risk of estrogen-positive breast cancer [11].

1.2.3 Contraceptive pills

Current or recent use of oral contraceptive pills increases the relative risk of breast cancer [12].

Post-menopausal hormonal replacement therapy (HRT) was associated with an increased risk for breast cancer [13]. Vaginal estrogens are considered an exception [4].

1.2.4 Obesity

Breast cancer is more common in obese women [6]. Obesity also affects breast cancer management; obese patients have lower treatment efficacy, more complications and higher recurrence rates [14].

Again, this supports the theory of linking breast cancer to the high estrogen states.

1.3 Lifestyle

1.3.1 Physical activity

A study held among Chinese women showed evidence that physical activity decreases breast cancer incidence; this is maybe due to the proposed effect of exercise on estrogen & insulin [15]. Education about this aspect seems reasonable for breast cancer prevention in high-risk groups.

1.3.2 Smoking

Both passive & active smoking are associated with an increased risk of breast cancer [16].

Also, women who were smoking at the time of their diagnosis have weaker outcomes and poorer survival [17]. However, there are inconclusive results about the smoking risk for the recurrence of the disease.

1.3.3 Alcohol

Just like smoking, it does increase the risk for breast cancer even in light to moderate intake in all ethnicities & with no association to estrogen hormonal status [18].

1.3.4 Dietary factors

Meat, caffeine, high fat diet, Low phytoestrogen all appear to increase the risk of breast cancer, in contrast to increment in vitamin D and calcium levels [6, 19].

1.3.5 Others

Living in stressful life/personality may appear to increase the breast cancer risk [20].

1.4 Drugs and radiation

- Non-steroidal anti-inflammatory drugs may appear to protect against breast cancer, although the evidence is not strong [21].
- Digoxin carries more pronounced research evidence to increase the risk of breast cancer, and all women should be informed about this relative risk before starting treatment [20, 22, 23]. This usually describes its use for more than four years and the risk is elevated by 21 to 40%.
- Radiation: patient's receiving radiotherapy as part of their treatment of Hodgkin lymphoma appeared to have an increased risk for breast cancer [6]. Routine chest X-ray and Computed tomography scans only have a little contribution to the risk [4].

2. Imaging in oncology

The first imaging modality to be discovered was X-ray by the German physicist Roentgen in 1895, the first use in oncology was to obtain a picture of sarcoma in an

amputated leg by German Surgeon Konig. the second imaging modality involved in oncology was ultrasonography, which was used for brain tumors, it Dussik used and called (hyper phonography) [24, 25]. The ultrasonography was then used in bowel, breast and obstetrics.

The history of mammography in breast cancer began in 1913 by Salomon who used it to evaluate 3000 mastectomies specimens [26]. He evaluated the role of radiological assessment correlated with the macrocalcifications and microscopic assessment of breast in order to differentiate between benign and malignant diseases [27].

The use of Xeromammography in 1960s shows improvement in mammogram diagnostic ability, the 1970s and 80s were the time to establish of screening mammography. In 1996 the Food and Drug Administration (FDA) established guidelines for commercializing digital mammography equipment [27].

Offering a screening mammography started in different times according to each country, for example, Australia had started screening by mammography every 2 years for women aged 50–69 years since 1991, while in Europe it started in 1986 [28, 29].

3. Screening

Screening is applied to many types of cancer, including mainly breast, colorectal, prostate, cervical and lung cancer. Breast cancer screening includes three main types screening mammography, clinical examination and ultrasound [30, 31].

Mammography is the most common screening modality for detecting breast cancers in asymptomatic women. The age and the frequency for screening mammogram is the subject of ongoing debate [32]. There is a considerable disagreement between guidelines regarding the recommendation for the age and frequency this might results from the wide variation in studies as found by Raichand et al. [32]. In a meta-analysis of 11 randomized clinical trials, the relative risk RR of breast cancer mortality for screening compared with controls was 0·80 (95% CI 0·73–0·89), with a 20% relative risk reduction [33].

The starting of 'Europe against Cancer' program in 1986, has led the committee of experts to start systematic population-based screening for cancer that shows decreased mortality with implementation. The effectiveness and benefits of mammography screening have been evaluated in randomized trials that showed decreased mortality by 20–35% in women 50–69 year [34].

If breast cancer is not diagnosed, the screening result is considered false-positive resulting in distress and anxiety among women [35]. The rates of false-positive results depend on many factors including screening interval, single versus double reading, sensitivity of the performance, participation patterns, equipment, and characteristics of the screening population [36]. Women who had false-positive results had a twofold increased risk of a later screen-detected cancer and might cause a reduced likelihood of reattendance [36, 37]. A recent meta-analysis had shown that a previous false-positive test does not influence participation in subsequent screening program [38].

It might better to encourage women with false-positive results to participate in regular screening, as the potential benefit is higher than in women who had negative tests [36].

The elements suggestive of a successful screening program are substantial reduction in cancer-related mortality, good participants' compliance, acceptability among participants, coverage, and high reattendance rate [37, 39].

Box 1 conditions required for successful mammogram screening.

1. It requires sufficient health system as well as financial resources to achieve a sustainable program with effective diagnostic and treatment capabilities including equipment, infrastructure, quality assurance, and monitoring processes.

2. It requires an administrative facilities responsible for the process of implementation and evaluation.

3. It requires validated protocols for screening steps, including recognizing the target population, inviting women who are eligible to be screened, applying screening tests, referral mechanism and its regulations, and management of each case accordingly.

4. It requires a good Communication and education of eligible women using culturally appropriate, objective information about the benefits and harms of breast cancer screening.

5. Ensuring good adherence to the guidelines for screening, diagnosis and treatment which are evidence based.

6. Information system for recording data of the screening process like calling the participants for follow up if abnormality was detected on screening.

7. Continuous regular monitoring, assessment and reporting of program performance and impact depending on reliable indicators like women's safety and satisfaction [40].

Box 1.
According to WHO, conditions for successful mammography screening.

3.1 Barriers to participating in mammogram

3.1.1 Personal beliefs

Fear of a positive result, pain and embarrassment related to the procedure, lack of knowledge about breast cancer and its screening, absence of trust in doctors and hospitals, lack of knowledge regarding mammography and its advantages, perception of being healthy, and fear of radiation exposure.

3.1.2 Accessibility and associated factors

Low-income population and lack of resources and health insurance, cost of mammogram, language barrier for minorities, lack of time required for mammogram, lack of transportation including personal and public transport, registration difficulties, and lower educational level.

3.1.3 Social factors

Lack of medical recommendation and advice regarding mammogram and discouragement from other people.

Other factors that affect participation include Age, Religiosity, family and personal history, and role of responsibility [41, 42].

3.2 Benefits and harms of breast cancer screening

Breast cancer mortality is generally reduced with mammography screening, although the magnitudes of effect are small. Advanced cancer is reduced with screening for women aged 50 years or older [43].

The detection of breast cancer in Australia increased in 2004 and mortality decreased [28]. On the other hand, possible harms of breast cancer screening may be related to false-positive results. According to a study published in 2011, most abnormal mammograms are actually false-positive. Follow-up testing adds additional cost [44].

3.3 Breast cancer overdiagnosis

The effectiveness of screening is mainly dependent on detecting cancer at early stage to promote early detection and better outcome, however, screening yields malignancies that may not have progressed during lifetime [45]. the lead time is the period between detection of cancer at screening and when it might be presented clinically, with stopping screening, the cancer incidence must fall, and at the end of screening time plus lead time, the cumulative incidence of the controlled and the screened populations should be the same. During the screening, some cancer detected might never progress throughout woman's life and might die from another cause before cancer becomes clinically detected. In another word overdiagnosis is defined as "detection of cancers that would never have been found without screening" [46–51] (**Tables 1** and **2**).

3.4 Clinical Breast examination (CBE)

Benefits: The current evidence does not support additional benefits and harms of CBE due to lack of evidence. CBE accuracy in the community screening might be lower than in the RCT [53].

Harms:

- False positives with additional testing and anxiety.
- False negatives with potential false reassurance and delay in cancer diagnosis.

3.5 Breast self-examination (BSE)

Benefits: BSE has been compared with no screening and has been shown to have no benefit in reducing breast cancer mortality [53].

Harms: There is solid evidence that formal instruction and encouragement to perform BSE leads to more breast biopsies and more diagnoses of benign breast

Risk stratification	Criteria
Low (L) risk	Category 1 breast density without or with only one risk factor (family history or breast biopsy) or Category 2 breast density with no risk factors
Medium-Low (ML) risk	Category 1 breast density with two additional risk factors, Category 2 breast density with only one risk factor, or Categories 3 or 4 breast density with no additional risk factors
Medium-High (MH) risk	Category 2 breast density with two additional risk factors, or Categories 3 or 4 breast density with only one risk factor
High (H) risk	Categories 3 or 4 breast density with two additional risk factors

Table 1.
Risk stratification for breast cancer screening. It is adopted from Yamamuro et al. [47].

Ages (Years)	U.S. Preventive Services Task Force [52]	American Cancer Society	American College of Obstetricians and Gynecologists	The Canadian Task Force	International Agency for Research on Cancer	European Commission Initiative for Breast Cancer Screening and Diagnosis guidelines (European Breast Guidelines)	American College of Radiology	American College of Physicians	American Academy of Family Physicians
Prior to 50	The decision should be individualized. Women who place a higher benefit than harms can start biennial screening between 40 and 49 years	Women have the choice of screening from age 40 to 44 once a year. Women should be screened from age 45 to 49 years.	If the individual prefers to screen and after taking consultation, mammography may be done once a year or once every two years with clinical breast exams once a year. Those choices should be taken after shared doctor with patient decisions.	For women aged 40–49 we recommend not routinely screening with mammography. (Weak recommendation; moderate quality evidence)	There is limited evidence that screening with mammography reduces breast cancer mortality in women 40–49 years of age.	For asymptomatic women aged 40 to 44 years with an average risk for breast cancer, the ECIBC's GDG suggests not implementing organized mammography screening	Screening with mammography is recommended once per year.	The choice of whether or not to screen with mammography before 50 years should be discussed by clinicians, taking into consideration the potential the benefit and harms and a woman's preferences. The potential risks outweigh benefits in most women between 40 to 49 years.	The decision to start screening with mammography should be an individual one. Women who place a higher value on the potential benefit than the potential harms may choose to begin screening.
50–74	Biennial screening mammography for women aged 50 to 74 years	Between 50 and 54, women should be screened with annual	Mammography is recommended once a year or every two years. Decisions should	For women aged 50–69 years we recommend routinely screening with	There is sufficient evidence that screening with mammography	For asymptomatic women aged 50 to 69 years with an average risk for breast cancer, the	Screening with mammography is recommended once a year.	Clinicians should offer screening with mammography once every two	Screening with mammography is recommended once every two years.

Ages (Years)	U.S. Preventive Services Task Force [52]	American Cancer Society	American College of Obstetricians and Gynecologists	The Canadian Task Force	International Agency for Research on Cancer	European Commission Initiative for Breast Cancer Screening and Diagnosis guidelines (European Breast Guidelines)	American College of Radiology	American College of Physicians	American Academy of Family Physicians
		mammography, While after 55 years, mammography is recommended once every one or two years. After 55 years, individuals should be transitioned to biennial screening or continue to screen annually.	be made after shared patient with doctor discussion Clinical breast examination can be done annually. .	mammography every 2 to 3 years. (Weak recommendation; moderate quality evidence) For women aged 70–74 we recommend routinely screening with mammography every 2 to 3 years. (Weak recommendation; low quality evidence)	reduces breast-cancer mortality to the extent that its benefits substantially outweigh the risk of radiation-induced cancer from mammography. There is inadequate evidence that clinical breast examination reduces breast cancer mortality. There is sufficient evidence that clinical breast examination shifts the stage distribution of tumors detected toward a lower stage.	ECIBC's GDG recommends mammography screening over no mammography screening, in the context of an organized screening program (strong recommendation, moderate certainty of evidence;		years. In average-risk women of all ages, clinicians should not use clinical breast examination to screen for breast cancer.	Current evidence is insufficient to assess the benefits and harms of clinical breast exams.

Ages (Years)	U.S. Preventive Services Task Force [52]	American Cancer Society	American College of Obstetricians and Gynecologists	The Canadian Task Force	International Agency for Research on Cancer	European Commission Initiative for Breast Cancer Screening and Diagnosis guidelines (European Breast Guidelines)	American College of Radiology	American College of Physicians	American Academy of Family Physicians
75 and older	The current evidence is insufficient to assess the balance of benefits and harms of screening mammography in women aged 75 years or older	Women should continue screening with mammography as long as their overall health is good and they have a life expectancy of 10 years or more.	The decision to stop screening should be based on a shared decision-making process. The decision-making process should include a discussion of the woman's health status and longevity.	_____	_____	For asymptomatic women aged 70 to 74 years with an average risk for breast cancer, the ECIBC's GDG suggests mammography screening over no mammography screening, in the context of an organized screening program (conditional recommendation, moderate certainty of evidence	The age to stop screening with mammography should be based on each woman's health status rather than an age-based determination.	Screening should be discontinued for average-risk women of 75 years or older, also in women of life expectancy of 10 years or less	Current evidence is insufficient to assess the balance of benefits and harms of screening with mammography.
Women with dense breast	Current evidence is insufficient to assess the balance of benefits and harms of	Evidence is insufficient to recommend for or against yearly MRI screening.	No routine use of other alternative tests is recommended, other than	_____	There is inadequate evidence that ultrasonography as an adjunct to	_____	In addition to mammography, contrast-enhanced breast MRI is also	There is insufficient evidence on the beneficial and harmful effects	Current evidence is insufficient to assess the balance of benefits and harms of

Ages (Years)	U.S. Preventive Services Task Force [52]	American Cancer Society	American College of Obstetricians and Gynecologists	The Canadian Task Force	International Agency for Research on Cancer	European Commission Initiative for Breast Cancer Screening and Diagnosis guidelines (European Breast Guidelines)	American College of Radiology	American College of Physicians	American Academy of Family Physicians
	adjunctive screening for breast cancer using breast ultrasonography, magnetic resonance imaging (MRI), digital breast tomosynthesis (DBT), or other methods in women identified to have dense breasts on an otherwise negative screening mammogram.		screening mammograph. State laws may require disclosure to women of their breast density as recorded in a mammogram report.		mammography reduces breast cancer mortality. There is limited evidence that ultrasonography as an adjunct to mammography increases the breast cancer detection rate. There is sufficient evidence that ultrasonography as an adjunct to mammography increases the proportion of false positive screening outcomes		recommended. After weighing benefits and risks, ultrasound can be considered for those who cannot undergo MRI	of screening for women with dense breast	adjunctive screening for breast cancer using breast ultrasonography, MRI, DBT, or other methods. Women

U.S: United state, ECIBC, GDG: The European Commission Initiative on Breast Cancer Guidelines Development Group.

Table 2.
Guidelines and recommendations for breast cancer screening mammogram. The references are enlighten between parentheses.

lesions. The biopsy rate was 1.8% among the study population compared with 1.0% among the control group.

3.6 Magnetic resonance imaging (MRI)

MRI has the greatest sensitivity of all imaging techniques, and it is considered a problem-solving modality, as a negative breast MRI can exclude malignancy. Only microcalcification seen on mammography cannot be excluded sufficiently by MRI and mammography in such case should be used to judge for biopsy indications. The role of MRI in screening high-risk patients is established, the sensitivity of MRI in high risk patients is between 71 and 100% compared with 16–40% in mammography, while specificity ranges 81–99% for MRI and 93–99% in mammography [54].

The American Cancer Society Guidelines recommends annual breast MRI screening starting from 25 to 30 years in women with a first-degree relative with a BRCA mutation, patients with a BRCA gene mutation, and women with 25% or greater lifetime risk of cancer [55].

European Society of Breast Imaging also advises annual screening with MRI for patients with breast cancer diagnosed under 50 years of age who have a 20% lifetime risk of recurrence and for patients who received radiation to the chest in their second or third decade of life and for patients with inherited syndromes, like Cowden and LiFraumeni syndrome, and their first-degree relatives [54].

Starting Screening at age 40 years may provide some benefits in average-risk populations, but offer higher levels of harm than strategies initiated at age 50 years. The age for cessation of screening can be based on the Comorbidity levels. Biennial screening strategies can be used and considered as the most efficient, but annual screening might be indicated from 40 to 74 years of age in groups with have a 2- to 4-fold higher risk than average [56].

3.7 Ultrasound (US)

Until the early 1990's, breast ultrasound was used primarily to distinguish solid from cystic lesions and image-guided interventions [57]. Ultrasound can be added to mammography in women with dense breasts so that, to increase the sensitivity of detecting the cancer. Ultrasound has relatively good specificity and sensitivity as a follow up tool in women with dense breast and negative mammogram, for that reason, ultrasound can be considered as an adjunct to mammography in screening women with dense breasts [58]. One meta-analysis results suggest the addition of US to mammography of women with dense breasts improves the sensitivity of detecting breast cancer, despite a slightly decreased specificity. Follow-up US also had good diagnostic sensitivity and specificity [59].

Ultrasound, when compared to mammography, is radiation-free, cheaper and less strenuous modality [60].

Using mammography alone for screening has been shown to have poorer diagnostic performance for high-risk women than when used for the general population. For high-risk women, mammography has lower sensitivity and a higher interval cancers rate that might be spread to the lymph nodes. Many factors described in the literature may be responsible for that; like higher breast density, younger age of onset, and increased tumor growth, breast cancer associated with genetic mutation may also be invisible on screening mammography. Supplemental screening with (MRI) significantly improves the detection rate of breast cancer in high-risk populations, compared to mammography alone. Ultrasound may be used instead in patients with a contraindication of MRI due to anxiety or severe claustrophobia, or metallic implants, or patients allergic to the contrast agents [61].

3.8 Artificial intelligence in breast screening

Computer-aided detection software for mammography was intimated in 1990s and since that improvement had been made to improve outcomes. The use of artificial intelligence in screening mammogram has been shown to provide an absolute reduction of 1.2–5.7% in false positives and 2.7–9.4% in false negatives [62]. Artificial intelligence use in screening has the potential advantages of reducing the interval cancer rate without any additional modality, the reduction in interval cancer risk is an important indicator for screening program efficacy [63]. The use of AI in screening requires acceptance to participate and trust in their results, many people as shown by Ongena et al. [64] do not supply the use of AI alone in screening.

4. Conclusions

As breast cancer is among the most common cancer in women, prevention represents an important step to decrease morbidity and mortality. Prevention can be applied on three levels primary, secondary, and tertiary. Screening mammogram has the main advantage of early detection leading to better management and decreased mortality.

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Conflict of interest

The authors declare no conflict of interest.

Notes/thanks/other declarations

Place any other declarations, such as “Notes”, “Thanks”, etc. in before the References section. Assign the appropriate heading. Do NOT put your short biography in this section. It will be removed.

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