



Management of Breast Cancer in Elderly Women

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Abstract

Introduction: Breast cancer is the most common malignant tumor among women (around 1.5 million women are diagnosed every year and 400,000 die) and is strongly dependant on age as 80% of its cases occur after the age of 50. Moreover, the mentioned feature is also observed in breast cancer mortality.

Materials and methods: The article reviews the literature using the Pubmed and Google Scholar databases as well as articles available on the Internet. Articles were analyzed using keywords: breast cancer, elderly women, radiotherapy, chemotherapy, targeted therapy. The article presents risk factors, possible therapies and the situation of older women experiencing breast cancer.

Results: In patients over 55 years of age, there was observed a relationship between age at the time of diagnosis and the presence of more beneficial biological features of the tumor. These features include a lower degree of proliferation, normal p53, and lack of expression of the epidermal growth factor receptor.

The typical therapy of breast cancer may include radiotherapy, the standard one – called teleradiotherapy – intraoperative radiotherapy or brachytherapy, chemotherapy, hormonal therapy and surgery or their combination.

Conclusions: The outcome of the treatment may be enhanced by novel modalities as targeted therapy and breast conserving surgery, followed

by appropriate oncological rehabilitation in order to improve the quality of life.

Key words

breast cancer, elderly women, radiotherapy, chemotherapy, breast cancer surgery

Introduction

Breast cancer is one of the most common cancers. In Poland, this disease is responsible for 25% of cancer cases. As much as 80% of cases occur after the age of 50 [1]. It is estimated that in the European Union member states in 2008 more than 330,000 women were diagnosed with breast cancer, about 89,000 died because of this. Additionally, it can be said that about 1.33 million women have lived with the diagnosis of breast cancer in the previous 5 years [2].

Recently, it was noticed that in patients over 55 years of age there was a connection between age at the time of diagnosis and the presence of more beneficial biological features of the tumor – including lower rates of proliferation, normal p53 and absence of epidermal growth factor receptor expression. In women aged 55 years or older, the advancing age is associated with a more favorable biology of cancer, and the survival of breast cancer in older women is similar to survival in the general population, regardless of the condition of the disease. This beneficial outcome should be considered when making clinical decisions in older patients [3].

According to the results received in the International Breast Cancer Study Group 10-93, patients aged 60 years and older diagnosed with hormone-dependent breast cancer (without clinically suspected lymph nodes), that are supplemented with tamoxifen, radical surgical therapy without axillary lymphadenectomy is proceeding of comparable effectiveness and ensures a better quality of life. An additional unquestionable argument is the fact that such treatment reduce the risk of postoperative complications in the form of pain or limitation of limb movement and lymphoedema [4].

It can be observed that standards and guidelines for the treatment of breast cancer in older women change all the time – more and more attention is paid to the prevention of the disease and the possible improvement of the functioning of these women after treatment [5].

Nowadays, when the incidence of breast cancer is growing rapidly, prophylaxis and decent knowledge of risk factors are very important. Risk factors include, among others, alcohol (high-percentage alcohol), obesity – especially in the post-menopausal and abdominal type and a diet high in saturated fat. At the other side, it is known that a diet rich in vegetables and fruits and regular physical activity are significant, because all of these factors reduce the risk of breast cancer [6, 7].

Breast cancer, unfortunately, can also have an impact on patients' lifetime after treatment. Oncological disease is a situation that promotes the occurrence of crises and mental disorders such as anxiety or depression. Presence of cancer also affects not only the mental state of patients – as it turns out, patients after menopause, who in their lives suffered from breast cancer – have a much higher risk of cardiovascular disease than women who have never coped with that illness. All of these examples show how much cancer treatment is valuable for older people and also how many small but meaningful factors affect the course of the disease and the condition of patients [8, 9].

Epidemiology and breast cancer characteristics

Breast cancer is a malignant tumor arising from breast cells, which develops locally in the breast and also metastasizes, usually to the liver, lungs and bones. It is the most common oncological problem in women. It is estimated that 1.5 million women are diagnosed with breast cancer every year in the world and 400,000 die of it [10]. Over the last three decades, the incidence of breast cancer has increased twice, and in 2012, the number of detected breast cancer exceeded 17000 in Poland [12].

80% of breast cancer cases occur after the age of 50, of which 50% are diagnosed between 50 and 69 years of age. The risk of breast cancer increases with age up to the age of 65, after which it gradually decreases. Also, mortality from breast cancer increases with age. Since the mid-1990s, the mortality rate for breast cancer in Poland has been falling. It is the third oncological cause of death in the Polish population, immediately after lung and colorectal cancer, with 90% of deaths from breast cancer affecting women over 50 years of age [10].

It is estimated that 20% of breast cancers are caused by risk factors that can be modified. These include alcohol consumption, overweight or obesity and lack of physical activity. Other risk factors for breast cancer

are: female sex, age, gene mutations (most common BRCA1 and BRCA2) and hormonal factors (use of oral contraception and hormone replacement therapy) [10, 11, 13].

Clinical symptoms depend on the stage of cancer. In the initial stage it is usually asymptomatic, recognized accidentally as a small lump in the breast. The first symptom in most women is the palpable tumor, usually placed in the upper outer quadrant. Other symptoms include breast asymmetry, nipple retraction, ulceration of the nipple or skin of the breast, orange peel-like pitting, burning or leakage from the nipple [10, 13].

The histopathological classification of breast cancer introduced by WHO divides breast tumors into pre-invasive cancers and invasive (infiltrating) cancers depending on the limitation of neoplastic lesion within epithelial cells or its further spread (infiltration). The most common morphological form of metastatic breast cancer is invasive ductal carcinoma, accounting for 65-80% of all cases. The second most common form is invasive lobular carcinoma, which accounts for 10-20% of breast cancer cases in women [10, 13].

Chemotherapy and radiation therapy

Radiotherapy uses ionizing radiation that destroys actively dividing cancer cells. Supplementary radiotherapy for patients with breast cancer is carried out in the case of a breast-conserving procedure and when breast amputation has been performed but there are indications for post-operative radiotherapy e.g. when the tumor has a diameter of more than 5 cm. Patients receive the appropriate dose to the surgical area in a cycle of 5 days a week for 6 weeks. The treatment is painless, but it has several side effects, including fibrosis in the area of the wound or temporary redness of the skin. Side effects may or may not come out after treatment [14, 15].

Standard radiation therapy, known as teleradiotherapy, is a preparation for radiotherapy and is carried out in several stages. The initial positioning and treatment plan is prepared on the basis of data obtained from computed tomography, thanks to this it is possible to save as much healthy tissue as possible. Most often, it takes several weeks, where the irradiation session takes about 10 minutes [15, 16].

Intraoperative radiotherapy is a modern type of radiotherapy and is increasingly used in breast cancer-saving therapy. The area around the

excised breast tumor during surgery is subjected to the first dose of targeted irradiation, which makes its operation more precise. The time of postoperative radiotherapy is reduced by at least a week. Currently, numerous scientific studies are being conducted to shorten the period of postoperative radiotherapy further or even in some cases to stop at intraoperative radiotherapy [14].

Brachytherapy is a method of a local radiotherapy used in treatment that saves the breast. The source of radiation are special catheters, which are temporarily placed during the surgery. The radiation is introduced on the second day after the operation, and after the irradiation procedure the catheters are removed. This method is more accurate and more effective than only standard radiotherapy with external fields. In patients after surgery, postoperative radiotherapy is significantly reducing the risk of recurrent breast cancer and death [17].

Chemotherapy is one of the methods of systemic treatment of cancer, consisting in the administration of cytostatic drugs, whose action is directed against rapidly dividing cancer cells. Chemotherapy is used at various stages of breast cancer treatment. It can be used as a single drug (monotherapy) or – it can be a combination of many drugs (polychemotherapy) much more often and is a curative program that prescribes types of drugs, their dose, dosing intervals, route of administration and auxiliary drugs to support treatment. Antineoplastic agents do not have a strictly selective nature, they also affect other rapidly dividing cells, including bone marrow and gastrointestinal tract cells. This form of treatment carries an undesirable effects which most often includes gastritis and myelosuppression. Currently, many cancer diseases are treatable by means of chemotherapy alone or combined with other treatment methods such as radiotherapy or hormone therapy [14, 16].

Adjuvant (complementary) treatment is used in patients after radical surgical procedures in which there is a high risk of dissemination of neoplastic disease due to the presence of unfavorable prognostic factors in histopathological examination. This treatment significantly affects the number of total heals. Neoadjuvant treatment is a pre-treatment used before a radical surgery, in many cases allows a radical operation, which was impossible before chemotherapy [14, 18].

Hormone therapy and targeted therapy

Hormone therapy is a form of systemic cancer treatment that is used when the cancer is hormone-dependent, meaning that estrogen and progesterone receptors are in its tissue. The target of hormonal treatment of patients with breast cancer is the elimination of estrogen effects on cancer development. The benefit of hormone therapy applies only to those who have confirmed the presence of steroid receptors in cancer tissue. In the diagnosis of the tumor type and its biological features, a thick-needle or vacuum assisted biopsy is used. In a situation where the studies did not reveal the presence of steroid receptors and HER2 overexpression, chemotherapy should be considered [14].

The basis of therapy is pharmacology. The common hormonal preparation is tamoxifen. Tamoxifen is an anti-estrogen drug and can be used in women, as in women after menopause. An important system is the exclusion of ovarian function. Pharmacology is currently used for this, for goserelin that is reversible. In postmenopausal women, estrogen production is inhibited by the ovaries and estrogen secretion is activated in tissues such as the liver, muscles and cancer. To eliminate those processes, non-steroidal aromatase inhibitors are used [14, 19].

The choice of the type of hormone therapy determines whether the woman is before or after menopause. Women who did not have menopause can be treated by pharmacological castration with tamoxifen. Tamoxifen or non-steroidal aromatase inhibitors – anastrozole, letrozole are for postmenopausal women. The contraindication to the injection of aromatase inhibitors is otosclerosis [5, 14, 19].

Targeted therapy, like hormone therapy, is a form of systemic cancer treatment. Targeted therapies for breast cancer block the major signaling pathways that stimulate the development of the disease: associated with epidermal growth factor receptors and vascular endothelial growth factor [20].

The epidermal growth factor receptor gene codes for the HER2 receptor. The HER2 receptor has a large role in signal transduction during cell proliferation and differentiation. HER2 overexpression is associated with: higher degree of malignancy of the disease, metastases to axillary lymph nodes and the lack of progesterone and estrogen receptors. The signal pathogenesis of vascular endothelial growth factor plays an important role in tumor formation, since the development of

new blood vessels in the tumor is a necessary condition for growth and metastasis [20, 21].

The epidermal and vascular endothelial receptors of the growth factor are composed of extracellular, endothelial and intracellular parts. Receptor inhibition can be achieved using monoclonal antibodies that bind to the extracellular portion or by using tyrosine kinase inhibitors that block the activity of the intracellular domain. Targeted drugs include trastuzumab, bevacizumab and a small molecule tyrosine kinase inhibitor – lapatinib [20].

Trastuzumab is the only targeted drug used in the standard treatment of breast cancer. Administration of this drug in the advanced stage of cancer allows to obtain remission, extend the time to progression, extend the survival time (by up to 25%) and allows the control of extracranial tumors. Resistance to trastuzumab occurs in 2/3 of patients with disseminated tumor and in a large proportion of patients receiving complementary treatment. The big advantage of trastuzumab and bevacizumab is the activation of the immune system against the tumor cells. The disadvantage of these drugs is the intravenous route of administration, the restriction of penetration at high tumor mass, lack of penetration across the blood-brain barrier, immunogenicity, high price of therapy, the possibility of cardiac complications, musculoskeletal disorders and renal dysfunction [20, 21, 22].

Lapatinib is a new promising drug from the group of small molecule inhibitors of tyrosine kinase. Patients treated with lapatinib have a lower number of brain metastases. The advantage of using this drug is the route of administration (oral), the ability to block other kinases and signaling pathways. The big disadvantage is the high price of therapy and the possibility of diarrhea, neutropenia and cardiovascular disorders occurring during treatment [20, 21, 22].

Breast cancer surgery

The main component of the treatment of breast cancer is surgical resection of the tumor. There are two main surgeries, such as mastectomy and breast conserving surgery with different variants of these procedures. The way of treatment depends on clinical and histopathological situation [23, 26].

The breast conserving surgery involves removing the tumor with a safe margin of ≥ 2 mm of healthy tissue and is associated with postope-

rative radiotherapy that reduces the possibility of local tumor recurrence [24, 25, 27]. Not every patient qualifies for this kind of surgery, it depends on many factors such as tumor size, location, histological malignancy, carrier of genetic mutations, cosmetic effect or patient's consent. The breast is amputated with the skin when there are contraindications to breast conserving surgery. Both types of surgical procedures for the treatment of invasive breast cancer also include lymph nodes. The first is a biopsy of sentinel lymph nodes then, if the metastases are present, the axillary lymph nodes are excised. Lymphadenectomy is a serious procedure with major complications that affect the future quality of life of the patient [23, 26].

Another option for the treatment of cancer infiltrating ≤ 50 mm may be axillary radiotherapy which is less invasive than lymphadenectomy [23, 26, 29]. These operations can be combined with breast reconstruction, but it should be postponed in the event of postoperative radiotherapy. In the case of local or regional tumor recurrence, the breast is amputated and only some patients can be offered a saving treatment again [23]. Elderly patients' surgery is associated with a higher risk of cardiovascular events and stronger negative effects of narcosis, but otherwise Yoshinari Ogawa et al. did not show any significant differences [25]. However, that treatment may be associated with greater systemic postoperative complications, such as severe infections [28].

Treatment method has a large impact on the quality of life of the patient, Rosenberg et al. prove that women who have mastectomy experience more negative symptoms in everyday life than women who have breast conserving surgery [24]. Moreover, the effects of treatment affect the sense of femininity, body acceptance and quality of the sexual life of the patient. Mastectomy has a more negative effect than breast-saving surgery, but in both cases psychological care after surgery is recommended [30, 31].

Rehabilitation and palliative care

Oncological rehabilitation is a key element in the management of breast cancer. It contains whole series of actions aimed at restoring the psychophysical fitness of patients treated for malignant tumors. Oncological rehabilitation can be divided into: preventive – prevents the effects of oncological treatment by reducing the risk of complications and physical

and mental disorders, increasing the probability of disability; healing – restores the proper functioning of the body and improves the quality of life of the patient; palliative – refers to the terminal phase of the disease and increases the independence of the patient [32, 33].

The overriding elements in rehabilitation include the work on restoring the ability of the Activities of Daily Living (ADL) to perform, such as dressing, eating meals, moving, by strengthening muscles and increasing the range of mobility. In the process of rehabilitation planning, real and achievable goals should be set [32, 34].

Before the operation (1-2 days before the procedure), rehabilitation involves learning the basic exercises that will be performed after the procedure. These include: correct positioning of the upper limb on the side operated on a special wedge, learning to breathe the rib and diaphragmatic traverse, and automassage of the limb to prevent lymph stagnation about the area of surgical intervention. In addition, the patient is informed about possible problems and inconveniences associated with axillary lymphadenectomy [32, 33, 34].

Proper hospital rehabilitation begins already on the first day after surgery and lasts about 5-7 days. On the first or second day after surgery, the verticalization is carried out, gradually changing the position from sitting to standing with the help of the therapist and independently. Exercises of the fingers of the hand, upper limb, shoulder girdle on the operated side are aimed at preventing muscular atrophy and assisting the drainage of the lymph. Breathing exercises with resistance and effective coughing help to prevent respiratory disorders. Anti-oedematous prophylaxis consists of lymphatic drainage techniques, limb bandaging and high limb placement on the side operated on a special wedge [32, 34, 35].

After the end of hospital treatment, patients should participate in outpatient rehabilitation conducted in rehabilitation centers or rehabilitation clinics. Thanks to the use of kinesitherapy and other physiotherapeutic methods, the aim is to increase muscle strength and the range of mobility of the upper limb. An important element is the prevention and reduction of lymphoedema by the application of Manual lymphatic drainage (MDL), limb bandaging, Kinesiology Taping and pneumatic massage. In addition, post-operative scar mobilization should be carried out [32, 35].

Palliative care concerns patients suffering from advanced cancer. It is an interdisciplinary activity of a team of specialists aimed at improving

the quality of life of the patient and his relatives. Comprehensive care is provided by a team including: doctors, nurses, medical caregivers, psychologists, social worker, physiotherapists, chaplains and volunteers. Palliative care activities are focused on controlling and eliminating persistent chronic pain, preventing contractures and decubitus ulcers and alleviating symptoms that cause suffering to patients [36, 37].

Discussion

The aim of the study was to show different ways of dealing with breast cancer in older women. Breast cancer in older women is usually detected at a more advanced stage, and these women are much less likely to be included in clinical trials. The same diagnostic and management strategies for younger patients can not be used to treat older patients with breast cancer. Increasing the possibility of enrolling in clinical trials could contribute to improving healthcare for this age group [38, 40].

Due to the presence of more favorable biological features of the tumor, older women are less treated than the standard treatment applied to younger women with breast cancer. Also specific coexisting diseases have an impact on the course of treatment. However, it is worth emphasizing that older women in good health tolerate surgical procedures well and all available screening, diagnostic and surgical procedures should be applied to them [38, 40].

A common dilemma complicating therapeutic decisions during treatment are limiting factors for older people, such as lack of social support, financial difficulties, inferior physical capacity, existence of comorbidities, barriers to providing medical care and side effects related to therapy in the context of life expectancy. Research suggests that age should not be the basis for a decision to treat cancer, as survival data show that older women have comparable results with younger women, in the case of localized and regional disease (within 8 years of follow-up). Unfortunately, older women are much more susceptible to destruction caused by cancer [39, 40].

Breast cancer in elderly women usually has a slow course, with low-grade tumors and estrogen receptors. Women who are in good health should be treated according to standard guidelines, however, those who can not stand or refuse surgery can choose the basic hormonal therapy that is the right option for them. The decision to administer chemotherapy in elderly women is dependent on many factors such as the decline

in the function of organs due to age, the existence of comorbidities, the toxicity associated with the treatment and the expected life expectancy. Unfortunately, the guidelines for chemotherapy for women with breast cancer are very poorly represented in clinical trials. People with severely impaired renal, heart and liver function are often excluded from research, despite the fact that fewer older people are included in them. This is a major problem in the treatment of elderly people and should lead to a lowering of criteria in relation to older people admitted to clinical trials, which could lead to a significant improvement in the treatment of this age group [41].

Conclusions

Breast cancer is a serious problem for many women, but especially the older ones. Its mortality is still at a high level. Obese women who lead unhealthy lifestyle are more expected to become ill, although the most important risk factor is genetic – BRCA1 and BRCA2 mutations. Invasive ductal carcinoma is the most common followed by invasive lobular carcinoma. Women should regularly examine themselves because the first sign of a cancer is a change in breasts and nipples look, symmetry and a tumor placed usually in upper quadrant.

There are a lot of ways to treat breast cancer and it is still a developing matter. Radiotherapy eliminates cancerous cells. It can be used in patients whose operation consisted of excision of the tumor with leaving the breast and in patients after mastectomy with regional lymph nodes removed depending on the histopathological result. It is usually used as an adjuvant therapy after surgery. More accurate is brachytherapy consisting in direct irradiation of lesions by placing the radiation source in the tumor or its vicinity.

Chemotherapy is also commonly used in treating breast cancer. It is possible to use one drug or several cytostatics in combination. Unfortunately, it can have serious side effects such as bone marrow damage or exhaustion. Adjuvant therapy is helpful in eradicating possible metastases and diffuse cancer cells.

Hormone therapy is a great choice of treatment when the cancer has estrogen and progesterone receptors. Women before menopause are treated with tamoxifen and pharmacological castration and postmenopausal women use tamoxifen with anastrozole or letrozol.

When the patient has HER2 receptor then the malignancy of the tumor increases. Trastuzumab is a monoclonal antibody which is a part of targeted therapy against breast cancer with HER2 expression and metastases. It significantly reduces the risk of relapse and increases the response rate. New targeted drugs, such as lapatinib, are being examined and they give promising results.

Breast cancer surgery can remove the whole breast but more common is the resection of the tumor itself. Lymphadenectomy is also performed and the lymph nodes are subjected to a biopsy. Clinical and histopathological situation is a basis of a taken action. Breast conserving surgery is a better option for patient, although it is not always sufficient and then mastectomy is needed.

To improve patient's health and comfort of life rehabilitation and palliative care are essential factors. They can help to achieve progress in activities of everyday life such as eating or moving. Special exercises, massages, drainage-technique and kinesitherapy are recommended to get the best therapeutic effects. Psychological support is usually forgotten but such an important factor in reducing stress, pain and increasing patient's quality of life.

All in all, breast cancer management is an extensive issue with various and still developing methods. Therefore, it undoubtedly will be further investigated so new ways of treatment can be offered and existing ones constantly upgraded.

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