REVIEW ON SCREENING AND PREVENTION OF BREAST CANCER

Essay

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Caroline Magued Elmaraghi

استعراض على الفحص والوقاية من سرطان الثدي

رسالة
توطئة للحصول علي درجة الماجستير
في علاج الأورام والطب النووى

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Breast cancer is the most common cancer and a leading cause of death in women worldwide. Its incidence is increasing in developing country due to changes in reproductive factors, lifestyle, and increased life expectancy.

There are number of established and potential risk factors associated with breast cancer, like age/gender, race/ethnicity, family history, hormonal/reproductive factors, proliferative breast disease, ionizing radiation, personal history of malignancy, life style factors, and mammographic density.

BRCA1 BRCA2 genes have important role in DNA repair, there mutation lead to increase the lifetime risk of breast cancer to between 40% and 85% and of ovarian cancer to between 20% and 50%.

There are several models for assessing a women's risk of having breast cancer, the most widely used is the Gail model. Identifying women at high risk is very important so as to present for them the appropriate method of screening and counsel them about the risk reduction method suitable for them.

Breast cancer screening has proved to be effective in reducing breast cancer mortality. The mammography is the gold standard method for screening. Breast self examination is no longer recommended but, breast awareness is encouraged instead, so as the women be familiar with their breasts and notice any changes early.

Major organizations vary in their recommendations for Clinical Breast Examination. Variation is by age at initiation,

breast cancer risk status, frequency of CBE performance, and the strength of language used to recommend CBE. The UPSET and WHO didn't recommend for it, on the other hand it's recommended annually by the ASCO and the NCCN.

Increased mammographic density in premenopausal women can obscure the radiological features of early breast cancer. Further, it has been suggested that cancers associated with BRCA mutations, in particular BRCA1, are more likely to have a benign appearance on mammography. Therefore magnetic resonance imaging is used in conjunction with mammography in proven BRCA mutation carrier or first degree relative to a proven BRCA carrier or those with 20% lifetime risk for breast cancer on the basis of family history and with Women with histories of chest irradiation.

Ultraonography in conjunction to mammography is used in all women with dense breast, and in high risk women when MRI is contraindicated.

Breast cancer can potentially be prevented in women considered at high risk for breast cancer. Life style modification like maintaining healthy body weight, being physically active and avoiding alcohol are simple way to reduce breast cancer and are recommended for all women at all risk levels .

Bilateral prophylactic mastectomy reduces the risk of breast cancer up to 95%. It has special indications.

Bilateral salpingo oophercetomy had decreased BC risk and Ovarian cancer risk but it showed an increase in all-cause

mortality, fatal and nonfatal coronary heart disease, and lung cancer, so BSO is an option for BRCA mutation carrier only in whom the potential benefit of the procedure are increased because of reduction in BC by 50% also of ovarian cancer.

Tamoxifen and Raloxifen are the recommended SERM used as chemoprevention, several trials were done, and they proved effectiveness in breast cancer risk reduction.

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LIST OF ABBREVIATIONS

ACS	American Cancer Society
ADH	Atypical Ductal Hyperplasia
ASM	Areola Sparing Mastectomy
ATM	Ataxia Telangectasia Mutated
ATR	ATM Related Kinase
BARD1	BRCA1-Associated Ring Domain 1
BC	Breast Cancer
BCPT	Breast Cancer Prevention Trial
BIRAD	Breast Imaging Report and Data system
BOADICEA	Breast and Ovary Analysis of Disease Incidence and Carrier Estimation Algorithm
BPM	Bilateral Prophylactic Mastectomy
BRCT	Breast Cancer Carboxyl Terminus
BSE	Breast Self Examination
BSO	Bilateral Salpingo Oopherectomy
CBE	Clinical Breast Examination
CORE trial	Continuing Outcome Relevant to Evista trial
DCIS	Ductal Carcinoma In situ
FDA	Food and Drug Administration
HRT	Hormone Replacement Therapy
IBIS	International Breast Cancer Intervention Study
IBR	Immediate Breast Reconstruction
LCIS	Lobular Carcinoma In Situ
MORE trial	Multiple Outcomes of Raloxifene Evaluation trial
MRN	Mre11-Rad50-NBS1
NBSI	Nijmengen Breakage Syndrome 1
NCCN	National Comprehensive Cancer Network
NCI	National Cancer Institute
NSABP	National Surgical Adjuvant Breast and Bowel Project

NSM	Nipple Sparing Mastectomy
OCP	Oral Contraceptive Pills
PTEN	Posphate Tensin homologue on chromosome Ten
RAP80	Receptor associated Protein 80 DKAa
RCT	Randomized Clinical Trials
RUTH trial	Raloxifen use for the heart trial
SEER	Surveillance, Epidemiology and End Results
SERM	Selective Estrogen Receptor Modulator
SSM	Skin Sparing Mastectomy
STAR trial	Study of Tamoxifen and Raloxifene
WHI	Women's Health Initiative Trial

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EPIDEMIOLOGY

Incidence and mortality rates world wide

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in females worldwide, accounting for 23% (1.38 million) of the total new cancer cases and 14% (458,400) of the total cancer deaths in 2008. About half the breast cancer cases and 60% of the deaths are estimated to occur in economically developing countries. In general, incidence rates are high in Western and Northern Europe, Australia/New Zealand, and North America; and low in sub-Saharan Africa and Asia (Fig. 1). The factors that contribute to the international variation in incidence rates largely stem from differences in reproductive and hormonal factors and the availability of early detection services ***(Jemal A et al, 2010).***

The number of deaths as a percentage of incident cases in 2008 was 48% in low-income, 40% in low middle- income, and 38% in high-middle-income countries, while it was 24% in high-income countries according to the most recent Globocan/IARC data (Fig 1) ***(Ferlay J et al, 2010).***

In the United States, the average lifetime risk of breast cancer has been estimated at 12.3% (i.e., 1 in 8 women). In 2009, an estimated 194,280 cases of invasive breast cancer (192,370 women and 1,919 men) and 62,280 cases of female carcinoma in situ of the breast will be diagnosed in the United States with 40,610 death from invasive breast cancer predicted ***(Jemal A et al, 2009).***

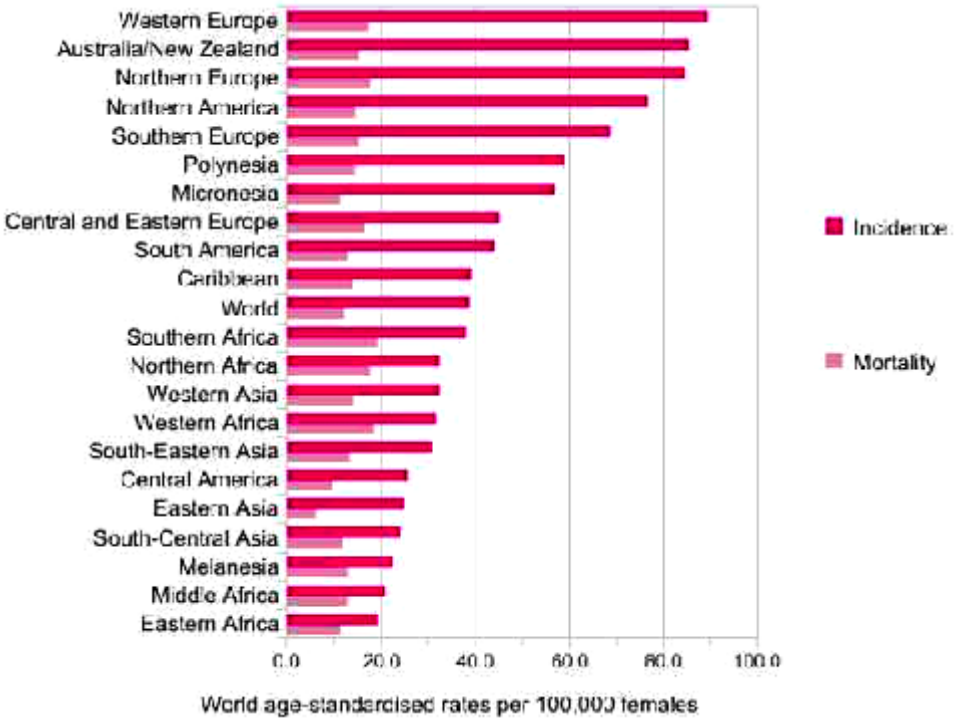

Figure 1. Age-standardized breast cancer incidence and mortality rates by world area. Source: GLOBOCAN 2008 ***(Ferlay J et al, 2010).***

Change of incidence and mortality

An analysis of data from the United States National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER) registries showed that the age-adjusted incidence rate of breast cancer in women in the United States fell sharply by 6.7% in 2003 as compared with the rate in 2002. The decrease in breast cancer incidence seems to be temporally related to the ensuing drop in the use of hormone-replacement therapy (HRT) among postmenopausal women in the United States. The decrease was evident only in women who were 50 years of age or older and was

more evident in cancers that were estrogen-receptor positive than in those that were estrogen-receptor-negative ***(Ravdin PM et al, 2007).***

Breast cancer mortality has been decreasing since 1990 by 2.3% per year overall. This decrease is largely attributed to the combination of mammography screening with improved treatment ***(Berry DA et al, 2005).*** However, this trend is primarily seen in white women, women with hormone receptor- positive tumors, and women younger than the age of 50 ***(Jatoi I et al, 2007).***

Despite declining mortality rates and the recent reduction in incidence, breast cancer still represents a significant burden to the health care system. Interventions that could further reduce the number of cases not only would be the appropriate measure but could potentially be cost-efficient ***(Tirona MT et al, 2010).***

Developing countries

In many developing countries, the incidence of breast cancer is now rising sharply due to changes in reproductive factors, lifestyle, and increased life expectancy. Today, more than half of incident cases occur in the developing world ***(Beaulieu N et al, 2009).***

The most widely cited reason for the global increase in breast cancer is the "westernization" of the developing world. Social factors like smoking, alcohol, and obesity are becoming more common in the developing countries and are increasingly accepted, also the wider adoption of the western diet and lower exercise levels. Hormonal risk factors like delayed parity, and

reduced breast feeding are now being observed in low and middle-income countries ***(Porter P, 2008).***

Available evidence on stage at diagnosis, though scarce, indicates that a very high proportion of cases in the developing world are detected in late stages ***(Porter P, 2008).*** In many underserved populations, a majority of women present with advanced disease. In contrast, in the United States the majority of cases are detected in localized stages of the disease (Stages I and II), a third is regionally advanced (Stage III), and only 5% are distant-stage metastatic (Stage IV) ***(Horner M et al, 2009)***.

Many reasons are given for the advanced stage at presentation and resultant poor survival rates in low- and middle-income countries: the stigma of breast cancer and the associated societal implications of its treatments (especially mastectomy) discourage women from seeking care early on; lack of knowledge about breast health; scant options for early detection due to limited access to routine care and examinations; and lack of access to mammography and to affordable, high-quality treatment options ***(Shulman NL et al, 2010).***

In Egypt, breast cancer is the most common cancer among women, representing 18.9% of total cancer cases (35.1% in women and 2.2% in men) among the Egypt National Cancer Institute (NCI) series of 10 556 patients during the year 2001 ***(Elatar I, 2001)***.

Data reported by Gharbiah population based cancer registry (2001) indicated that breast cancer ranked first among females