RADIATION THERAPY CONTRIBUTION IN BREAST CANCER TREATMENT

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ABSTRACT

Breast cancer has a high incidence, prevalence and mortality, representing a serious public health problem, demonstrating the need for early diagnosis and effective treatments for it to become a curable disease. Against this background radiation is presented as an important therapeutic tool. The objective of this study was to describe what is the contribution of radiotherapy in the treatment of breast cancer, using as a methodological approach to literature. The therapeutic approach to breast cancer can vary depending on multiple factors such as individual characteristics, disease staging and the psychological characteristics of the patient, prioritizing the quality of aftercare life. Radiation therapy is considered a method able to control or cure cancerby inhibiting cell growth and division, and their application is basically in two ways, brachytherapy or teletherapy, depending on the location of the tumor. This therapeutic method plays a key role because it can prevent local recurrence of breast cancer operated after conservative treatment or chest wall following mastectomy, and also prevent relapse in the areas of lymphatic drainage when there is lymph node involvement. To avoid local recurrence, radiotherapy increases the chance of cure patients, contributing effectively in the treatment of breast cancer.

KEYWORDS: Treatment, radiotherapy, breast cancer.

1. INTRODUCTION

The cancer is in a disease with a multifactorial etiology and natural history, often providing cellular mutations of genes that control cell growth and mitosis. Neoplastic diseases are developed progressively from any tissue within any organ, when normal cells lose their functional capacity dividing uncontrollably, to give a mass of cancerous tissue[1].

Breast cancer is the second among cancer cases, both globally and in Brazil[2], has been estimated for 2015 in the country, the occurrence of about 57,120 new cases[3]. Every year, approximately 1.3 million women are affected by breast cancer in the world[4]. The incidence rates increase reflecting the global trend towards the predominance of lifestyles that encourage exposure to risk factors[5].

Control of breast cancer is a concern for public health services[5], characterized as the primary malignancy that affects women in Brazil[6]. The severity of the disease is a challenging situation and requires changes, especially when considering the relationship between early detection, therapeutic perspectives and women's quality of life[2].

As for the origin of breast cancers, it is believed that 90% to 95% of them are sporadic (non-family) and arising from somatic mutations that occur during life, and 5% to 10% are hereditary (family) due the nucleotide mutations perpetuated in the family line by germ cells, which confers susceptibility to breast cancer[7].

Early diagnosis is one of the main prognostic factors and therapeutic choice will depend on the clinical stage of the disease, the anatomical and pathological characteristics, clinical conditions, age and desire of the patient[8].

The most effective means of early detection of breast cancer are: the systematic examination of the breast, or clinical examination, done by specialized professional, mammography and self-breast examination[6].

The treatment typically comprises performing surgery to remove the tumor mass, chemotherapy (chemotherapy), radiation therapy (RT) and in some cases hormonotherapy[5].

Radiotherapy is a treatment for cancer locoregional, painless performed by the application of ionizing radiation, damaging the structure of deoxyribonucleic acid (DNA) cell and thereby interfering with tumor growth and metastasis[9], reducing the risk of local recurrence and increase survival[10]. The application of radiotherapy is basically performed in two ways: the external called teletherapy, and internal, brachytherapy[11].

Considering radiotherapy as an important adjunct in the treatment of malignancies, the aim of this study was

o describe his contribution to the treatment of breast cancer.

2. MATERIAL AND METHODS

This study is a literature review made through literature searches using the datas of Google Scholar and SciELO data. The keywords used were: treatment, radiotherapy and breast cancer.

We performed a reading and selective analytical sources of interest according to the quality and relevance of the content to the proposed theme then was the construction and subsequent presentation of the article

3. LITERTURE REVIEW

Cancer

Etymologically the word cancer, cancer of the Latin meaning crab, must have been employed in analogy to penetrant growth mode, which can be compared to the legs of the crustacean, which introduces the sand or slurry to settle and hinder its removal[12].

Cancer can be defined as a set of more than 100 diseases that have in common the uncontrolled growth of cells that invade tissues and organs and can spread (metastasize) to other parts of the body[13].

These cells divide rapidly and tend to be very aggressive and uncontrollable, causing the formation of tumors or malignancies. On the other hand, a benign tumor is characterized as a localized mass of cells which multiply slowly and resemble the original tissue, constituting rarely life threatening[14].

According to the National Cancer Institute José Alencar Gomes da Silva (INCA), the factors that can cause cancer are varied and may be internal or external to the body, both of which are interrelated. External causes concern for the environment and the habits and customs of their own social and cultural environment. The internal causes are most often pre-determined genetically and are linked to the body's ability to defend itself from external aggressions. These causal factors may interact in various ways, increasing the probability of malignant transformation in normal cells[14].

Establishing itself as a global public health problem[15], cancer affects both the developed countries, the developing ones, merits further research in order to get better quality and humanization in care for patients with this disease[16].

It is estimated that by 2020, the number of new cases per year to reach 15 million, of which about 60% occur in developing countries[17]. Already for the year 2030, with an expected 27 million incident cases of cancer[18].

In Brazil, two main indicators characterizing cancer as a public health problem. First, the gradual increase in the incidence and cancer mortality in proportion to population growth and socioeconomic development. Second, the challenge this poses to the health system, especially in the population's access guarantee to diagnosis and treatment[19].

Gutiérrez *et al.*(2009)[20]notes that economic development, technological development, industrial growth, women's entry into the labor market, aging population are factors that, deprived of educational conditions capable of generating in the population aware of the risk factors related to cancer, as well as the right to make use of diagnostic tests and proven effective treatments become ingredients for the unfavorable condition in cancer advancement of control in our society.

According to Hazin*et al*. (2015)[21], developing countries still face significant barriers to curing cancer, among which can be highlighted the delay in diagnosis, high early mortality and treatment abandonment.

It should be noted that the late cancer diagnosis difficult treatment with curative purpose, reducing the length of survival and quality of life[22], may cause permanent states of mutilation, loss of organic functional capabilities leading to early retirement or death of the individual, in a continuous cycle of personal suffering, emotional and financial family breakdowns and resource commitment of the social area of health and the country's own economy[20].

Regarding the treatments for cancers, which have the objective to cure, prevent recurrence and increase survival with quality for the patient, there are the surgery, radiotherapy, chemotherapy, hormone therapy and immunotherapy[23].

The most common symptoms resulting from treatment are: depression, anxiety, insomnia, fatigue, psychological stress, vomiting, nausea and limitations of skills. Fatigue is the most debilitating symptom, increasing the time to return to work, while anxiety and depression cause the withdrawal from normal activities[23].

It is observed that patients with malignant diseases have been increasingly admitted to the intensive care unit (ICU) due to complications of the cancer itself or the side effects of treatments[15].

The cancer approach represents a major challenge with regard to confronting the problem fully, demanding more skilled workers and improved to cope with the new demands of professional practice, directed to the epidemiological reality of our country[17].

Breast cancer

Breast cancer is defined as a group of malignant epithelial tumors characterized by invading adjacent tissue prone to distant metastasis[24].

The most common forms of breast cancer are ductal and lobular invasive carcinomas. Other rarer types of invasive breast cancer are: medullary carcinoma, mucinous carcinoma, papillary carcinoma, inflammatory carcinoma[25].

Breast cancer is in a heterogeneous group of diseases with different behaviors. The heterogeneity of this cancer can be observed by various clinical and morphological manifestations, different genetic signatures and consequent differences in therapeutic responses[14].

INCA data indicate breast cancer as the most common cancer among women worldwide and in Brazil, second only to nonmelanoma skin, accounting for about 25% of new cases each year. Breast cancer also affects men, but it is rare, accounting for only 1% of all cases of the disease[14].

For the year 2015, in Brazil, estimated the occurrence of about 57,120 new cases of breast cancer and is considered a major public health problem[3]. It adds that, mortality rates remain high, most likely because the disease still it is diagnosed in advanced stages[26].

This type of cancer is relatively rare before the age of 35 and above that age its incidence is growing rapidly and steadily[27], especially after 50 years[14].

According to Garcia *et al.*(2015)[28], the breast cancer can trigger many negative feel ments in women and may be strongly related to changes in their quality of life. Among them, you can highlight the fear of diagnosis, possible surgery, the uncertainty of the prognosis and recurrence of the side effects of treatment, suffer the pain and face the possibility of death.

Among the risk factors of the disease, it should be noted that the changes in women's lifestyle tend to increase them, associated with events such as: the absence of motherhood, achieving hormonal intervention, motherhood after 30 years of age, sedentary lifestyle , poor diet, obesity, smoking and excessive alcohol consumption, in addition to family history of cancer and age, the main risk factor for the diagnosis of breast cancer, in which the age of incidence is more common in women over 40 years[4,13,25,27,29].

Is worth mentioning that the presence of cancer in women may not exactly be avoided because it also depends on genetic factors that are beyond the woman's control in its entirety[13].

It is estimated that 30% of cases the disease can be prevented when healthy practices are adopted as practice regular physical activity, eating healthily, maintaining proper body weight and avoid alcohol consumption. Breastfeeding is also an important protection factor[14].

The proper prognosis of breast cancer occurs typically when it is detected early, leading to a reduction in mortality and physical, psychological and social effects caused by this type of cancer[25].

Early diagnosis being prioritized, mainly from guidance, information and consistent care practices can significantly alter the reality of late diagnosis of breast cancer, as well as faster access to health services, optimizing the therapeutic steps[4].

Breast cancer, diagnosed and treated in time, it reveals a good prognosis tumor and the five-year survival rate reaches 85%. Late treatments bring harm to the quality of life, it requires more aggressive approaches, the need to use multiple therapeutic modalities, and results in overlapping consequences. In Brazil, the high mortality rate can be partially explained by the fact that, on average, 60% of breast cancers are diagnosed in advanced stages[30].

Currently, the guidance is that women do self-palpation of the breasts whenever you feel comfortable to do so (in the bath at the time of change of clothes or other daily situation), without a specific technique of self-examination. Early detection of breast cancer can also be done by mammography. The recommendation in Brazil, updated in 2015, is that women between 50 and 69 years do a mammogram every two years. The diagnostic mammography, with the purpose of investigating suspicious breast lesions may be requested at any age, the doctor's discretion[14].

The results of mammography are classified according to the BreastImaging Reportingand Data System (BI-RADS®), published by the American College of Radiology and translated by the Brazilian College of Radiology[31].

This system uses categories 0-6 to describe see the survey findings and provides recommendations of conduct.

The most common symptom of breast cancer is the lump of onset, usually painless, hard and bumpy, but there are tumors that are soft consistency, globular and well defined. Other breast cancer signs are skin edema similar to orange peel, skin retraction, pain, nipple inversion, hyperemia, desquamation or ulceration of the nipple, and papillary secretion, especially when it is unilateral and spontaneous. The secretion associated with cancer is generally transparent and may be pinkish or reddish due to the presence of red blood cells. There, may also be palpable lymph nodes in the armpit[14].

The therapeutic approach to breast cancer can vary depending on multiple factors such as individual characteristics, disease staging and psychological characteristics of the patient, prioritizing the quality of aftercare life[3].

The most common forms of cancer treatment include surgery, chemotherapy, radiation therapy or hormonal therapy, and usually more than one way can be used in a

complementary manner[32].

Surgical procedures include mastectomy and breast conservative surgery (lumpectomy and quadrantectomy), which change the appearance, sensitivity and functionality of the breasts[33], complications may arise as local infections, skin necrosis, scarring complications, disorders of the range of motion, lymphedema, functional disorders, nerve damage, pain and sensitivity of upper limb ipsilateral to the operated breast disorders[34].

The other modalities of treatment (chemotherapy, radiotherapy and hormone therapy) can cause side effects like nausea, vomiting, fatigue, alopecia, induced menopause, reduced vaginal lubrication, decreased sexual arousal, dyspareunia and anorgasmia[33].

A radical mastectomy was the standard treatment for breast cancer for years, regardless of any associated factor. However, from the 1980s, change was observed in the therapeutic approach, following the trend of treatments more conservative, but without having compromising oncological safety[8].

Radiotherapy

Radiation therapy is a method to control or cure cancer by inhibiting cell growth and division, which has three distinct purposes: to cure cancer when it is used to eradicate a tumor order; be palliative, acting in reducing symptoms such as pain, bleeding and respiratory distress; and have an adjuvant role when applied in order to eradicate cancer cells that may possibly lead to relapse. The radiotherapeutic treatment time varies according to the type of cancer being treated, its staging and therapeutic objective sought[9].

The RT can be used as adjuvant therapy or neoadjuvant surgery[34], and for the most part, is performed on an outpatient basis[35]. It is a technique to remove local tumor cells by beams of ionizing radiation produced by apparatus or emitted by radioisotopes natural. A pre-calculated dose of radiation is delivered in a given time and in a given tissue volume[34]. The total dose is fractionated in daily applications for a variable time up to two months[35].

Ionizing radiation conceptualized itself as radiation having sufficient energy to ionize molecules by the release of electrons from atomic structure, such as x-rays, beta particles, alpha particles and others for the treatment of cancer and certain benign diseases[11]. Ionizing radiation is electromagnetic or corpuscular and to interact with the tissues, giving rise to fast electrons which ionize the medium and form chemical effects, such as the water hydrolysis and breakdown of DNA chains[36].

Radiation therapy may act on the cell's DNA, preventing it from multiplying (reproductive death) or inducing a direct death by apoptosis[11]. The molecular mechanism of interaction with the nucleic acid can be direct or indirect by means of free radicals[9].

Each cell responds to radiation in different proportions, equivalent to its specific radiosensitivity. The sensitivity of a cell to radiation results from their mitotic activity and degree of differentiation, i.e., the less differentiated and a larger number of divisions the cell will be more sensitive to radiation[9].

It is emphasized that the radiation also affects the regions of normal tissue, causing side effects such as pain, fatigue, sensory and skin changes, such as radiodermatitis. About 90% of patients may experience a dose-dependent skin reaction[34], yet have the possibility of repair with greater efficiency than the malignant cell. Thus they are achieved positive results by the total or partial removal of tumors treated with radiation[11].

Patients treated with radiotherapy may also experience other side effects such as loss of self-esteem and confidence, changes in mobility and sensation on the affected side, emotional shock, confusion, anxiety, fear, feelings of isolation, changes in routine[35], lack of appetite, hair loss, nausea, diarrhea[9].

The application of radiotherapy happens in two ways basically: external, called teletherapy, and internal, brachytherapy[11]. The choice depends on the tumor location[36].

External radiation therapy: Teletherapy

The radiotherapy is the most common application technique, in which the ionizing radiation passes through various tissues before reaching the tumor area and thereby normal organs and tissues are subject to the toxic effects of the emitted rays. The absorption of radiation can cause biochemical changes and damage at the cellular level both immediately as late[10].

In teletherapy, the ionizing radiation beam is directed to the target region of the body called field, at a distance. External radiation therapy uses radioactive sources from nuclear or linear accelerators, which give rise to radiation by accelerating electrons[11].

The radiations are generated by devices that are remote from the patient. The cobalt pump is a container containing a source of cobalt, a device with a small window that opens and lets the radiation beam leaving monitored, allowing tumor treatment. In this case, the treatment time and all others involved physical parameters are carefully monitored and examined by a permanent quality control program[36].

The linear accelerator operates very similarly to a device x-rays, or radiation is only generated when the apparatus is connected to a source of electrical energy. Radiation of the formation mechanism is more complex, but the net effect is equivalent to: a controlled radiation

beam impinges on the target to be treated[36].

Internal Radiotherapy: Brachytherapy

In brachytherapy the radioactive element is positioned next in contact or inside the organ to be treated[11]. Often it is a surgical procedure and should be performed in the operating room with anesthesia[36].

There are two types of brachytherapy treatment. The high dose rate (High Dose Rate - HDR) is fractionated, makes use of programming via computer, and has shorter exposure to radiation, which allows outpatient treatment. The high dose of radiation delivered increases the tumor cure chances. Low dose rate (Low Dose Rate - LDR) is a continuous treatment, with longer period of exposure, which requires hospitalization of the patient[11].

We emphasize that, in brachytherapy the radiation is applied directly to the tumor site by means of molds, catheters, implants[11], or prostheses that act as guides for application on site[36], which enables radiate small target volumes with high dose radiation. This technique makes it possible to save neighboring structures not affected by the disease, as it presents a significant drop dose as it departs from the sources[11].

Radiotherapy in breastcancer

Breast cancer because of its high incidence, prevalence and mortality requires early diagnosis and effective treatments that can become a curable disease. RT presents itself as a valuable tool in this therapeutic context where most patients with breast cancer to receive as part of their treatment, reducing significantly the mortality due to cancer[37].

Radiotherapy has in order to prevent local recurrence of breast cancer operated after conservative treatment or chest wall following mastectomy, and also prevent relapse in the areas of lymphatic drainage when there are lymph nodes. To avoid local recurrence, radiotherapy increases the chance of cure for patients[38].

Radiotherapy in breast-conservingsurgery

The breast conservation is based on surgical excision of the tumor (setorectomy or quadrantectomy) and axillary management (sentinel lymph node with or without axillary dissection) followed by radiation therapy, and is currently considered the standard local treatment for the disease in early stages[8].

After conservative treatment, the patient usually needs to receive radiation therapy to prevent relapse occurs in the operated breast. Patients over 70 years with small tumor (less than two centimeters), no nodes in the engaged armpit and with positive estrogen receptors, may not need radiotherapy even after treatment with preservation of the breast, since the local recurrence in these situations is considered low (about 7%), provided that treated with hormone[38].

Survival rates after conservative surgery followed by breast irradiation are similar to those observed after modified radical mastectomy. As a result, the use of conservative surgery has increased steadily in recent decades, with a corresponding increase in the use of the mammary radiation[37].

The method usually used for RT breast, conservative therapy is teletherapy, but the reinforcement can be accomplished with teletherapy or brachytherapy. In radiotherapy, the most commonly used is electron energy variable, depending on the breast size and depth of the tumor bed; brachytherapy, iridium-192 may be used by placing plastic catheters or needles, usually two planes for broad coverage of the target volume. They can be placed at the time of surgery, with subsequent loading of radioactive sources[8].

The best way to define the reinforcement of the place is the view of metal clips placed in the surgical procedure. In the absence thereof, can be used imaging tests (ultrasound, mammography or MRI of the breast) to provide guidance on the location of the tumor bed, associated to the surgical scar information. A common practice is to treat the whole quadrant headquarters of the primary lesion[8].

Post-mastectomyradiotherapy

After lumpectomy or radical mastectomy with reconstruction, radiotherapy is performed when the tumor is larger than five centimeters, where the nodes of the axilla are compromised when there is invasion of skin and existence of more than one breast tumor removed. In these situations, the patient receives the applications both in the chest wall or in the reconstructed breast as well as in lymph drainage[38].

Even after total mastectomy, a relevant local recurrence risk (in the chest wall or regional lymph nodes) may remain in certain groups of patients. If there is lymph node involvement (or the armpit has not been adequately assessed), RT after mastectomy can enable effective reduction and delay in the occurrence of local recurrences following both simple as radical mastectomies[37].

Radiotherapyadjuvant

Adjuvant radiotherapy is a local treatment modality applied in breast cancer to reduce local recurrence after surgical treatment, however the application of ionizing radiation in the primary tumor site may cause systemic effects[37].

The result of the application of adjuvant radiotherapy is beneficial for women with younger age, in tumors in advanced stage and lymph node involvement. The lore-

gional radiation is also known where no adjuvant chemotherapy indication, since the addition of this therapy is important for achieving higher cure rate and survival[4].

For patients who did not receive chemotherapy, it is proposed that the RT starts within a period of eight weeks after surgery. When both RT as CT are indicated, the following sequences are executable: RT followed by CT, CT followed by RT, RT and CT and RT simultaneously between CT cycles. However, despite the effectiveness of RT can be increased by concomitant CT, toxicity may also increase[37].

Collateral effects resulting from the application of Radiotherapy in breast cancer

Radiation therapy, especially in patients with breast cancer, can damage the long-term function of the shoulder joint ipsilateral to the irradiated site, with even greater impact when the axillary fossa also receives radiation. Another commonly described side effect of radiation therapy is fatigue, regardless of tumor location[9].

Radiotherapy when associated with radical treatment for breast cancer, is admittedly significant for significant morbidity in the ipsilateral to the site of disease. Injuries to the lymphatic system, venous thrombosis of axillary and subclavian veins, limiting cicatricle retraction are well known complications. A serious and poorly understood complication is critical ischemia of the upper limb due to arterial injury in these patients[39].

The combination of factors triggered by surgical elementand RT can negatively impact the daily lives of these women, causing pain in the upper limb, functional disorder and impairment in activities of daily living and the possibility of these symptoms worsen after RT[34].

Side effects of RT applied to the treatment of breast cancer, such as subcutaneous fibrosis, expose women to the risk of lymphedema, brachial plexus injuries and limitation in shoulder movement. The physical suffering affects survival, as it may hinder the coping strategies in women undergoing radiotherapy treatment, in which it observed high prevalence of tension, nervousness, feeling of loneliness, anxiety and depression, and social changes in lifestyle and self-image, directly influencing the health andwellness, damaging the quality of life of these women[40].

The skin changes resulting from RT can interfere with superficial sensitivity of the irradiated region, but it is believed that the main reason for sensory change is due to the total or partial damage to the intercostal nerve sensory (NICB) during surgery. The NICB is derived from the lateral cutaneous branch of the second and third nerves intercostal and his injury is responsible for frequent complaint of discomfort or unpleasant feeling, or can promote dysesthesia in the posteromedial edge of the upper arm, underarm or chest wall the affected side, which may cause complaints hypoesthesia, anesthesia, burning, pitting localized pain and even hiperestesia[34].

Rehabilitation programs for women for breast cancer assist in improving the quality of life. How many physical complications occur simultaneously at RT for breast cancer, it is important that effective prevention strategies are identified and well targeted[40].

4. CONCLUSION

Radiotherapy contributes valuable in the treatment of breast cancer and may act in palliative treatment, curative and adjuvant helping to improve the quality of life and increased survival rate of patients suffering from cancer.

The cancer, especially breast, is a public health problem in Brazil, and is for the health system a challenge to ensure is full, accurate diagnosis, appropriate treatment and necessary support for health recovery of individuals affected by cancer.

We emphasize the need to structure a network of regionalized and hierarchical services to ensure comprehensive care to the population, which requires qualified professionals to meet the demand of the population.

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