

A Review of Breast Cancer

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Breast cancer is the second most common cancer worldwide. It is the most common cancer among women. And it is the leading cause of cancer mortality, and one of the leading causes of morbidity and mortality in women worldwide [1, 2].

Fifty years ago cancer of the cervix and child-bearing complications were the leading health care problems of women.[3] Breast cancer is a multifactorial disease and various factors contribute to its occurrence.[5]

Breast cancer occurs all over the world,

its incidence, mortality, and survival rates vary considerably among different parts of the world, which could be due to many factors such as population structure, lifestyle, as well as both genetic and environmental factors.[6] The main risk factors are age, low parity, and a low rate of breast feeding. This is why it is common in high resource nations, however it is increasing in almost all countries. [4]

Changes in risk factors have led to an increase in the prevalence of breast cancer. [7]

The world population continues to rise and the life expectancy for women has reached 80-plus year in most nations, especially western.

The single most important demographic factor determining future health care burdens will be age. One oncological disease certain to increase in all nations is breast cancer.

Breast cancer is an individual tragedy for those affected. It is a highly curable disease when detected early, and an inevitably fatal disease when discovered too late. Access to high-quality care leading to early diagnosis and proper surgical and medical treatment can mean the difference between life and death. [7]

Breast cancer is a major health care burden. Screening programs are costly and difficult to organize, involving major logistic and quality control issues.

Proper surgical treatment requires appropriate operating room facilities and highly qualified healthcare providers. Local radiation requires facilities beyond the scope of most health care systems in low income countries.

Adequate systemic treatment with chemotherapy and hormonal therapy is costly both in itself, as well as in management of their potentially severe adverse effects. All sophisticated breast cancer treatment requires the resources of advanced pathological laboratory investigation including immunohistochemistry and molecular pathology analysis.

New targeted therapies remain an evolving field where only one thing is certain, individual treatment costs are already threatening the best founded healthcare system.[8]

Breast cancer is a challenge for all countries. Organizing and centralizing breast cancer care around integrated breast cancer centers can potentially provide optimal care to individual patients within different health care systems; the reverse will strain healthcare systems.

Screening and Imaging

Early diagnosis is the key to the successful treatment of breast cancer. T1 tumors measuring less than 2cm in size have a ten years survival of approximately 85%. While T3 tumor have a ten years survival of less than 60% [9] Four diagnostic procedures lead to the ultimate detection of breast cancer: (1) clinical examination (2) mammography; (3) breast ultrasound; and (4) breast magnetic resonance imaging (MRI)

Clinical examination is the most readily available method of diagnosis. It is a simple form of early detection, capable of diagnosing tumors between 1 and 2 cm and bigger, depending on tumor location and

breast size. It remains the most frequent way breast tumors are first detected, usually by the affected woman herself.

Awareness of the breast is one of the key concepts in the fight against breast cancer. [10]

Healthcare providers who are in regular contact with women need to be aware of breast disease, as well as willing to examine women on a regular basis.

Healthcare providers need to be recruited for breast cancer detection, and women themselves need to be aware of the disease threat. They need to be informed and willing to expose themselves to routine breast examination. With regard to early diagnosis and systematic screening, only mammography provides the

key advantages of easy to perform minimal technical set-up, easy standardization, as well as the potential of review and direct comparisons.

Many countries with highly developed health system have introduced systematic mammography screening for women usually every two years, between 50 and 70 years of age in an effort to reduce breast cancer mortality. Acceptance among women has been variable and the systematic screening approach remains controversial. Many women are afraid of the procedure, which is often painful and cannot avoid some radiation exposure. [12]

Breast ultrasound is an excellent tool in the management of breast diseases. Most, but not all, breast cancers seen on mammography or MRI can also be visualized on ultrasound and subsequently biopsied using ultrasound-guided core biopsy techniques. The quality of breast ultrasound depends on a variety of variables, including breast size, glandular tissue density, previous surgeries, or radiation, and examiner experience. It has not been used as a large-scale screening tool. [13]

MRI of the Breast is the most expensive and logistically demanding breast examination modality, with the best sensitivity, but overall low specificity. Radiologists appreciate its accuracy, while clinicians have to deal with the clinical management of nonspecific and often benign findings that require extensive patient counseling. On the other hand to rule out malignancy particularly in questionable cases and within breasts heavy or scar tissue, MRI remains second to none. [14]

Diagnosis

Breast examination, mammography, breast ultrasound, and MRI only raise the suspicion of breast cancer. Ultimately, a lump is detected, an area of microcalcification, a suspicious area on ultrasound, or a gadolinium-enhanced area on the MRI scan. The next step is key to the diagnosis: histologic confirmation or exclusion of malignancy.

Some 80% - 90% of breast cancers can ultimately be identified on ultrasound, even if the primary diagnosis is made by one of the other imaging modalities. Breast ultrasound allows direct, ultrasound-guided biopsy. Core biopsies allow an exact histologic diagnosis: grading, as well as a determination of estrogen- and progesterone-receptor status and HER2 receptor status

Treatment Stratification

all the relevant information to determine appropriate treatment is available: tumor location, tumor size, histology, and tumor-specific properties. Lymph node status can be assessed clinically, sonographically, and—if necessary—using cytology. Together with patient age and overall health status, a treatment

course can be discussed.

If chemotherapy is needed, it is used as an adjuvant therapy, or after surgery as an adjuvant treatment.

Surgery is breast conserving surgery if possible, unless the breast needs to be removed totally (mastectomy). As with prognosis, the earlier the diagnosis, the smaller the tumor, the lower the percentage of mastectomies, and the lower the number of costly breast-reconstructive procedures. Again, early detection remains key both at an individual level as well as at a financial level.

Surgical Treatment

Radical mastectomy as introduced by Halstead was modified and still remains standard therapy in many countries where healthcare systems lack a specialized focus for breast disease.

Later the concept of breast conserving surgery was introduced proving that the removal of the tumor, combined with local radiation provides the same cure rates as mastectomy. This concept has improved the lives and the fate of hundreds of thousands of women worldwide. [15 16]

By introduction of oncoplastic surgery, breast conserving surgery has become a challenging area of surgery. It requires an intimate knowledge of what is and what is not possible. It requires an understanding of the breast as a physiologic and aesthetic entity that is composed of two different parts: the skin and the glandular tissue, which need to be treated almost separately, only to be reconnected within a new breast shape at the end of the procedure.

Surgeons performing other types of surgery usually have no time nor interest to focus on this small but aesthetically challenging area of surgery. [17] So, only a specialist breast surgeon will develop, the necessary competence to provide acceptable breast conserving solutions for up to 70% of patients with a small tumor.

In countries without a strong specialization for breast and breast conserving surgery, there is fragmentation of care thus rendering treatment decisions unnecessarily complicated for patients. The higher the skill of the surgeon and the smaller the tumor, the lower the mastectomy rate.

What kind of mastectomy is performed determines what kind of reconstruction is necessary or possible. The most advanced versions of mastectomy are skin-sparing mastectomy or nipple-sparing mastectomy, allowing direct reconstruction with artificial implants. Again a specific kind of training is required. An insufficient resection, leaving behind too much subcutaneous tissue, will also leave behind too much breast tissue, while a too radical resection will lead to excessive thinning of the skin and subsequent necrosis.

Autologous reconstruction techniques are either vascularized skin/muscle flaps (latissimus dorsi flap,

TRAM flap), or free flaps (DIEP, superior gluteal flap), and allow either reconstruction after a skin-sparing mastectomy, or a plastic reconstruction after the loss of the breast skin as part of a traditional mastectomy. Management of the axilla is an integral part of breast cancer surgery.

Axillary dissection along anatomic levels is an important part of adequate staging, and is thought to be an important part of curative surgery.

The introduction of the sentinel lymph node biopsy is one of the major advances to reduce nontherapeutic morbidity.

As molecular profiling improves, future treatment concepts might be able to do without any kind of axillary exploration. [18]

Systemic Treatment

Chemotherapy for oncologic diseases was introduced in the 1950s.

During the 1970s the concept of adjuvant therapy was developed and remains one of the cornerstones of breast cancer treatment. In spite of that this locally cured disease has the potential to recur systemically after one or more years as metastatic and incurable breast cancer. Things to be answered include: where exactly in the human body do these breast cells with oncologic potential "hide," how do they survive, and why do they ultimately metastasize? [19]

The theory of micro metastatic tumor cells that have left the primary breast tumor and spread into the body led to the concept of adjuvant chemotherapy. After appropriate local treatment, almost all breast cancer patients are clinically free of disease.

Depending on prognostic factors such as tumor size, lymph node status, hormone receptor status, HER2 receptor status, and grading, some of the patients are initially cured but later have systemic treatment failure over the course of 5–10 years.

The treatment failure rates vary between 5% to up to 50%, depending on the factors mentioned above.

Adjuvant chemotherapy effected a measurable decrease in long-term systemic failure and mortality of between 10% and 20%.

It remains difficult to determine exactly which patients will benefit, leading to over treatment of some patients.

Over the years, different chemotherapeutic regimens have developed, beginning with the CMF regimen (cyclophosphamide, methotrexate, and 5-fluorouracil) and leading to today's standard of epirubicin and cyclophosphamide, followed by paclitaxel (EC-paclitaxel). [21]

Other therapeutic agents have been tested, mostly in the metastatic but also in the adjuvant phase.

Targeted Therapy

Such as anti estrogens "tamoxifen" and fulvestrant were introduced and, later, aromatase inhibitors. The effect of oophorectomy on the disease progression of

metastatic breast cancer was already established in the 1890s.

Adjuvant chemotherapy with anti hormonal drugs in patients positive for estrogen and progesterone receptors has proven as successful as adjuvant chemotherapy in over 60% of patients. [22] Recently for about 15% of breast cancer patients positive for the HER2 receptor an additional targeted therapy was introduced. Specialized breast cancer centers needed to coordinate the surgical, systemic and radiation therapies available.

Radiation Oncology

Breast radiation is an integral part of breast conserving surgery in the elderly population. Both the extent of and the necessity for radiation are undergoing considerable changes.

Breast conservation is key to educating women how to detect breast cancer early (the breast is a major aesthetic symbol) which does not need to be removed. On the other hand, breast radiation remains a problem in low income countries.

Breast radiation requires modern, state-of-the-art, high-cost facilities to avoid considerable adverse effects.

Follow Up

In advanced health systems, 80% – 85% of breast cancer patients will be cured. Owing to long-term relapse follow-up becomes a major issue as patients with previous breast cancer are at high risk of developing subsequent breast cancers, i.e. in the contralateral breast.

Breast cancer survivors are breast cancer advocates. They show how this increasingly common disease can be cured. Raising awareness of breast cancer within different cultures is the main challenge, particularly in emerging economies with developing healthcare systems. Management of breast cancer survivors will play an integral part.

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