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A REVIEW ON BREAST CANCER

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ABSTRACT

Although breast cancer is uncommon in women, it can cause significant morbidity and mortality. The current review was undertaken to determine whether strategies applied for the evaluation and treatment of breast cancer in females are appropriatein breast cancer. Female breast cancer has biological differences compared with male breast cancer, including a high prevalence in certain parts of Africa, a higher incidence of oestrogen receptor positivity and more aggressive clinical behaviour. It responds to hormonal manipulation and chemotherapy, but optimal treatment regimens in female are unknown. Female breast cancer remains an uncommon disease. Most of our current knowledge regarding its biology, natural history and treatment strategies has been extrapolated from its female counterpart. Much research is needed to further characterize the molecular biological properties of female breast tumours and their prognostic significance, and to devise treatment strategies, including optimal chemotherapy regimens.

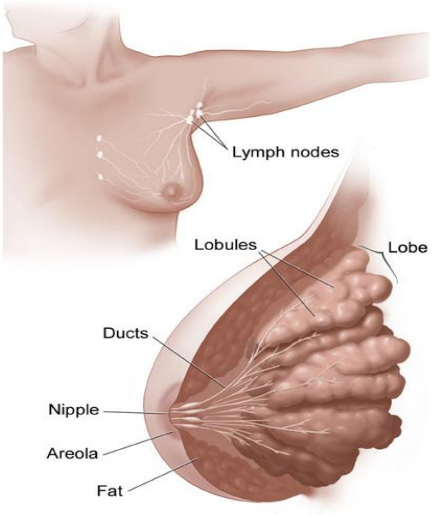
KEY WORDS

Breast cancer, appropriatein breast cancer.

INTRODUCTION

Breast cancer is a malignant tumor that starts in the cells of the breast. A malignant tumor is a group of cancer cells that can grow into (invade) surrounding tissues or spread (metastasize) to distant areas of the body. The disease occurs almost entirely in women, but men can get it, too.The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries. Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn't die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does. People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment.



Types of breast cancer

There are several types of breast cancer, but some of them are quite rare. In some cases a single breast tumor can be a combination types or be a mixture of invasive and in situ cancer.

1. ***Ductal carcinoma in situ***

Ductal carcinoma in situ (DCIS; also known as *intraductal carcinoma*) is considered noninvasive or pre-invasive breast cancer. DCIS means that cells that lined the ducts have changed to look like cancer cells. The difference between DCIS and invasive cancer is that the cells have not spread (*invaded*) through the walls of the ducts into the surrounding breast tissue. About 1 in 5 new breast cancer cases will be DCIS. Nearly all women diagnosed at this early stage of breast cancer can be cured.

2. ***Lobular carcinoma in situ***

This is not a true cancer or pre-cancer. A risk factor is anything that affects your chance of getting a disease, such as cancer. Different cancers have different risk factors. For example, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx (voice box), bladder, kidney, and several other organs

3. ***Invasive (or infiltrating) ductal carcinoma***

This is the most common type of breast cancer. Invasive (or infiltrating) ductal carcinoma (IDC) starts in a milk duct of the breast, breaks through

4. ***Invasive (or infiltrating) lobular carcinoma***

Invasive lobular carcinoma (ILC) starts in the milk-producing glands (lobules). Like IDC,it can spread (metastasize) to other parts of the body. About 1 invasive breast cancer in10 is an ILC. Invasive lobular carcinoma may be harder to detect by a mammogram thaninvasive ductal carcinoma. The wall of the duct, and grows into the fatty tissue of the breast.

Less common types of breast cancer

1. ***Inflammatory breast cancer***

This uncommon type of invasive breast cancer accounts for about 1% to 3% of all breast cancers. Usually there is no single lump or tumor. In its early stages, inflammatory breast cancer is often mistaken for an infection in the breast (called *mastitis*) and treated as an infection with antibiotics. If the symptoms are caused by cancer, they will not improve, and a biopsy will find cancer cells. This type of breast cancer tends to have a higher chance of spreading and a worse outlook (prognosis) than typical invasive ductal or lobular cancer.

2. ***Triple-negative breast cancer:*** This term is used to describe breast cancers (usually invasive ductal carcinomas) whose cells lack estrogen receptors and progesterone receptors, and do not have an excess of the HER2 protein on their surfaces. Breast cancers with these characteristics tend to occur more often in younger women and in African-American women. Triple-negative breast cancers tend to grow and spread more quickly than most other types of breast cancer. Because the tumor cells neither lack these certain receptors, neither hormone therapy nor drugs that target HER2 are effective treatments.

3. ***Paget disease of the nipple:*** This type of breast cancer starts in the breast ducts and spreads to the skin of the and then to the areola, the dark circle around the nipple. It is rare, accounting for only about 1% of all cases of breast cancer. The skin of the nipple and areola often appears crusted, scaly, and red, with areas of bleeding or oozing.The woman may notice burning or itching.

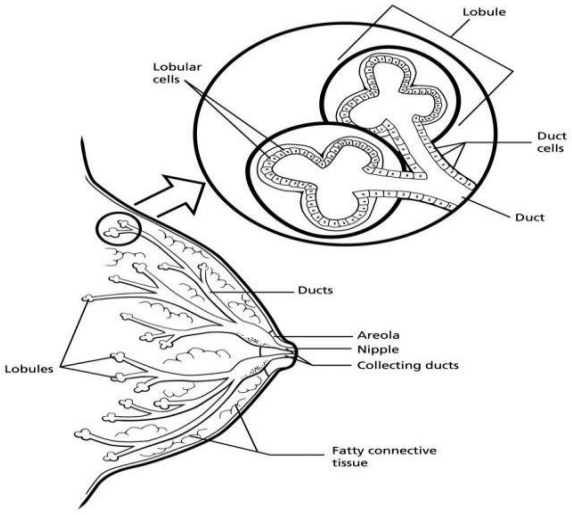
4. ***Phyllodes tumor:*** This very rare breast tumor develops in the stroma (connective tissue)of the breast, in contrast to carcinomas, which develop in the ducts or lobules. Other names for these tumors include *phylloides tumor* and *cystosarcoma phyllodes*. Thesetumors are usually benign but on rare occasions may be malignant. Benign phyllodes tumors are treated by removing the tumor along with a margin of normal breast tissue.

5. ***Angiosarcoma:*** This form of cancer starts in cells that line blood vessels or lymph vessels. It rarely occurs in the breasts. When it does, it usually develops as a complication of previous radiation treatments. This is an extremely rare complication of breast radiation therapy that can develop about 5 to 10 years after radiation. Angiosarcoma can also occur in the arms of women who develop lymphedema as a result of lymph node surgery or radiation therapy to treat breast cancer.

Special types of invasive breast carcinoma

There are some special types of breast cancer that are sub-types of invasive carcinoma. These are often named after features seen when they are viewed under the microscope, like the ways the cells are arranged. Some of these may have a better prognosis than standard infiltrating ductal carcinoma. These include:

- Adenoid cystic (or adenocystic) carcinoma
- Low-grade adenosquamous carcinoma (this is a type of metaplastic carcinoma)
- Medullary carcinoma
- Mucinous (or colloid) carcinoma
- Papillary carcinoma



Symptoms of Breast Cancer

Widespread use of screening mammograms has increased the number of breast cancers found before they cause any symptoms. Still, some breast cancers are not found by mammogram, either because the test was not done or because, even under ideal conditions, mammograms do not find every breast cancer.

The most common symptom of breast cancer is a new lump or mass. A painless, hard mass that has irregular edges is more likely to be cancerous, but breast cancers can be tender, soft, or rounded. They can even be painful. For this reason, it is important to

have any new breast mass or lump or breast change checked by a health care professional experienced in diagnosing breast diseases.

Other possible signs of breast cancer include:

- Swelling of all or part of a breast (even if no distinct lump is felt)
- Skin irritation or dimpling
- Breast or nipple pain
- Nipple retraction (turning inward)
- Redness, scaliness, or thickening of the nipple or breast skin
- Nipple discharge (other than breast milk)

CAUSES OF BREAST CANCER

Hormones seem to play a role in many cases of breast cancer, but just how this happens is not fully understood.

DNA is the chemical in each of our cells that makes up our genes—the instructions for how our cells function. We usually look like our parents because they are the source of our DNA. But DNA affects more than how we look.

Some genes control when our cells grow, divide into new cells, and die. Genes that speed up cell division are called *oncogene*s. Others that slow down cell division, or cause cells to die at the right time, are called *tumor suppressor genes*. Certain changes (mutations) in

DNA that "turn on" oncogenes or "turn off" tumor suppressor genes can cause normal breast cells to become cancerous.

- ***Inherited gene mutations***

Certain inherited DNA mutations can dramatically increase the risk for developing certain cancers and are responsible for many of the cancers that run in some families. For example, the *BRCA* genes (*BRCA1* and *BRCA2*) are tumor suppressor genes. A mutation in one of these genes can be inherited from a parent. When one of these genes are mutated, it no longer suppresses abnormal growth, and cancer is more likely to develop.

Mutations in tumor suppressor genes like the *BRCA* genes are considered "high penetrance" because they often lead to cancer. Although many of the women with high penetrance mutations develop cancer

- ***Acquired gene mutations***

Most DNA mutations related to breast cancer occur in single breast cells during a woman's life rather than having been inherited. These *acquired* mutations of oncogenes and/or tumor suppressor genes may result from other factors, like radiation or cancer causing chemicals. But so far, the causes of most acquired mutations that could lead to breast cancer are still unknown. Most breast cancers have several acquired gene mutations.

Tests to spot acquired gene changes may help doctors more accurately predict the outlook for some women with breast cancer. For example, tests can identify women whose breast cancer cells have too many copies of the *HER2* oncogene. These cancers tend to be more aggressive. At the same time, drugs have been developed that specifically target these cancers and improve outcomes for patients.

DIAGNOSIS OF BREAST CANCER

Breast cancer is sometimes found after symptoms appear, but many women with early breast cancer have no symptoms. This is why getting the recommended screening tests (as described in the section, "Can breast cancer be found early?") before any symptoms develop is so important.

During your regular physical examination, your doctor will take a thorough personal and family medical history. He or she also will perform and/or order one or more of the following:

• ***Breast examination.*** During the breast exam, the doctor will carefully feel the lump and the tissue around it. Breast cancer usually feels different (in size, texture and movement) than benign lumps.

• ***Mammography.*** An X-ray test of the breast can give important information about a breast lump.

• *Digital mammography.* This is a technique in which an X-ray image of the breast is digitally recorded into a computer rather than on a film. This may be better for women with dense breasts.

• ***Ultrasonography.*** This test uses sound waves to detect the character ofa breast lump — whether it is a fluid-filled cyst (not cancerous) or a solid mass (which may or may not be cancerous). This may be performed along with the mammogram.

Based on the results of these tests, your doctor may or may not request a biopsy to get a sample of the breast mass cells or tissue. Biopsies are performed using surgery (excisional biopsy) or a needle (core biopsy). Your surgeon will advise you on the most

appropriate type of biopsy for your individual case. After the sample is removed, it is sent to a lab for testing. A pathologist — a doctor who specializes in diagnosing abnormal tissue changes — views the sample under a microscope and looks for abnormal cell shapes or growth patterns. When cancer is present, the pathologist can tell what kind of cancer it is and whether it has spread. Laboratory tests, such as hormone receptor tests (estrogen and progesterone)and human epidermal growth factor receptor (HER2/neu) can show whether hormones or growth factors are helping the cancer grow.

TREATEMENT OF BREAST CANCER

Your doctor will work with you to develop a personalized plan to treat your breast cancer, to reduce the chance of cancer returning in the breast and to reduce the chance of the cancer traveling to a location outside of the breast. Treatment generally follows within a few weeks of the diagnosis.

The type of treatment recommended will depend on the size and location of the tumor in the breast, the results of lab tests done on the cancer cells, and the stage or extent of the disease. Your doctor usually will consider your age and general health, as well as your feelings about the treatment options.

Breast cancer treatments are local or systemic. Local treatments are used to remove, eliminate or control the cancer cells in a specific area. Surgery and radiation treatment are local treatments. In most cases, surgery is the first course of action, with additional treatment decisions made based on surgical findings, including extent of disease. Systemic treatments are used to destroy or control cancer cells all over the body. Chemotherapy and hormone therapy are systemic treatments. A patient may have just one form of treatment or a combination, depending on her needs.

The main types of treatment for breast cancer are:

- Surgery
- Radiation therapy
- Chemotherapy
- Hormone therapy
- Targeted therapy
- Bone-directed therapy

1. Surgery

It is followed by paclitaxel(Taxol) or docetaxel (Taxotere),Epirubicin, and cyclophosphamide.

Most women with breast cancer have some type of surgery. Surgery is often needed to remove a breast tumor. Options for this include breast-conserving surgery and mastectomy. The breast can be reconstructed at the same time as surgery or later on. Surgery is also used to check the lymph nodes under the arm for cancer spread. Options for this include a sentinel lymph node biopsy and an axillary (armpit) lymph node dissection.

2. Radiation therapy

Radiation therapy is treatmentwith high-energy rays or particles that destroy cancer cells. Radiation to the breast is often given after breast-conserving surgery to help lower the chance that the cancer will come back in the breast cancer or nearby lymph nodes. Radiation may also be recommended after mastectomy in patients either with a cancer larger than 5 cm, or when cancer is found in the lymph nodes. Radiation is also used to treat cancer that has spread to other areas, for example to the bones or brain.

3. Chemotherapy

The most common chemo drugs used for early breast cancer include the anthracyclines (such as doxorubicin/Adriamycin and epirubicin/Ellence) and the taxanes (such as paclitaxel/Taxol and docetaxel/taxotere). These may be used in combination with certain other drugs, like fluorouracil Someofthemostcommonlyuseddrug combinations for early breast cancer are:

- Cyclophosphamide, doxorubicin (Adriamycin), and fluorouracil (5-FU)
- *Docetaxel (Taxotere), doxorubicin (Adriamycin), and cyclophosphamide*
- Doxorubicin (Adriamycin) and cyclophosphamide by docetaxel (Taxotere) or paclitaxel (Taxol)
- Docetaxel (Taxotere) and cyclophosphamide
- Docetaxel, carboplatin, and trastuzumab (Herceptin) for HER2 / neu positive tumorer combinations that are less often used include

- cyclophosphamide (Cytoxan), methotrexate, and 5-fluorouracil (fluorouracil, 5-FU)
- Doxorubicin (Adriamycin), followed by CMF
- Epirubicin (Ellence) and cyclophosphamide
- Doxorubicin (Adriamycin) and cyclophosphamide

4. Hormone therapys

Tamoxifen:Tamoxifen blocks estrogen receptors in breast cancer cells. This stopsestrogen from binding to them and telling the cells to grow and divide. While tamoxifenacts like an anti-estrogen in breast cells, it acts like an estrogen in other tissues, like theuterus and the bones. Because it acts like estrogen in some tissues but like an antiestrogenin others, it is called a *selective estrogen receptor modulator* or SERM.

Toremifene (Fareston): Toremifene is a drug similar to tamoxifen. It is also a SERM and has similar side effects. It is only approved to treat metastatic breast cancer. This drug is not likely to work if tamoxifen has been used and stopped working

Fulvestrant (Faslodex): Fulvestrant is a drug that first blocks the estrogen receptor and then also eliminates it temporarily. It is not a SERM – it acts like an anti-estrogen throughout the body.

5. Targeted therapy

Trastuzumab (Herceptin): Trastuzumab is a type of drug known as a *monoclonal antibody*—a man-made version of a very specific immune system protein. It attaches to

HER2 and can help slow the growth of cancer cells with too much HER2. It may also stimulate the immune system to more effectively attack the cancer. Trastuzumab is given as an injection into a vein (IV), usually once a week or as a larger dose every 3 weeks.

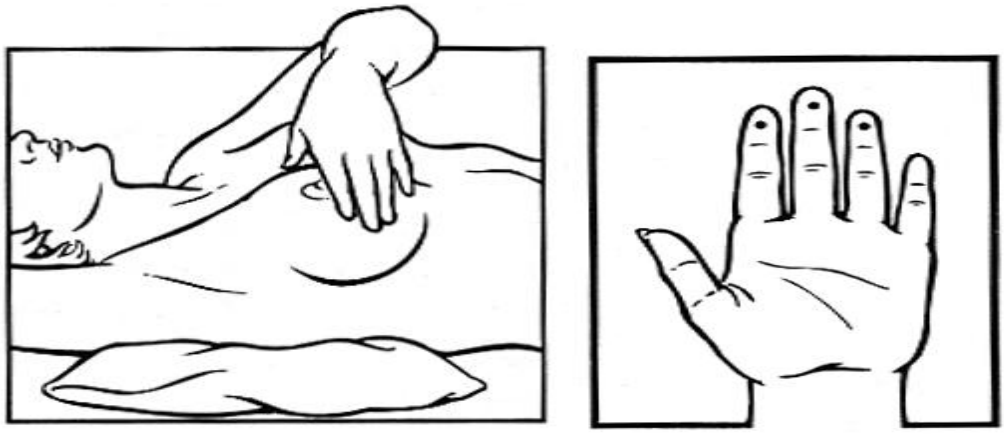
Ado-trastuzumab emtansine (TDM-1, Kadcyl):Ado-trastuzumab emtansine is atype of drug known as an antibody-drug conjugate. It is made up of the same monoclonalantibody found in trastuzumab attached to a chemo drug known as DM-1. In this type ofdrug, the antibody acts as a homing device, taking the chemo drug directly to the cancer cells.

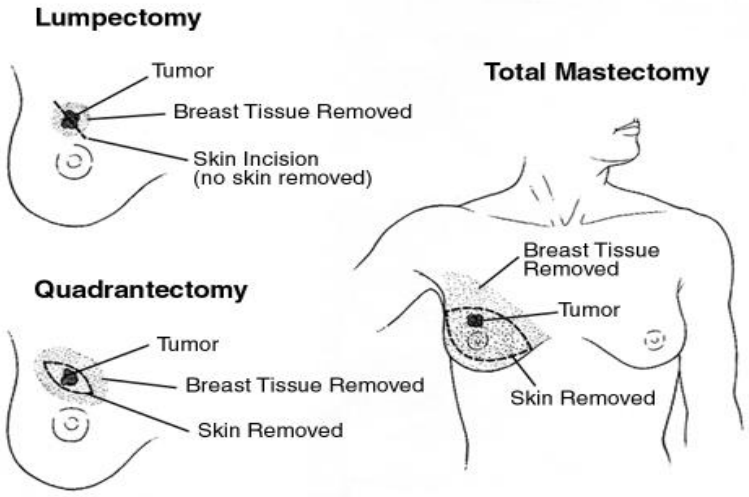
Pertuzumab (Perjeta): Like trastuzumab, pertuzumabs is a monoclonal antibody thatattaches to the HER2 protein. It seems to target a different part of the protein thantrastuzumab does. This drug can be used along with docetaxel (Taxotere) andtrastuzumab to treat advanced breast cancer. This 3 drug combination can also be used totreat earlier-stage breast cancers before surgery (as neoadjuvant therapy).

6. Bone-directed therapy

Denosumab:

A newer drug called *denosumab* (Xgeva, Prolia) is also now available to help reduce the risk of problems from breast cancer metastasis to the bone. It works differently from bisphosphonates. In studies of patients with breast cancer that had spread to the bone, it seemed to help prevent problems like fractures (breaks) better than zoledronic acid. It also can help bones even after bisphosphonates stop working. In patients with cancer spread to bones, this drug is injected under the skin every 4weeks. Side effects include low blood levels of calcium and phosphate, as well as ONJ. This drug does not seem to affect the kidneys, so it is safe to give to patients with kidney problems.





DISCUSSION

Many risk factors can increase your chance of developing breast cancer; cells divide into new cells, and die. Genes that speed *up* cell division are called oncogenes. Others that slow down cell division something suspicious is found during a screening exam, or if you have any of the *symptoms* of breast cancer described in the previous section, your doctor will use one or *more* methods to find out if the disease is present. If cancer is found, other tests will be done to determine the stage because cells to die at the right time are called tumor suppressor genes. Certain changes (mutations) inDNA that "turn on" oncogenes or "turn off" tumor suppressor genes can cause normal breast cells to ecomeancerous. Mecancerous. This is followed by a discussion of the typical treatment options based on the stage of the cancer (and a small section on breast cancer treatment ring pregnancy). Hormones seem to play a role in many cases of breast cancer, but just how this Breast cancer is sometimes found after symptoms appear, but many women with early breast cancer have no symptoms is not fully understood.

Systemic therapy refers to drugs which can be given by mouth or directly into the blood stream to reach cancer cells anywhere in the body. Patients who have no detectable cancer after surgery are often given additional treatment to help k cancer cells may break away from the primary breast tumor and begin to spread. It is important to understand that having a mastectomy instead breast conserving surgery plus radiation only lowers your risk of developing a second breast cancer in the same breast. It does not lower the chance of the cancer coming back in other parts of the body. It is important that you don't rush into making a decision. These cells can't be felt on a physical exam or seen on x-rays or other imaging tests, and they cause no symptoms. But they can go on to become new tumors in nearby tissues, other organs, and bones. Most patients see their surgeon about 7 to 14 days after the surgery. Your doctor should explain the results of your path Treatment to relieve symptoms depend on where the cancer has spread. For example, pain from bone metastases may be treated with external beam radiation therapy and/or bisphosphonates such as pamidronate (Aredia) or zoledronic acid (Zometa). Most doctors recommend bisphosphonates or denosumab (Xgeva), along with calcium and vitamin D, for all patients whose breast cancer has spread to their bones. Report and talk to you about the need for further treatment.

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