ejpmr, 2020,7(8), 752-759

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

BREAST CANCER

Mansi S. Pandit*, Akshay B. More, Shreegita R. Jadhav and Archana R. Gavit

Kasturi Shikshan Sanstha College of Pharmacy Shikrapur, Pune 412208.

***Corresponding Author: Mansi S. Pandit**

Kasturi Shikshan Sanstha College of Pharmacy Shikrapur, Pune 412208.

Article Received on 12/06/2020 **Article Revised on 22/07/2020** **Article Accepted on 02/08/2020**

ABSTRACT

The following article is based on the investigation of different dimension. Based on breast cancer and factors (risk and genetic) associated with it. Staging, detection, treatment and diagnosis of breast cancer. Breast cancer is the most frequent malignancy in women worldwide all over 25% death is due to cancer. 14% arise from breast cancer. Breast cancer is an heterogenous disease an molecular level. Which is curable in 70-80% of patient cancer associate with early stage and non-metastatic. This molecule level cancer include activation of human epidermal growth factor receptor 2, activation of harmone BRCA receptor. Treatment is based on according molecular subtype with different in strategies. This is huge impact on women physical and mental health. Breast cancer's etiology is unknown, treatment associated with identification of risk factors. Normal surgery, radiation therapy and chemotherapy allow a good prognosis where screening measure are in place.

KEYWORDS: Cancer, Breast Cancer, Risk factor, Staging, Screening.

INTRODUCTION

Cancer comes from overproduction and malfunction of the body's own cell. It is an uncontrolled growth of abnormal cells in any where any part of body. These abnormal cells are termed cancer cells, malignant our tumor cell. In normal cell if there is insufficient blood supply then the cell function get slower than normal. These cell get damaged/unrepair cell do not die so it become cancer cell.

There are various type of cancer

1. Bladder
2. Breast (male- female)
3. Colorectal cancer
4. Kidney (renal cell/ renal pelvis)
5. Leukemia (all types)
6. Lung (including bronchus)
7. Melanoma
8. Non-Hodgkin Lymphoma
9. Pancreatic
10. Prostate
11. Thyroid

According to estimates more than 7 million people globally die due to cancer. The cancer cases rises from 10 to 15 million by 2020. Meanwhile breast cancer is most prevalent type of malignant neoplasm among women.[1]

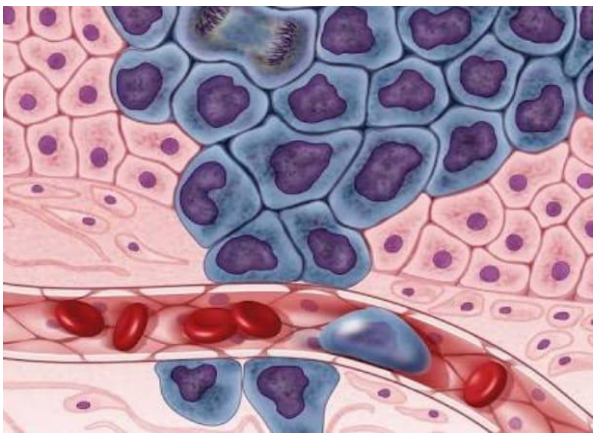

Fig no. 1: Growing cancer cell(purple) is surround by healthy cell (pink).

What is breast cancer?

Breast cancer is the most common type of cancer and second leading cause of death due to cancer. Breast cancer is type of tissue cancer that mainly involves inner layer of milk gland /lobules, and duct. Breast cancer is multi-stage disease in which viruses play a role in one stage of this pathogenic process. Breast cancer cells usually form tumor that can often see through x-ray/ felt has a lump.

It's important to understand that most breast lumps are benign and not cancer(malignant). Non cancerous breast tumors are abnormal growth, but they do not spread outside of the breast. They are not life threatening but some type of benign breast lump increase woman's risk.

Where breast cancer starts?

Breast cancer can start from different parts of breast.

Most breast cancer begin in the duct that carry milk to nipple (ductal cancer).

Some start in the gland which produce milk (lobular cancer).

Also there is some cancer that s less common like phyllodes tumor and angiosarcoma.

Also some cancers start from other tissue of breast.

Although many types of breast cancer can cause lump in breast, but not all. Many breast cancer are also found on screening mammogram which detect cancer at early stages.[1,2]

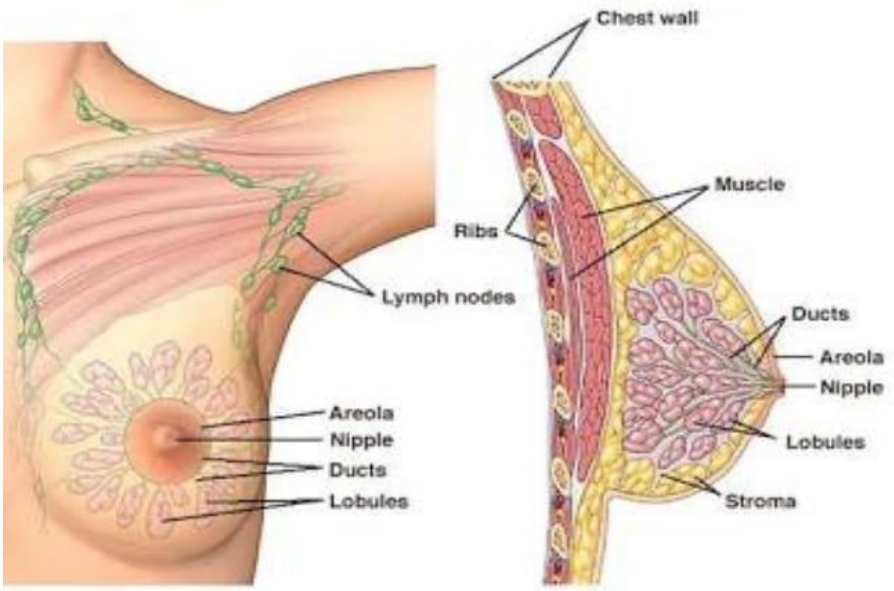

Fig No 2: Structure of normal breast tissue.

Types of breast cancer

There are many different types of breast cancer and most common involve ductal carcinoma in situ (DCIS) and invasive carcinoma. Others phyllodes tumor and angiosarcoma is less common.

Starting biopsy are done then breast cancer cells are tested for protein called estrogen, progesterone receptors and HER2.

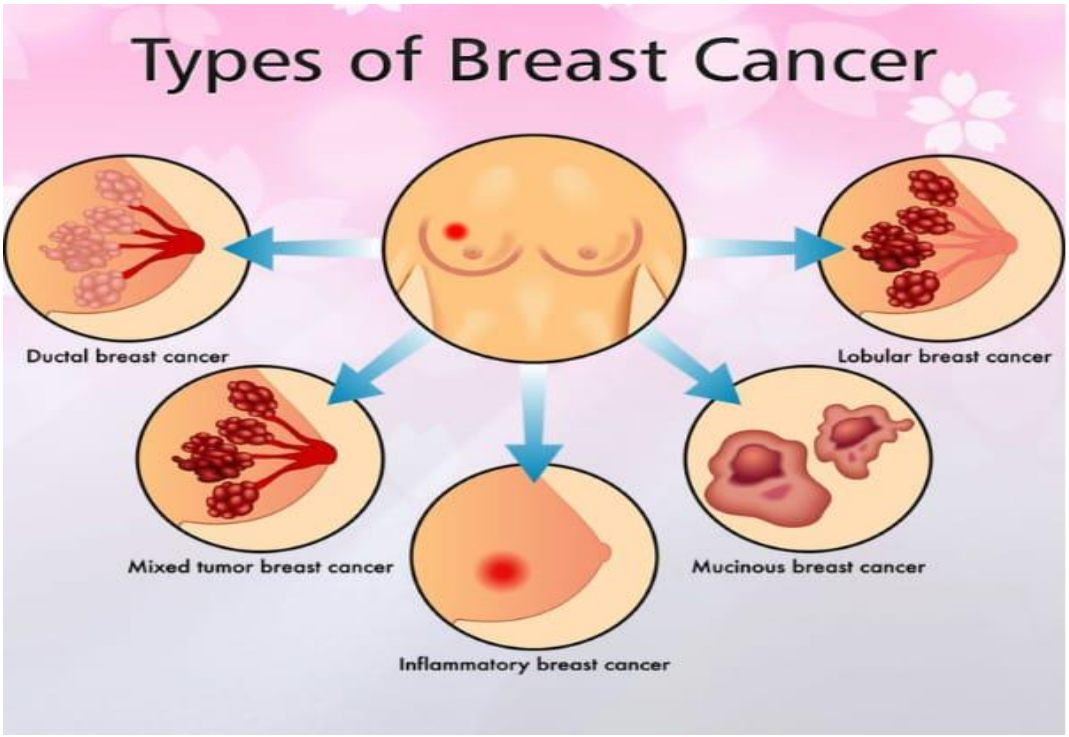

Fig No. 3: Types of breast cancer.

Types of breast cancer include ductal carcinoma in situ, invasive ductal carcinoma, inflammatory breast cancer, and metastatic breast cancer, Mucinous breast cancer, complex, tumor breast cancer.

Metastatic Breast Cancer

Metastatic breast cancer are also classified as Stage 4 breast cancer. The cancer is spread to other parts of the body. This usually includes the lungs, liver, bones or brain.

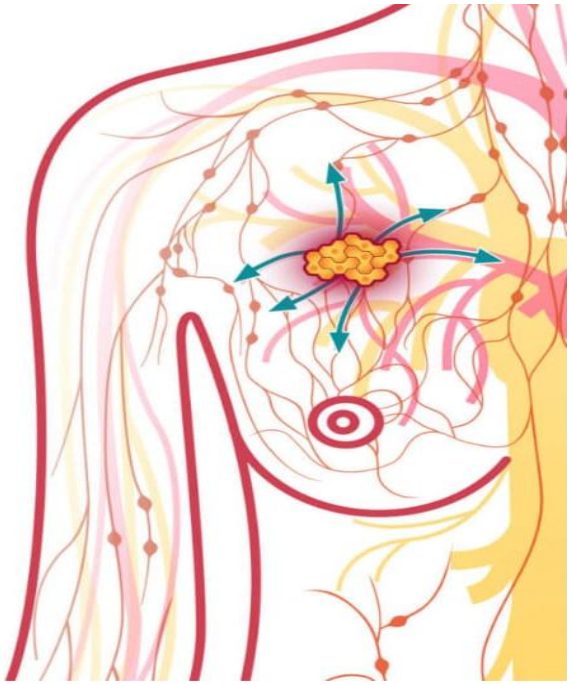

Fig no4: Metastatic breast cancer.

Spreading steps

- Cancer cells invade not far away healthy cells. When the healthy cell has taken over, it too can replicate more abnormal cells.
- Cancer cells inflow into the circulatory or lymph system. Cancer cells travel through the walls of nearby lymph vessels or blood vessels.
- Migration through circulation, Cancer cells are carried by the lymph system and the bloodstream to diffrent parts of the body.
- Cancer cells lodge in capillaries. Cancer cells stop moving as they are lodged in capillaries at a distant location and divide and evacuation into the surrounding tissue.
- New little tumors increase. Cancer cells form small tumors at the new location known as micro metastases.

Symptoms of metastatic cancer

Symptoms vary depending how far cancer tissue spread and what type of tissue involves in new cancer cells.

Symptoms of metastasis may vary depending on where cancer spread.

➢ **Metastasis in the bone may cause**

- Severe, progressive pain
- Swelling
- Bones that are more easily fractured or broken

➢ **Metastasis to the brain may cause**

- Persistent, progressively worsening headache or pressure to the head
- Vision disturbances
- Seizures
- Vomiting or nausea
- Behavioral changes or personality changes

➢ **Metastasis to the liver may cause**

- Jaundice
- Itchy skin or rash
- Abnormally high enzymes in the liver
- Abdominal pain, appetite loss, nausea, and vomiting

➢ **Metastasis to the lungs may cause**

- Chronic cough or inability to get a full breath
- Abnormal chest X-ray
- Chest pain

Other nonspecific systemic symptoms of metastatic breast cancer can include fatigue, weight loss, and poor appetite, but it's important to remember these can also be caused by medication or depression.

Ductal Carcinoma In Situ

Ductal carcinoma in situ (DCIS) is a non-invasive cancer where abnormal cells have been found in the lining of the breast milk duct. The atypical cells have not spread outside of the ducts into the surrounding breast tissue. Ductal carcinoma in situ is very early cancer that is highly treatable, but if it's left untreated or undetected, it can spread into the surrounding breast tissue.

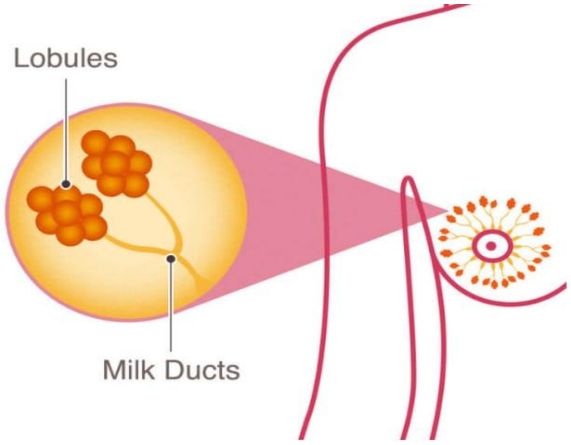

Fig no5: Ductal carcinoma In Situ.

Invasive Ductal Carcinoma (IDC)

The abnormal cancer cells that starded forming in the milk ducts have spread beyond the ducts into other parts of the breast tissue. Invasive cancer cells can also scattered to other parts of the body. this is also sometimes called infiltrative ductal carcinoma.

IDC is the common type of breast cancer, making up nearly 70- 80% of all breast cancer diagnoses. this can most commonly affects men

The Difference Between Invasive Ductal Carcinoma (IDC) And Ductal Carcinoma In Situ (DCIS)?

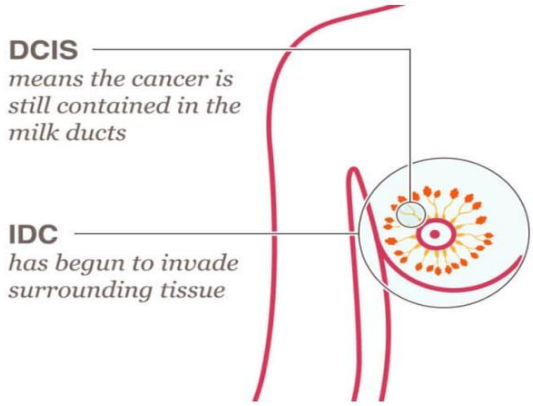

Fig no. 6: The Difference Between Invasive Ductal Carcinoma (IDC) And Ductal Carcinoma In Situ (DCIS).

DCIS means the cancer is still comprise in the milk duct and has not invaded any other area. IDC is cancer that began expanding in the duct and is invading the surrounding tissue. Cancer staging done by a physician, along with a physical exam and medical history can help to perceive the best treatment options.[3]

RISK FACTORS AND RISK PREDICTION

Age, reproductive factors, personal or family history of breast disease, genetic pre-disposition and environmental factors are associate with an increased risk for the development of female breast cancer.

- **Age**

The risk of developing breast cancer increases with age. By using the Surveillance, Epidemiology, and End Results (SEER) database, the possibility of a woman in the United states developing breast cancer is a lifetime risk of 1 in 8; 1 in 202 from birth to age 39 years of age, 1 in 26 from 40-59 years, and 1 in 28 from 60-69 years.

- **Personal history**

A personal history of breast cancer is also a luminous risk factor for the development of a second ipsilateral or contralateral breast cancer. In fact, the more common cancer amongst breast cancer survivors is a metachronous contralateral breast cancer. Factors associated with an increased risk of a second breast cancer include an primary diagnosis of DCIS, stage IIB, hormone receptor negative cancers, and young age.

- **Breast pathology**

Proliferative breast disease is attach with an increased risk of breast cancer. Proliferative breast lesions without atypia, involving usual ductal hyperplasia, intraductal papillomas, sclerosing adenosis and fibroadenomas confer only a small increased risk of breast cancer development, approximately 1.5-2 times that of the general population. Atypical hyperplasia including both ductal and lobular, usually incidentally found on screening mammography, confers a substantial increased risk of breast cancer. Women with atypia have an approximately 4.3 times greater risk of developing cancer compared to the general population.

- **History**

A woman's risk of breast cancer is increased if she has a family history of this disease. In the Nurses' Health Study follow-up, women with a mother diagnosed before age 50 are an adjust relative risk of 1.69 and women with a mother diagnosed at 50 or older had a relative risk of 1.37 compared to women without a family history of breast cancer. A history of a sister with breast cancer also demonstrated an increased relative risk of 1.66 if the diagnosis was made previously to age 50 and a relative risk of 1.52 if diagnosed after age 50 compared to patients without a family history. The highest risk is attached with increasing number of first degree relatives diagnosed with breast cancer at a young age (under age 50). Compared with women who had no blatant relative, women who had one, two or three or more affected first degree relatives had risk ratios of 1.80, 2.93 and 3.90, respectively.

- **Genetic predisposition**

Approximately 20%-25% of breast cancer patients are a positive family history but only 5%-10% of breast cancer cases demonstrate an autosomal dominant inheritance. Genetic predisposition alleles are describe in terms of clinical significance. High-risk predisposition alleles conferring a 40%-85% lifetime risk of developing breast cancer involve BRCA1 and BRCA2 mutations, mutations in TP53 gene resulting in Li-Fraumeni syndrome, PTEN resulting in Cowden syndrome, STK11 causing Peutz-Jegher's syndrome, Neurofibromatosis (NF1) and (CDH-1) E-Cadherin. Half of the breast cancer predisposition syndromes are associated with mutations in BRCA1 and BRCA2. Women with BRCA1 or BRCA2 damage mutations have a significantly higher risk of developing breast cancer. Lifetime breast cancer risk ranges from 65% to 81% for BRCA1 mutation carriers and 45% to 85% for BRCA2 carriers. Moderate risk genes including homozygous ataxia-telangiectasia (ATM) mutations, somatic mutations in tumor suppressor gene CHEK2, and BRCA1 and BRCA2 modifier genes BRIP1 and PALB2 confer a 20%-40% lifetime risk of breast cancer. Numerous lowrisk common alleles are identify mostly through genome-wide association studies and the clinical application in the presence of these mutations is yet to be determined.[4,5]

CANCER DETECTION PROGRAM

Cancer screening

Screening (often used synonymously with "early detection") programmes aim to find individuals during asymptomatic stages for possible detection of cancer

during preclinical phases of the disease. Screening programmes enable betime diagnosis, more effective treatment and increased possibility of a complete outcome. In developing and implementing screening programmes, three factors should be considered.

a) Characteristics of the cancer

The cancer that is screened should have significant and serious health and economic consequences for the normal population. Mortality are the most important consequence to be considered. In addition, it is important to understand the natural history and cellular growth characteristics of the cancer being screened and whether it responds favourably to screening. Therefore, there must exist a detectable preclinical phase of some duration (lead time) when the cancer are discover through testing well before actual symptoms develop. It was noted that individual cancers have differing natural histories. Cancers with long natural histories and long lead times are most likely to be detected in a screening programme.

b) Screening tests

The screening tests used can be acceptable and cushy for the patient. They can be also be accurate, user-friendly for health workers and cost-useful.

c) Screening evaluation

Evaluation of the programme can focus on measurable goals: early diagnosis of the disease, patient benefit from treatment facilities and services, and mimic mortality to an acceptable rate. This evidence-based valuation process should be utilized as an indicator of the programme's efficacy and outcomes. The success of screening programmes depends on a number of fundamental principles:

- The target disease can be a common form of cancer, of public health importance, and associated with high morbidity and mortality;
- There should be virile evidence that the screening tests adopted can result in reduced mortality and morbidity in the target population;
- Test procedures can be acceptable, safe and relatively inexpensive;
- There should be ethical, acceptable and effective procedures for detecting the disease at an early stage to provide an opportunity for intervention;
- The benefits of screening should outweigh any adverse cost;
- The implementation of screening, diagnostic and intervention activities should strengthen the health system and social development;
- a specific and sensitive test for the early detection of the disease should be available;
- There should be suitable facilities for the diagnosis and treatment of detectable abnormalities.

Screening for breast cancer

Breast cancer are most easily and effectively treated in its early stages. Survival rates drop dramatically when women present with advanced cases regardless of the setting; that is why, a primary strategy for reducing breast cancer mortality is enhansing the proportion of cases that are detected during the early stages of the disease. Unfortunately, women in resource-poor countries are present at a later stage of disease than women elsewhere, in part due to the absence of mass screening programmes in many such countries. Regular screening of all women aged 50 and over has the potential to sharply increase the proportion of cancer cases are diagnose in their earliest stages.

The goals of screening guidelines are

- To provide guidance regarding the exactly use of screening tools for breast cancer detection;
- To help physicians and patients make informed decisions regarding screening for breast cancer in asymptomatic women of all ages.

SCREENING MAMMOGRAPHY

Overview

This is another screening tool utilized for detecting early breast cancer. Screening mammography is defined as a standard two-view mammogram found in an asymptomatic woman with the motive of early detection of breast cancer. The objective of population-based mammography screening is to mimic mortality and morbidity from breast cancer through the early detection and treatment of malignancies. There are ample evidence from a variety of well-documented sources that annual or biannual mammography is effective in reducing breast cancer mortality in women aged 50–69 years. Women who are no family history of breast cancer or prior diagnosis of cancer and who have under the age of 50 are considered to be low risk, although they may benefit from regular mammograms at the discretion of their physician. Women with a family history of premenopausal breast cancer in a first-line relative, those with a history of breast or gynaecological cancer, and those who are over 50 years of age are considered to be at high risk and in progress countries are advised to have screening mammography every 1–3 years. Despite all the cited benefits, it should be noted that mammography alone, with a false negative rate of 12%, is not an effective screening tool. This false-negative rate is higher among younger patients. A working group of the International Agency for Research on Cancer has evaluated the efficacy of breast screening.

They concluded

- These is sufficient evidence for the efficacy of screening women aged 50–69 years by mammography as the sole screening modality in reducing mortality from breast cancer. There is evidence of a 25% reduction in women aged 50–69 years.
- There is limited evidence for the efficacy of screening women aged 40–49 years by mammography as the only screening modality in reducing mortality from breast cancer. When all

valid trials were included there was evidence of a 11% reduction in women 40–49 years of age.

- No direct conclusion are possible for the efficacy of mammography in women younger than 40 or older than 69. Mammograms Mammography is an X-ray technique that are develop specifically for breast lesion examination. Diagnosis, evaluation and determination of the results is based on the different absorption of X-rays between different types of breast tissue, such as fat, fibro glandular tissue, cysts, tumours and calcifications. During the procedures, the imaging system must be optimized to provide the small radiation dose as required. The level of radiation can be standardized based on national and international guidelines. The mean absorbed dose in the breast gland per mammographic film is in the order of 1.0–1.5 mGy for the average breast examined with modern equipment.

- Following points remember regarding mammographic density are that:
- Breast parenchymal density as seen on a mammogram are the determinant of the sensitivity of mammography;
- Breast parenchymal density are decreases with age;
- Hormone replacement therapy of the combination type may result in growth breast density;
- Tamoxifen may be reduce breast density. In reading mammographic images, most authors recommend a double reading, which enhance the sensitivity of the reading by 10%–15% compared to single readings. In recent years, digital mammography are also use as an alternative to traditional mammography. In digital mammography, the image receptor used in conventional mammography is replaced by a digital receptor. The imaging techniques are remaining the same in all other respects. From the point of view of the woman being screened, a digital mammogram are similar to a conventional mammogram, as breast compression and positioning are unchanged. Digital mammography was the potential to provided images with lower doses of radiation than screen-film mammography. Also, computer-aided detection can be incorporated into the workstation and the results of the computer analysis added into the image, thereby assisting the radiologist in detecting suspect lesions. Computer-aided detection has been evaluate in several studies, which suggest an incremental value in terms of sensitivity, though the evidence on specificity is conflicting. Some data suggest that computer-aided detection could replace a second reader. Many women recommended for this type of screening are voice concerns regarding the risk of radiation from mammograms. Studies are shown that the average dose per examination (single view per breast) is approximately 2 mGy, the dose being dependent on breast thickness and exposure factors. The risk from radiation are cumulative, greatest for adolescent exposure and decreasing with an increase in age. Mammograms should be performed by radiographers who have completed a postgraduate course in mammography and be present courses on mammographic techniques and procedures. In addition, radiologists with appropriate training, especially in breast diseases, should be part of the multidisciplinary team.[6,7]

DIAGNOSIS

History and physical examination

The clinical history is directed at assessing cancer risk and promoting the presence or absence of symptoms indicative of breast disease. It should include age at menarche, menopausal status, previous pregnancies and use of oral contraceptives or post-menopausal hormone changes. A personal history of breast cancer and age at diagnosis, as well as a history of other cancers treated with radiation. In addition, a family history of breast cancer and/or ovarian cancer in a first- degree relative should be established. Any significant prior breast history should be elucidated including previous breast biopsies. After the estimated risk for breast cancer has been appoint (see above), the patient should be assessed for specific symptoms like breast pain, nipple discharge, malaise, bony pain and weight foil. Physical examination should involve a careful visual inspection with the patient sitting upright. Nipple changes, asymmetry and obvious masses will be noted. The skin must be inspected for changes such as; dimpling, erythema, peaud' orange (associated with local advanced or inflammatory breast cancer). After careful inspection and with the patient in the sitting position the cervical, supraclavicular and axillary lymph node basins are palpated for adenopathy. When naked the size, number and mobility should be ascertained. Palpation of the breast parenchyma itself is performed with the patient supine and the lateral arm keeped over the head. The sub areolar (central quadrant) and each quadrant of both breasts is palpated specifically. Masses are noted with respect to their size, shape, location, accuracy and mobility.[8,9]

Treatment options for breast cancer

Treatment are depend upon the size, location and number of tumours and the pathology (subtype, grade and presence of biomarkers) of the tumour, as well as your age and general health. The choice and intermix of treatments will be discussed with you and your preferences will be taken into account. One of the most important decisions you will have to make is where to be treated. Treatment within a multidisciplinary and reform team improves survival and quality of life, as opposed to being treated by a single doctor. All of your treatment resolution should be taken after discussion in a multidisciplinary meeting, where doctors from different specialties, nurses and other health professionals intricate in your care will discuss your case and decide which treatment is the best option for you.

- **Surgery**

The two types of surgery for breast cancer are breast conserving surgery, in which the surgical team eliminate the tumor but tries to keep as much of the breast as possible, or mastectomy, in which the whole breast is eliminate. If the lymph nodes in your armpit look like they are clear of cancer in imaging tests, then a technique called sentinel lymph node biopsy should be carry out. This identifies the most important (sentinel) lymph node and examines it; if no cancer is detected, then no other lymph nodes will be removed, but if cancer is found in that lymph node, more nodes may have to be removed (called axillary dissection). Patients undergoing mastectomy should usually be offered immediate or delayed breast reconstruction, except in the case of inflammatory breast cancer.

- **Radiotherapy**

Radiotherapy is a type of treatment that consume ionising radiation, which damages the DNA of cancerous cells, causing the cells to die. Radiotherapy is usually given after breast-conserving surgery and that also also be given after mastectomy. Radiotherapy may also be given to patients with locally-advanced disease which remains inoperable after systemic treatment and may be considered in certain patients with metastatic disease to attend the symptoms of the primary tumour or distant metastases and reform quality of life. Radiotherapy after breast-conserving surgery is usually given as whole breast radiotherapy (WBRT). In patients considered to be at high risk of recurrence who have already undergone WBRT, a radiotherapy 'boost' may be given – this is an extra, lower dose of radiation directed specifically to the area that the tumour are remove from. This are done similarly to WBRT with external radiotherapy or with brachytherapy, in which a radiation source is placed into the breast tissue for a short time to provide internal radiotherapy focused only on a little margin of tissue surrounding the site of surgery. Patients who are considered to be at a low risk of recurrence may hence receive a short course of radiotherapy using a technique called accelerated partial breast irradiation (APBI) (Cardoso et al. 2018 [in press]). This treatment is shorter than WBRT and mimic the exposure of healthy breast tissue and other organs in the chest (e.g. heart, lungs) to radiation, reducing the risk of long-term side effects. Some patients also require radiotherapy after mastectomy, because of the presence of factors that enhance the risk of the cancer coming back. This is done similarly to radiotherapy after breast-conserving surgery.

- **Systemic therapy**

There are several types of systemic therapy that you may be treated with, depending on the type and stage of cancer you have.

- **Chemotherapy**

Chemotherapy despatch cancer cells and is used to treat most triple negative, HER2 positive and luminal B-like breast cancers. Chemotherapy are usually given every 1–3 weeks as intravenous infusions. Some patients are also be offered additional oral chemotherapy following completion of standard intravenous chemotherapy.

- **Endocrine therapies**

Endocrine therapies aim to minimize the effects of oestrogen in ER positive breast cancers. This is the important type of systemic treatment for ER positive tumours, also known as hormone-dependent tumours. Number of types of endocrine therapy available, which are taken orally or administered as an injection:

- Selective oestrogen receptor modulators (SERMs) block ER on breast cells to stop oestrogen attaching to the receptors. Tamoxifen is a type of SERM.
- Selective oestrogen receptor downregulators (SERDs), such as fulvestrant, work in a similar way to SERMs, but also reduce the number of ERs.
- Ovarian function suppression by gonadotropin-releasing hormone analogues or by surgery may be offered to pre- and perimenopausal women to reduce the supply of oestrogen from the ovaries to the tumour.
- Aromatase inhibitors minimize the production of oestrogen in tissues and organs other than the ovaries, and is therefore effective only in postmenopausal women, unless the function of the ovaries is suppressed (oestrogen levels are artificially lowered) in premenopausal women. Anastrozole, letrozole and exemestane are all aromatase inhibitors.[10]

CONCLUSION

Breast cancer since from past and continue be an most prevalent and growing malignant disease.Its huge impact seen in women's physical and mental health.It can occur in both male and female, but very rare in male.

REFERENCES

1. www.cancer.org
2. www.nature.com
3. www.ncbi.nlm.nih.gov
4. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin., 2013; 63: 11-30. [PMID: 23335087 DOI: 10.3322/caac.21166]
5. Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker DG, Edwards BK, Tucker MA, Fraumeni JF Jr., editors. New
6. Ford D, Easton DF, Stratton M, Narod S, Goldgar D, Devilee P, Bishop DT, Weber B, Lenoir G, Chang-Claude J, Sobol H, Teare MD, Struewing J, Arason A, Scherneck S, Peto J, Rebbeck TR, Tonin P, Neuhausen S, Barkardottir R, Eyfjord J, Lynch H, Ponder BA, Gayther SA, Zelada-Hedman M. Genetic heterogeneity and penetrance analysis of the BRCA1 and BRCA2 genes in breast cancer families. The Breast Cancer Linkage Consortium. Am J Hum Genet, 1998; 62: 676-689. [PMID: 9497246 DOI: 10.1086/301749]
7. Antoniou A, Pharoah PD, Narod S, Risch HA, Eyfjord JE, Hopper JL, Loman N, Olsson H,

Johannsson O, Borg A, Pasini B, Radice P, Manoukian S, Eccles DM, Tang N, Olah E, Anton-Culver H, Warner E, Lubinski J, Gronwald J, Gorski B, Tulinius H, Thorlacius S, Eerola H, Nevanlinna H, Syrjäkoski K, Kallioniemi OP, Thompson D, Evans C, Peto J, Lalloo F, Evans DG, Easton DF. Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case Series unselected for family history: a combined analysis of 22 studies. Am J Hum Genet, 2003; 72: 1117-1130. [PMID: 12677558 DOI: 10.1086/375033]

8. Cardoso, F., et al. (2018 [in press]). "Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up." Annals of oncology: official journal of the European Society for Medical Oncology.
9. Breast imaging reporting and data system, 2nd ed. Reston, Virginia, American College of Radiology, 1995.
10. Cardoso, F., et al. (2018). "4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4)." Annals of oncology: official journal of the European Society for Medical Oncology 29: doi.org/10.1093/ annonc/mdy192