

EPIDEMIOLOGY, PREVENTION AND MANAGEMENT GUIDELINES FOR BREAST CANCER IN ARAB COUNTRIES

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Abstract

Background: Breast cancer is the most common cancer among women in Arab countries. Management varies according to human and financial resources, as well as available facilities.

Materials and Methods: Literature review of publications on the epidemiology, prevention and treatment of breast cancer in Arab countries. Presentations and discussions summarized from various oncology meetings.

Results: Breast cancer represents an average of one-third of female cancers in Arab countries. Incidence continues to rise and has reached up to 50/100.000 women in Gulf countries and highest in Lebanon at 69/100000 women per year. Around 50% of cases are below the age of 50 years. Over 60% of cases present with advanced disease. However, number of advanced cases has started to decrease and more cases are being diagnosed at earlier stages because of recent awareness and early detection campaigns done in many Arab countries. Radiation therapy remains concentrated in major cities and large numbers of patients have to travel long distances to get adequate care. Multidisciplinary management is practiced only in major university hospitals and in the few available cancer centers.

Conclusions: More efforts towards primary prevention are recommended. Secondary prevention includes awareness campaigns and early detection. Raising awareness, promoting attention to breast symptoms, breast self-examination and clinical breast examination are recommended to reduce locally advanced breast cancer. In addition, screening mammography is recommended in countries with adequate resources. Although the starting age of screening mammography is controversial, we recommend to start at age 40 because 50% of cases of breast cancer in Arab countries occur in women below the age of 50. More group discussions and multidisciplinary management between individual physicians caring for women with breast cancer are needed.

Introduction

Cancer prevention and early detection are the most effective ways to control disease, alleviate sufferings, prolong survival, and eventually cure patients with cancer. Cancer prevention and early detection ultimately reduces the incidence of cancer as well as morbidity and mortality from cancer. Early detection of breast cancer is considered as an important element of prevention of the disease. The improvement in breast cancer survival observed in industrialized nations in recent decades have been attributed to early detection by screening as well as to timely and effective treatment.(1)

Consequently, breast cancer mortality which had been relatively unchanged from 1930s through 1980s has dropped by 1.4% to 3.1% / year between 1990 and 2003 in the US. (2) Cancer has

become a national health priority according to the WHO in the Eastern Mediterranean Region. The general public, as well as healthcare professionals have noted that breast cancer has become one of the most important health problems for women in Arab countries. (3, 4, 5)

Approximately, 15% of all breast cancer cases can be attributed to familial and genetic influences.(6) Most known risk factors for breast cancer can be linked to hazardous effects of prolonged exposure to estrogens⁷ such as early age at menarche, late age at menopause,(7) small number of children and nulliparity, late age at first birth⁸ and little or no breast feeding (9,10) which have all been associated with an increased risk of developing breast cancer. Although several retrospective studies have suggested that induced abortion is related to an increased risk of this disease, this is not seen in prospective studies (11) and its status as a breast cancer risk is unclear. Long term use of hormone replacement therapy has been associated with increased risk of developing breast cancer (12) but apparently not use of oral contraceptives. (12-15)

However, meta-analysis of all the data (Leslie Bernstein, et al) \geq ten years of use of the relative risk 1.38 (these women were 1.38 times as likely to get breast cancer as those who had not used the pill). The primary concern is for women who start their period before age eleven. Those who also begin having regular periods much faster, so, prolonged use of estrogen containing pills is more likely to harm this subgroup.(16) So far, there is no evidence that the use of mega-dose of hormone infertility treatment are hazardous to the breast.(15,17) High breast density has been described as an important marker of breast cancer risk.(18,19)

History of proliferative benign breast disease is also related to increased risk of breast cancer (20) especially those who underwent biopsies and those women in whom a typical hyperplasia was found in such biopsies. (21) Therefore, in summary, breast cancer risk can be allocated to one of four groups: family history/genetic, reproductive/hormonal proliferative, benign breast disease with dysplasia, and mammographic density. Recently, it is believed that high-fat diet is not related per se to breast cancer risk (22, 23) but overall caloric intake and obesity in particular with weight-gain pattern, are related to increased breast cancer risk with differentiate effects between pre and post menopausal women.(24, 25)

Women with breast cancer may have advanced disease at diagnosis and some of reasons for such presentations are summarized in Table 1.

Table 1: Reasons For Presentation As Advanced Disease

- Lack of knowledge on breast cancer risk factors
- Misconception about breast cancer screening
- Fear of cancer
- Shyness and fear of social implications
- Beliefs and fatalistic attitudes
- Lack of health care facilities

2. Disease Epidemiology

Breast cancer is the most common cancer diagnosed in US women and the second leading cause of death of cancer in US women. (1) The good news is that mortality from breast cancer has recently dropped slightly. This decrease has been attributed, in part, to mammographic screening. (1, 2) Breast cancer has been reported as the most common cancer among women from many hospitals and medical centers in Arab countries. Hospital-based registries, several regional and national registries have recently been in place and reported their data. Researchers have reported data in either abstract form or meeting presentations and some reported in peer-reviewed local or international journals. Many national registries now publish their data as annual reports in a booklet format. In this manuscript, we review and update the available data on breast cancer epidemiology from Arab countries. (26, 27)

Breast cancer is the most frequent cancer in Arab women constituting 14% to 42% of all women cancers. Age-Adjusted Standardized incidence rates (ASR) were reported to vary from 9.5 to 50 cases per 100,000 women per year. Median age at presentation is 48-52 years and 50% of cases are below the age of 50; whereas only 25% of cases in industrialized nations are below the age of 50 years, and 50% of the cases are above the age of 63 years, 1, 2 thus it appears breast cancer in Arab countries presents almost 10 years younger than that in USA and Europe (26, 27).

Age-adjusted standardized incidence rates (ASR) for breast cancer have increased in many Arab countries such as Lebanon (from 20 in 1996 to 46.7 in 1998 and even 69 in 2003), Jordan (ASR increased from 7.6/100,000 women in 1982 to 32.8/100,000 in 1997), Palestinians (ASR up by 93%), Egypt ASR up to 49.6. Reports from the Gulf Center for Cancer Registration (GCCR) which represented data from six Gulf countries: Kingdom of Saudi Arabia, United Arab Emirates, Kingdom of Bahrain, Sultanate of Oman, State of Qatar and State of Kuwait, revealed that breast cancer is the most common in the GCC states between January 1998 to December 2004. 6,882 breast cancer cases were reported from all GCC states accounted to 11.8% from all cancer and 22.7% from cancers among women. Bahrain reported the highest incidence.

The ASR per 100,000 women was 46.4 followed by Kuwait 44.3, Qatar 35.5, UAE 19.2, Oman 14.4 and KSA 12.9. 28 Despite the low breast cancer incidence in the Kingdom of Saudi Arabia (KSA), it is the most common cancer and it ranked number one in Saudi female population for the past 5 consecutive years (Saudi National Cancer Registry, 2000 – 2004). Data on female patients with invasive breast carcinoma reported from different regions in Saudi Arabia revealed that most patients were between 40 – 50 years of age and were predominantly premenopausal. Although the rates are still below those in industrialized nations, they are rising and expected to reach the same levels. Changes may be due to Westernized life style changes including dietary habits, lack of exercise and urbanization, delay of ages of marriage and first pregnancy from the late teens and early twenties to the late twenties and even early thirties, respectively, as well as and decrease of the practice of breast feeding by Arab women. Advanced disease is commonly seen at presentation and in young women, diagnosis of breast cancer may be delayed because of decreased awareness as well as and low index of suspicion from their primary physicians. (29) Young age at presentation has been shown to be a bad prognostic factor in two publications from Lebanon and Saudi Arabia. (30-31 (Figure-1)

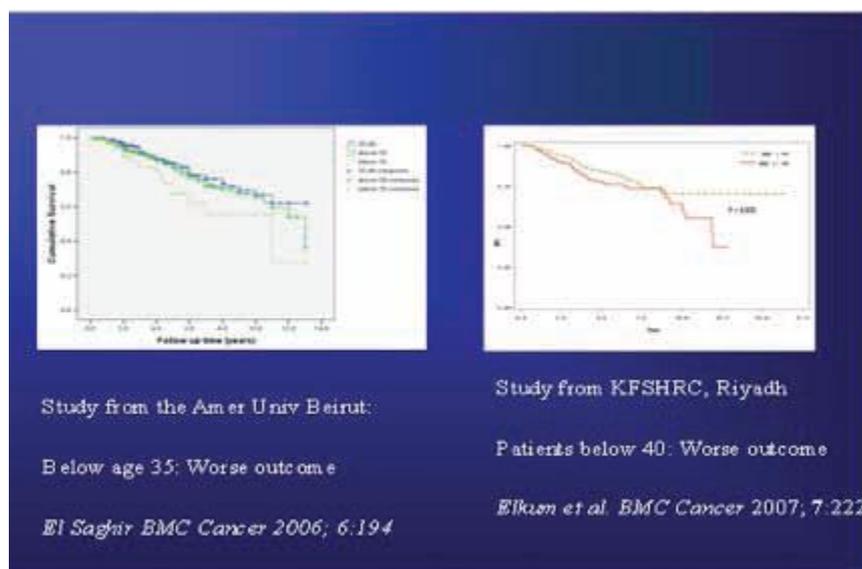


Figure-1 Young Age Confers a Worse Prognosis in Breast Cancer

3. Risk Factors

A number of breast cancer risk factors have been well established for many decades, notably

those related to hormonal and reproductive exposures. (7-8) For example, nulliparity late age at first childbirth, early age at menarche and use of hormone replacement therapy are all associated with increased risk. (7-11) Additionally, the association of a family history of breast cancer with increased risk of the disease has long been established.(32-33) The increased awareness of family history is enhanced partly by the establishment of the high risk, high penetrance BRCA1 and BRCA2 germline mutations.(34) Other risk factors pertaining to personal medical history has been established. These include diagnosis of atypical ductal hyperplasia and lobular carcinoma in situ. (35) Prolonged exposure to birth control pills in premenopausal women, and especially hormone replacement therapy in post-menopausal women increase the risk of breast cancer. Other risk factors include radiation exposure, pollution and exposure to carcinogenic compounds such as pesticides and even smoking are suspected. Westernized dietary habits, increase consumption of animal fats and decreased fibers, fruits and vegetables, as well as overweight and lack of exercise are known to increase breast cancer incidence among Asian immigrants to USA, Europe and Australia. Many of those risk factors are thought to apply to women in Arab countries. Only scattered studies on genetic mutations of BRCA-1, BRCA-2 and other oncogene mutations are available from Arab countries. (36-37)

4. Presenting Signs and Symptoms

The most common presentation in our countries is a breast lump or nodule, usually non-painful but may be associated with pain. Size of the lump depends on whether it was accidentally noted or whether the woman examines her breasts regularly. Other symptoms include changes in color or shape of the skin such as redness, ulceration and therapy of skin, nipple retraction or discharge of blood may be presenting complaints. A palpable mass in the axilla is not an uncommon presentation in cases of locally advanced breast cancer or without breast mass. Inflammatory breast cancer presents with a rapidly growing inflamed, thickened and red overlying breast skin. The data has shown that in many Arab countries that 50-80% of breast cancer is Arab countries present with advanced disease at presentation. More than 50% were Stage II and III while ductal carcinoma insitu represents <5% of reported cases. (27) However, with the massive campaigns of awareness and efforts at screening, more patients are presenting with early disease such as small lumps or abnormal mammography findings.

5. Breast Cancer Prevention in Arab Countries

The goal of prevention is to reduce the incidence of breast cancer and to reduce breast cancer associated mortality. Primary prevention refers to methods aiming to reduce incidence by eliminating causes and carcinogens, either through dietary changes, exercise, reducing obesity or by offering surgery to BRCA carriers for example, or the use of certain drugs. Chemoprevention drugs such as tamoxifen or raloxifen are offered for high risk women. The use of hormone replacement therapy should be controlled and regulated. Pharmacists should not be allowed to sell these medications without a physicians' prescription.

Reduction of incidence and mortality from breast cancer may be achieved by secondary prevention which refers to screening and early detection. Screening is designed to discover small tumors before they manifest themselves clinically. However, an important task for us in Arab countries is to detect tumors before they get large or involve the skin or chest wall, or metastasize to other organs. We refer to this strategy as "prevention of advanced disease at presentation."

To achieve goals of screening and early detection, i.e., reduce incidence and mortality, society should plan on discovering tumors at early stages and be able to treat them successfully. Therefore, improving quality of diagnosis and treatment is also an essential part of a national plan to control breast cancer.

Population screening is rarely practiced in most Arab Countries. This screening should include a monthly breast self exam (BSE) start age 20, clinical breast exam (CBE) every three years between the ages of 20 and 39 years and annually after the age of 40, and annual screening mammography starting at age 40 if resources are available. Guidelines for low and middle-income countries are published (38-40)

Sporadic screening, also called opportunistic screening is a relatively common practice of many Arab women. However, there is no epidemiologic study on this issue in Arab countries. In countries where screening mammography is done, there should be a policy for regular inspection, quality control and licensing of screening centers. Centers should be inspected yearly for radiation emission, film development, technologist performance and education, radiologist reading and possibly double reading. Every effort should be made to study detection rates, screen-initiated tests and biopsies, and outcome.

Prevention of locally advanced breast cancer requires continuous awareness campaigns and advocacy efforts. New clinical programs and special innovative methods such as the Cairo Breast Cancer Screening Trial, (41) which involved training social workers and nurses to perform home visits and classes and teach and examine breasts of women at their homes and community centers, is a good example to follow.

Locally advanced cases could be easily seen and/or palpated and should not be left to grow larger and become potentially devastating to the single woman, the married woman, her husband and even children and family. Fears should be alleviated. Proper information should be disseminated to both women and their husbands and families and they should be informed that early small breast cancer can be cured, and that small tumors usually do not require mastectomy and its associated deformity. Small tumors can be successfully treated with partial breast surgery and breast conservation with little deformity of the body. Reducing the incidence of locally advanced disease at presentation, should help alleviate sufferings, improve cure rates, reduce the current high rates of mastectomy and reduce economic burden of breast cancer. At the American University of Beirut, and in several other centers throughout Arab countries, more early breast cancer cases are being diagnosed, more partial mastectomies, and survivals over 90% are reported. (42)

In summary, screening breast self-exam and clinical breast exam are recommended for all women in all Arab countries. Annual screening mammography starting age 40 is recommended where resources are available and where adequate diagnostic and therapeutic modalities are available. Awareness campaigns should be directed at reducing the incidence of locally advanced disease at presentation. Awareness campaigns should be directed at both women and men. Men should be asked to encourage their wives to enroll in screening campaigns.

Radiation Therapy in Arab Countries

Radiation therapy centers in Arab countries are scarce and are mostly concentrated in major cities. Many young women in Arab countries do not undergo breast conserving surgery because of the unavailability of radiation therapy centers near their residence and cities. Although some Arab countries have adequate radiation therapy centers, most countries do not. In a comparison of radiation therapy centers, equipments, radiation technologists and radiation therapists between the United States of America and the entire Arab countries which are equivalent in population number according to WHO 2007 (Population is 301.227.000 people in the USA 298.213.000 people in Arab countries), there are 87 radiation therapy centers, 325 radiation therapists, and 490 radiation technologists in Arab countries, as compared to 1875 centers, 3068 radiation therapists, and 5155 technologists in the USA. (Table 2).

Table 2: Radiation Therapy Centers in Arab Countries Compared to USA (Equivalent in population numbers)

Countries	Population	RT Centers	Radiation Oncologists	Radiation Technologists
US Arab	301,227,000	87	325	490
USA	298,213,000	1875	3068	5155

6. Management and Treatment Guidelines: Multidisciplinary Approach

Breast cancer management must be composed of a multidisciplinary team that involves different specialty: breast surgeon/oncologist surgeon, medical oncologist, radiation oncologist, pathologist, psychologist, social worker, health educator and plastic surgeon. If a full team is not available, multi-disciplinary approach should be practiced by whoever is present. Even if the hospital where a breast cancer patient is treated has only a surgeon and a radiologist and pathologist, or a surgeon and radiologist and an oncologist, or a surgeon and a radiologist and a radiation oncologist, they should meet and discuss their patient's management. Every effort should be made to have a pathologist available. Discussion and exchange information with physicians working at major cancer centers should be encouraged.

If there is no multi-disciplinary clinic where the patient is seen by the full oncology team, every hospital that treats breast cancer should have a weekly Tumor Board conference where cases are discussed between available specialists.

As a general rule, the primary treatment is surgery. Partial mastectomy plus radiation therapy is equivalent to modified radical mastectomy for primary breast cancer. When partial mastectomy is performed, special attention should be made to obtain comfortably negative margins. Young women are at a higher risk of having local recurrences after long-term follow-up and should have continued long term follow-up. The treatment with mastectomy and reconstruction remains a viable option, particularly in younger women.

Adjuvant therapy includes chemotherapy, targeted therapy with trastuzumab, and hormonal therapy. Guidelines are referenced below. (42-43) Anthracyclines and taxanes are the most commonly used drugs, either separately, or in sequence, or combination. Classical oral CMF remains a viable option. Attention to resources and health care planning in countries with limited resources are presented by Breast Health Global Initiative (BHGI). (44)

Locally advanced breast cancer is treated with neoadjuvant therapy, preferably and more clearly called pre-operative therapy. Pre-operative therapy is usually anthracycline-based. (45) Taxanes improve breast conservation rates and increase complete pathological remissions (46) Patients with less residual disease tend to have better survival. (47) Higher rates of clinical and pathological remissions may be obtained with chemotherapy and targeted therapy in the presence of HER2 positive tumors. Hormonal preoperative therapy gives good clinical responses produces but rarely produces complete pathological remissions and is useful in older postmenopausal patients. Preoperative therapy requires adequate radiological and pathological evaluations to be available. (48)

Guidelines for the treatment of metastatic disease are referenced below. In general, hormonal therapy is indicated for hormone-receptor positive metastatic disease with bone and soft tissue metastases. Chemotherapy is used in patients with visceral metastases such as in the liver and lung. Chemotherapy is generally used when patients have aggressive and rapidly progressive disease particularly in young patients. Ovarian ablation (surgical, or by radiation therapy, or more the more costly ovarian suppression by LHRH analogs is preferred in premenopausal women. Tamoxifen with ovarian ablation is better than tamoxifen alone. Tamoxifen is effective anti-estrogenic therapy also in post-menopausal patients. Aromatase Inhibitors, particularly letrozole has been shown to be more effective than tamoxifen. Attention to resources and availability of therapy is important in countries with limited resources and has started to gain attention in major medical conferences and journals as referenced below. (48)

Targeted therapy with anti-HER2 agent trastuzumab has become an essential component of the treatment of CerebB2 (HER2/neu) positive disease. Trastuzumab may be combined with hormonal therapy (TanDEM trial) or chemotherapy particularly docetaxel, paclitaxel and vinorelbine. More recently, lapatinib, a dual anti-Her2 and tyrosine kinase inhibitor has been reported to be beneficial in trastuzumab-resistant patients and also upfront when effectively combined with hormonal therapy in combination with letrozole and lapatinib in breast cancer

(Abstract #81/ 31st Annual San Antonio Breast Cancer Symposium, 2008).

Modern treatment of breast cancer should include research and clinical trials to find better answers for many questions. Modern chemotherapy, targeted therapy, and new hormonal therapy require more research and participation in international phase III trials. The medical community in the Arab World is urged to establish nationwide and hospital computerized databases and publish its findings and its research in peer-reviewed scientific journals. Multidisciplinary approach to cancer management is currently practiced only in few major medical centers and should become standard practice in all hospitals that treat breast cancer. More cooperation between various specialists to improve care of breast cancer patients is direly-needed. A few cancer centers exist in Arab countries and many more are needed. Encouragement and funding of cancer research should become a priority in Arab countries. Readers are referred to Breast Health Global Initiative BHGI resource-oriented guidelines published in the October 2008 issue of Cancer. (48)

7. Prevention Through Risk Factor Modification

It is clear that modern therapy for breast cancer has become more effective and more expensive. Prevention and early detection may save major parts of costs of adjuvant and metastatic disease therapy. Several strategies are available for reducing breast cancer risk in countries with lower resources, but few of them have completed rigorous testing in clinical trials.²⁸ Strategies to increase the prevalence and length of lactation may reduce risk for breast cancer in mothers in addition to providing nutrition benefits for infants and small children. Increased adiposity, a sedentary lifestyle and moderate to high levels of alcohol use are associated with increased risk of breast cancer. The evidence of a role for specific dietary components is less clear. For individual women, counselling should include increasing physical activity and balancing energy such that weight remains stable over a lifetime and, preferably, with the body mass index remaining <25 kg/m². The provision of community-level and workplace facilities to enable these activities should be encouraged.⁴⁹ Counselling should include avoiding alcohol intake and to quit smoking whether cigarette or hubble bubble (argila).⁴⁹⁻⁵⁰ The routine use of combined estrogen/progesterone menopause hormone replacement therapy (HRT) which has been shown to increase the risk of breast cancer should be stopped and women should not be allowed to buy them without prescriptions. HRT use should be limited to women with refractory menopausal symptoms and for as short a period as possible. (Table 3)

Table 3: Prevention Through Risk Factor Modification

Risk Factors	Suggested Modification
Breast feeding	To prolong lactation $\geq 1 \frac{1}{2}$ years at least as many studies proved its beneficial protection.
Lifestyle and diet	Increase mobilization, avoid weigh gain specially after menopause, regular exercise.
Smoking, alcohol	Avoid smoking and alcohol.
Hormone Replacement Therapy (HRT)	Should not be given routinely to postmenopausal women. Should not be dispensed from pharmacies without prescription.

These behaviors, although they have not been proven in clinical trials to reduce risk, are likely to be beneficial. Information on them can be provided as a prevention strategy in limited resources societies, although the methods of information delivery and follow-up will depend on financial and personnel resources. The magnitude of absolute risk reduction based on risk factor management is somewhat unclear. However, any of these health behaviors can reduce risk for other chronic diseases, so they may be of high interest for general public health in both low and middle-income countries and high-income countries.

8. Early Detection: Experience in Arab Countries

In the majority of Arab countries, screening is not standard of care. However, few promising

screening initiatives emerged recently in some countries. The Cairo Breast Cancer Screening Trial was reported in 2005. It included training nurses and social workers to provide lectures and demonstrations, breast examinations, and referring women with suspicious findings to a nearby Italian Hospital in Cairo. More early breast cancer cases and less mastectomies were reported by the investigators.³⁹ Another major effort is being conducted with the Ministry of Health.

8.1. Early Detection: Experience in Saudi Arabia

In Saudi Arabia, several studies were done evaluating the perceptions of women regarding breast cancer screening. In addition to physician barriers to breast cancer screening, studies identified the following factors: lack of knowledge about mammography as it is the standard screening test, breast cancer risk factors and lack of knowledge of practice BSE.^{51, 52}

The study that targeted primary health care physician concluded that the main barriers to breast cancer screening were: the unavailability of a national screening program, lack of women cooperation and compliance, lack of allocated time by physicians, and lack of knowledge regarding screening recommendations. ⁵³

Recently, two screening programs were developed; one in Al-Qaseem region where investigators developed a program for early detection of breast cancer that included staffing by trained nurses, pathologists and radiologist and target 75,000 female ages 35-60 in the region. The program has five permanent screening centers and a mobile one. So far, they completed three years since they started but no official results, for their findings are available yet (Alhabdan, personal communication).

The second screening center is the Abdul-Lateef Center for Screening in the capital city of Riyadh, which opened in October 2007. The center is equipped with a digital mammogram machine, an ultrasound and two radiologists for double reading of mammographies, in addition to general practitioner and health educator who will interview the women and provide them with the screening questionnaires. For women with average risk factors using Gail Model questionnaires, a mammogram will be done based on BIRADS System (taken from <http://www.imaginis.com/breasthealth/acrbi.asp>). After a screening mammography is generated, the women are contacted. Those who need further evaluation are sent to King Abdulaziz Medical City or King Fahad Medical City in Riyadh.. So far, over 1,800 females were screened and 22 women were confirmed to have malignancies. A few of those malignancies were ductal carcinoma insitu (DCIS) and Stage 1 disease. Investigators are encouraged and women are reassured that we see early breast cancer rather than the usual advanced disease. Challenges facing the investigators include refusal of many women to do further investigations, and even some women refused to have treatment. Those issues highlight the importance of breast health education for the general population. Results of this program are accepted presentation in ASCO 2009.

8.2 Experiences from Lebanon

In addition to general public awareness campaigns, there is a systemic campaign that started in 2003, in collaboration with the Ministry of Health, Lebanese Society of Medical Oncology, Non-Governmental Organization Faire Face (Facing Cancer), and pharmaceutical company Hoffman-La Roche. Every October, the campaign runs billboard ads, TV ads, intense TV and newspaper and magazine interviews about breast cancer screening and education. The campaign recently evolved into getting offers for low-cost mammography offered once a year for women over 40. The Campaign and Ministry of Health offer classes and guidelines for quality mammography for participating centers. In parallel to the campaigns, there has been a noticeable increase in mammography-detected cancers, small tumors, and less total mastectomies being performed at major institutions.⁴² A National Breast Cancer Task Force has evolved to plan further actions

8.3. Breast Cancer Screening Recommendations

The recommendation of breast cancer early detection/screening in average risk and high risk women are depicted in Tables 4 and 5. These guidelines should be followed in the Arab countries

until future relevant evidences prove the need to modify these guidelines.

Table 4: American Cancer Society (ACS) and National Comprehensive Cancer Network (NCCN) Recommendations for the Early Detection of Breast Cancer in Average-Risk Asymptomatic People

Population	Test or Procedure	Frequency
Women, aged ≥20 years but <40 years	Breast self-examination (BSE)*	Beginning in their early 20s, women should be told about the benefits and limitations of BSE. The importance of prompt reporting of any new breast symptoms to a health professional should be emphasized. Women who choose to do BSE should receive instruction and have their technique reviewed on the occasion of a periodic health examination. It is acceptable for women to choose not to do BSE or to do BSE irregularly.
	Clinical breast examination (CBE)	Recommended that CBE be part of a periodic health examination, preferably at least every 3 years
	Mammography	Not recommended
Women, aged >40 years	Breast self-examination (BSE)	Optional
	Clinical breast examination (CBE)	Annually
	Mammography**	Annually

* The ACS no longer recommends monthly (BSE) and women should be informed about the potential benefits, limitations and harms (the possibility of false positive result). Also, women should receive instructions in the technique and/ or have technique reviewed periodically.

** There is no specific upper age at which mammography screening should be discontinued, decision to stop annual mammography screening should be individualized based on potential benefits and risk of screening in the context of overall health status and estimated longevity.

Table 5: American Cancer Society (ACS) and National Comprehensive Cancer Network (NCCN) Recommendations for the Early Detection of Breast Cancer in High-Risk Asymptomatic People

Population	Test or Procedure	Frequency
Prior thoracic radiation therapy (RT) for age <25 years 25 years	Breast self-examination (BSE)*	Periodic monthly
	Clinical breast examination (CBE)	Annually
	Clinical breast examination (CBE)	Every 6 – 12 months
	Mammography	Annually, to start 8-10 years after RT or age 50 whichever first
Lifetime risk of 20 – 25% in women age ≥35 as defined by models such as BRCAPro or Gail. That depends on personal and family history	MRI	As adjunct to mammogram and CBE every 6-12 months
	Clinical breast examination (CBE)	Every 6-12 months
	Mammography	Annually
BRCA1 or BRCA2 mutation or untested first degree relative (i.e. mother, sister) for age <25 years	MRI (Consider referring to oncology centers for risk reduction)	As adjunct to mammography every 6 – 12 months
	Clinical breast examination (CBE)	Annually
Age ≥25 years	Clinical breast examination (CBE)	Every 6-12 months
	Mammography	Annually, should be 5-10 years prior to youngest breast cancer case for

		strong family history
	MRI (Consider referring to oncology centers for risk reduction)	Every 6-12 months as adjunct to mammography
Atypical hyperplasia	Clinical breast examination (CBE)	Every 6-12 months
	Mammography/MRI	Annually
Prior history of breast cancer	Clinical breast examination (CBE)	Every 6-12 months
	Mammography	Annually
	MRI	Annually

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