

Advances in the surgical treatment of breast cancer and postoperative physiotherapy

Postępy w chirurgicznym leczeniu raka piersi i fizjoterapia pooperacyjna

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Abstract

In recent years, radical surgical techniques have been replaced with conserving ones, and a sentinel lymph node biopsy was introduced in the case of routine lymphadenectomy. Subcutaneous amputation with an immediate breast reconstruction or radical breast amputation in Madden modification are used in advanced tumours. Breast conserving surgery and effective neoadjuvant therapy reduce the range of the operation and postoperative complications. Similarly, breast reconstructions do not increase the risk of cancer development, and they do not impede the detection of a local recurrence. This paper presents the most commonly used types of surgery used to treat breast cancer, and the possibility of a surgical reconstruction of the breast. The methods of physiotherapeutic management in particular stages of treating women both after radical surgeries and reconstructions, including the aspect of maintaining their physical activity and mental balance are discussed.

Streszczenie

W ostatnich latach radykalne techniki chirurgiczne zostały zastąpione oszczędzającymi, a w odniesieniu do rutynowej limfadenektomii wprowadzono biopsję węzła wartowniczego. W zaawansowanych nowotworach stosuje się amputację podskórną z jednoczesną rekonstrukcją piersi lub amputację piersi radykalną w modyfikacji Maddena. Leczenie oszczędzające oraz skuteczna terapia neoadiuwantowa zmniejsza zakres operacji oraz powikłań pooperacyjnych. Analogicznie rekonstrukcje piersi nie zwiększają ryzyka rozwoju choroby nowotworowej i nie utrudniają wykrycia wznowy miejscowej. W pracy przedstawiono najczęściej stosowane rodzaje operacji wykorzystywanych w leczeniu raka piersi oraz możliwości chirurgicznego jej odtworzenia. Omówiono metody postępowania fizjoterapeutycznego na poszczególnych etapach leczenia kobiet zarówno po zabiegach radykalnych, jak i po rekonstrukcjach, z uwzględnieniem aspektu utrzymania aktywności fizycznej i równowagi psychicznej.

Introduction

Treatment of breast cancer involves a series of activities, the choice of which depends on the histopathological form and progression of the disease. The most important procedure is surgical management. Currently, the standard in breast cancer surgery is breast conserving surgery with a sentinel lymph node biopsy or lymphadenectomy. In advanced tumours subcutaneous amputation with an immediate breast reconstruction or radical breast amputation in Madden modification are performed. Progress in the wide use of oncoplastic operations was possible thanks to the creation of specialized centres called Breast Cancer Unit. Both after radical surgery, causing many undesirable consequences, as well as after more common oncoplastic surgeries, all the women need to have a comprehensive physiotherapy and psychological support.

Surgical methods of breast cancer treatment

In recent years, radical surgical techniques have been replaced with conserving ones, and sentinel lymph node biopsy SLNB was introduced in routine lymphadenectomy [1].

The choice of treatment method depends on the progression of the disease, individual indications, the patient's will, and the surgeon's skills as well as access to systemic treatment. Breast conserving therapy (BCT) is the way recommended according to the TNM staging system based on the assessment of clinical stage. The method of BCS involves excision of the tumour together with an adequate margin of tissue unchanged by the disease and a sentinel lymph node biopsy, or with excision of regional lymph nodes of the armpit – axillary lymphadenectomy [2–4] (Figure 1).

In pre-invasive cancer, breast conserving surgery such as lumpectomy – a local removal of the tumour (Figure 2) or quadrantectomy (Figure 3) – excision of a segment or quadrant of the breast are performed [4].

In this surgery, regional lymph nodes are not subject to excision if the tumour size does not exceed 4 cm. In the case of changes improperly treated, i.e. without a radical excision or supplement radiotherapy and hormone therapy, there is an increased risk of invasive breast cancer – it develops 10 years after the diagnosis in approximately 25–50% of patients [1, 4].

The criterion for the choice of the way of treatment is, among others, Van Nuys Prognostic Index (VNPI), which takes into account the tumour size, the



Figure 1. A patient after breast conserving surgery (BCS) of the left and right breasts with SLNB. Holycross Cancer Centre, Department of Rehabilitation in Kielce



Figure 2. A patient after lumpectomy surgery of the right breast with SLNB. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

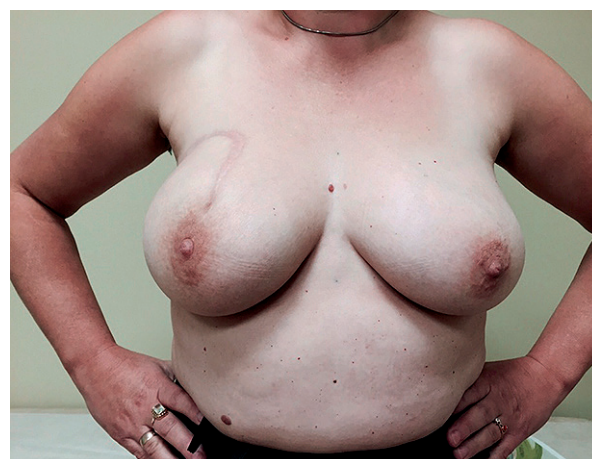


Figure 3. A woman after quadrantectomy surgery of the right breast with SLNB. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

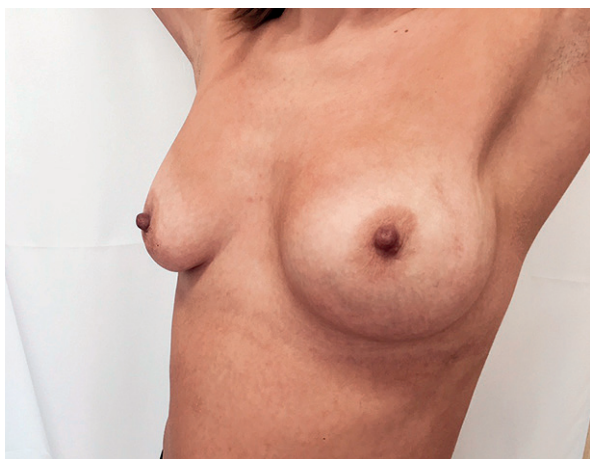


Figure 4. A patient after an immediate reconstruction – left-sided subcutaneous mastectomy which spares the areola and nipple (NSM) and implantation of a prosthesis. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

width of excision margins, the grade of neoplasm malignancy, the presence of necrosis, and the patient's age. The sum of points on the VNPI scale, not exceeding 10, means that a radical excision of a local lesion with a complementary radiotherapy and hormone therapy in the case of positive steroid receptors can be carried out [5].

However, in women with a total score exceeding 10, a straight or subcutaneous amputation with a sentinel node biopsy with an immediate reconstruction of the breast with the use of a prosthesis or expander is performed [1, 6] (Figure 4).

When the presence of risk factors (the presence of mutations of BRCA 1 and 2 genes) is confirmed, a bilateral subcutaneous amputation (mastectomy) with an immediate reconstruction of the breast with the use of an expander or prosthesis is recommended [1].

Reconstructive surgery can be offered to the patients subjected to amputation of the mammary gland. On the other hand, preliminary systemic therapy (neoadjuvant chemotherapy) can be considered in the case of locally advanced cancer, and if there is tumour regression, an attempt to save the breast and even the lymphatic system of the armpit can be made [7].

Studies that compare the effects of radical surgery and breast conserving surgery followed by complementary radiotherapy are still conducted. Their results show that, regardless of the procedure selection, similar results in terms of survival and disease control can be obtained. However, the most noticeable breakthrough has been made in terms of surgery. Surgeries conserving the breast and lymph nodes of the armpit are successfully performed instead of mutilating mastectomy. Comparative studies clearly show that this treatment has similar distant results, both in relation to local recurrence and time free of the disease as

well as total survival. Radical mastectomy is no longer a standard method of local treatment of breast cancer. Breast conserving therapy and effective neoadjuvant treatment reduce the range of the operation and post-operative complications. Similarly, breast reconstructions neither increase the risk of cancer development nor impede the detection of local recurrence [8–10]. Oncoplastic breast surgery (BCT new) is based on two widely used techniques:

- movement of skin-gland flaps to the place of defect,
- replacement of the removed parenchyma with the patient's own tissues [8].

New BCT technique depends on the size of the breast. Movement of the surrounding tissues makes it possible to fill small or medium-sized defects after the excision of breast tumour. The most common method is marginal mobilisation involving the use of tissue advanced flaps. The flaps are formed by separating the adipose tissue located behind the gland at the level of the fascia, which makes it possible to release and move the breast parenchyma to a new location (in relation to the greater pectoral muscle and the chest wall). Preparation of tissues over-fascially needs great cautiousness towards the blood vessels, which are important for blood flow in the prepared flaps [8].

One of many types of oncoplastic surgery is the technique of a so-called flap turned from the glandular tissue, a block excision of tissue around the nipple-areola complex (NAC). The created defect is filled by the displacement of the patient's own tissue. These methods are used primarily for large defects in small breasts, in which too little tissue remains after the surgery. Then, the following is applied, among others: transfer of the pedunculated latissimus dorsi muscle with or without the skin insula, free cutaneous-muscular or muscular flaps based on microsurgical anastomosis (a free TRAM flap – a flap whose pedicle is the rectus abdominis with transversal cutaneous-fatty insula, deep inferior epigastric perforator (DIEP) a flap based on lower abdominal vessels, SGAP – a flap based on the vascularisation from the perforators of the top gluteal artery) [6, 8, 12].

Breast restoration surgery refers to the women who are after mastectomy, and after breast conserving surgeries, if their aesthetic result was not satisfactory. Breast reconstruction should not hamper the assessment of the local state during check-ups after the treatment. These operations can be immediate or delayed. An immediate reconstruction is recommended in the case when the patient expresses her strong will to have it performed, and in the case of not very advanced cancers or regressions of bigger lesions after a successful neoadjuvant therapy. A delayed reconstruction is performed at least 4–6 months after finishing chemotherapy and 12–24 months after finishing radiotherapy, and earlier in patients who do not have adjuvant therapy. Selecting the optimum time for the surgery after radiotherapy is conditioned

by the return of normal function of the bone marrow and the regression of local lesions after irradiation (inflammation, vascular lesions, and fibrosis) [1, 5, 6].

Reconstructive surgery is carried out with the use of the patient's own tissues or synthetic materials – breast implants. An immediate reconstruction has two stages. First, in accordance with the technique of oncological treatment, the mammary gland is removed, but a large part of skin is spared (skin-sparing mastectomy – SSM) – Figure 5, and in some cases, also the areola is spared (areola-sparing mastectomy – ASM) or the nipple-areola complex (nipple-sparing mastectomy – NSM). The second stage includes the reconstruction of the breast eminence and involves a full range of surgical techniques from expanders, prostheses, expander-prostheses to the use of the patient's own tissues. The choice of the method depends on the size and shape of the breast, preferences of the patient, the surgeon's experience, and the expected adjuvant therapy. In patients with a good qualification for surgery, an immediate reconstruction is safe and brings satisfactory aesthetic results without an increased risk of oncologic complications – recurrence of the disease as a result of incomplete excision of the cancer [6].

The delayed technique of the breast reconstruction consists of many stages, which is associated with the applied method. The choice of procedure depends on the appearance and size of the other breast, indications or contraindications of the use of the patient's own tissues, or the use of silicone implants, as well as the patient's preferences [6].

There are three groups of delayed surgery:

- autologous reconstruction, relying on the formation of a breast from pedunculated or free transplants of the patient's own tissues,



Figure 5. A female after subcutaneous reduction surgery of two breasts with sparing of the nipple-areola complex (SSM), with the removal of the sentinel lymph node on the left side. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

- implantation of silicone endoprotheses/expander-prostheses,
- mixed reconstructions, connecting both above techniques.

One of the autologous methods is breast reconstruction with a transverse rectus abdominis myocutaneous flap (TRAM flap) [12, 13].

The advantage of this method is obtaining a breast with a natural look and the ability to rebuild the greater mammary glands. The operation is burdened with the risk of side effects in the form of hernias in the places after the moved rectus muscle of abdomen used as a pedicle. The created long scar and the weakening of the abdominal wall are the major drawbacks of this method. It is rarely performed now [13].

Another more frequently used autologous technique is reconstruction with the use of the latissimus dorsi flap (LD flap), which is moved from the back to the chest by rotation – Figure 6. Thoracic-dorsal vessels are the source of the blood supply. This method is used in women with a small mammary gland or as a complement to an implant (expander or prosthesis) due to the smaller volume of tissue than in the TRAM technique [12, 13].

An alternative to pedunculated flaps are reconstructions, during which skin-muscle flaps from more remote regions of the body can be used. In this case, blood vessels are combined with thoracic internal or thoracic-dorsal vessels and provide better blood circulation in a larger area, e.g. free TRAM flap. Free flaps are often the only chance for smokers, diabetics, and obese women [14].

Breast reconstruction surgery with the use of a tissue expander and implant is performed in women with a small volume of the breast. The expander is positioned below the greater pectoral muscle, and then



Figure 6. A patient after breast reconstruction of the right breast with an LD flap. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

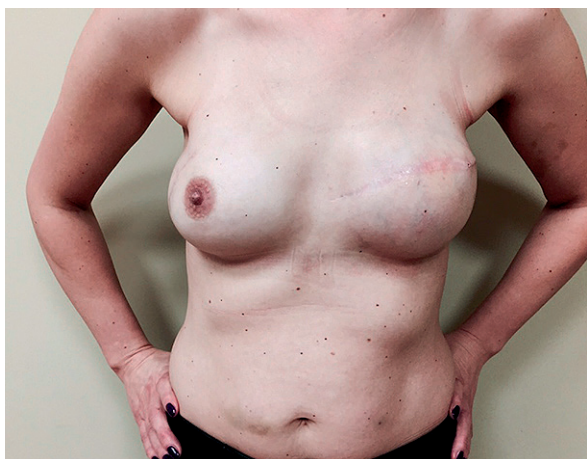


Figure 7. A patient after subcutaneous mastectomy of the right side and the breast reconstruction of the left breast with an expander. Holycross Cancer Centre, Department of Surgical Oncology in Kielce

once every few days it is filled up with physiological saline through a valve placed under the skin. After achieving the desired volume, the expander is left for 3–6 months to fix the stretched tissues. After this period, the patient is subjected to the second stage of treatment. The expander is exchanged for a permanent breast implant through the incision of the old scar [15] – Figure 7.

Another solution in implantation is Becker's expander-prosthesis. It is a dual-chamber device that enables the execution of a single-stage reconstruction surgery and completing one of the chambers with physiological saline up to the expected stretch of the tissues and obtaining the appropriate volume of the breast [15, 16].

A muscle flap or musculo-cutaneous flap from the LD with a silicone implant is mostly used in mixed reconstructions. This muscle is used as a cover of the implant constituting the filling of the breast. The last stage of the delayed surgery is reconstruction of the NAC, often overlooked by patients. It is performed after the final formation of the breast. A suitable size and shape of the nipple is achieved by local plasticity of the skin and the areola by intradermal tattoo [6, 13, 17].

For women with a big asymmetry between the healthy and reconstructed breasts, the recommended treatments are those that restore symmetry: mastopexy (breast lifting), reduction (breast reduction), or augmentation (breast enlargement) [6, 18].

A safe alternative to the existing methods of breast reconstruction is to fill the defect of the breast with transplantation of fat enriched with adipose-derived stem cells (ADSCs) using the Celution 800/crs technology. In contrast to the previously used autologous fat transplantation, this is a method for obtaining a permanent, patient satisfying effect without the necessity

of repeating the surgery [19]. The surgery that uses stem cells involves taking fat from the abdominal area or thighs with the use of liposuction. Stem cells, which are extracted from a part of the obtained fat, are able to transform themselves into the tissue of the body. In the place of the uptake, a network of blood vessels is created, and the fat is implanted. Tissues prepared in this way do not die after transplantation and they are not subject to pathological hypertrophy, which causes unexpected results. A similar method, used mainly in plastic surgery, is transplantation of fat – lipotransfer. After this surgery, atrophy of fat or its growth may occur. This technology is designed for women who, as a result of cancer treatment, have a significant loss of tissue surrounding the scar, and the other breast is small in size. Another indication is post-radiation damage of the skin and soft tissue [18, 19].

Physiotherapeutic management after breast cancer treatment

The primary goal of rehabilitation of women after radical surgical treatment of breast cancer is to prevent complications (lymphoedema of the upper extremity, functional disorders), and to return to full psychophysical health. In Poland, to achieve this, the model of complex physiotherapy developed in the Oncology Centre of the Institute in Warsaw is used [20].

The program includes specific actions implemented during the following periods of treatment: early – hospital, ambulatory – post-hospital, and late – maintaining [21].

Because of the progress of physiotherapy, this model is subject to adaptation, particularly in the scope of post-hospital treatment, in connection with the emergence of new opportunities of using specialised methods in the improvement of mobility, reduction of lymphoedema or pain, and many other dysfunctions in this group of patients [22–24].

Early rehabilitation relies on the introduction of an educational strategy based on the transfer of basic information about the risks and consequences of the removal of lymph nodes of the armpit, and the instruction of motion exercise used in hospital conditions. During this period, rehabilitation should include kinesitherapy of the chest, active and self-supporting exercises of the upper limb in drainage positions, stimulating trophics, and self-service exercises [25].

Exercises introduced on the first days after the surgery facilitate coughing up secretion, reduce the risk of thromboembolic complications, especially in older women, and also have a positive influence on the process of wound healing. During the first 3 days it is recommended to maintain the upper limb on the operated side in elevation in a special wedge in a recumbent position and perform simple active movements in the area of the hand and elbow joints, as well as as-

sisted exercises of the shoulder joint. Such gymnastics should also include breathing exercises through the thoracic and diaphragmatic track and learning how to cough up secretion. Already on the first day after the surgery, in the absence of contraindications, tilting the patient to an erect position takes place. On successive days, the scope and degree of motor exercise difficulty in the area of the shoulder girdle increases. It is recommended to do exercises every 2 h for at least 10 min. Active exercises of the brachial joint in the sagittal plane, with a straight elbow joint in a recumbent position, are added on the second day, and in the other planes of motion on the following day. It is not until the fourth day that the patient can perform the mentioned exercises in a sitting position [21, 25, 26]. Before leaving the surgical ward, the patient should be given a special brochure with instructions of antiedematous and rehabilitation management at home. This is extremely important for patients at risk of lymphoedema, i.e. after armpit lymphadenectomy. The SLNB procedure does not pose a significant risk of the emergence of this complication, because it is only recognised in 3–7% of women after the surgery [27, 28].

After removing the stitches and healing the wound, the patient can launch into ambulatory physiotherapy. At this stage of physiotherapy, the patient is mostly qualified to do self-supportive exercises in relief, to learn self-massage and individual exercises, in which manual therapy techniques, as well as specialised kinesitherapy methods are used [20, 23, 29].

Functional disturbances of the fascial system after radical surgery may appear in the form of painfulness of the scar and its restriction in different directions, which also contributes to myofascial pain in other parts (trunk, limbs, head, and neck). Because of that, it is necessary to introduce techniques of myofascial relaxation to the treatment [29].

Women who have obtained, as a result of earlier rehabilitation, greater range of motion and have a better performance are directed to group exercises that improve their general condition. The duration of ambulatory rehabilitation can vary widely – from several months to several years, until the best possible efficiency is achieved.

In the late period after the operation, it is possible to introduce physical stimuli that depend on the indications and on the individual condition of the patient. Also during progression of the disease and its terminal period, physiotherapeutic treatment brings relief to patients and it is helpful in removing the symptoms of lymphoedema. Because of the chronic nature of the disease, its treatment is another difficult challenge for physiotherapists. Complete decongestive therapy (CDT) is mentioned among the most commonly used and most effective methods of conservative therapy of late complications after breast cancer treatment. The

method is based on simultaneous introduction of four elements: manual lymphatic drainage (MDL), skin care, compression therapy (multi-layer bandaging), and exercises that restore patency. In the first phase of the treatment, these techniques are carried out every day, and as a result the volume of the limb is reduced. After stabilisation of its size, in the second phase of the treatment, the obtained results are sustained by wearing elastic compression products (compression sleeves) and the use of self-massage and exercises, which restore patency at home [30, 31].

There are many discrepancies in establishing a coherent system of measuring lymphedema associated with the treatment of breast cancer (breast cancer related lymphedema – BCRL). Therefore, there is a problem in the unification of the standard rules of treatment [31–33].

Despite this, the described method remains the most commonly used in clinical practice. It may be further combined with other techniques.

One of them is intermittent pneumatic compression – pneumatic massage, which is introduced after manual lymphatic drainage, but before applying multilayer bandages to the upper extremity. The treatment consists of cyclical filling of the chambers with the air, and then emptying them with the use of a pump. Under the pressure, the hydrostatic pressure, lowered in tissues as a result of oedema, increases and the muscle pump facilitating the outflow of the excess of liquid and proteins from endothelium, as well as its penetration and transport to lymph vessels, is supported. Other physical treatments supporting the treatment of secondary lymph oedema are: whirl massage of limbs and instrument vibratory massage (in the case of hard consistency of oedema), and deep oscillation (electrostimulation of lymphatic vessels). In turn, lymphatic applications of kinesiology taping cause the improvement of blood and lymph circulation, which results in an effective reduction of stasis and lymphoedema [30, 34, 35].

They can be used both as an independent treatment method as well as a perfect complement to KFTU [36].

If left untreated, lymphoedema is the cause of complications dangerous to health and life due to the risk of developing recurrent inflammatory states of vessels, paresis and paralysis, elephantiasis, and lymphatic angiosarcoma (Stewart-Treves syndrome) [25, 37].

A slightly different range of improvement applies to patients undergoing reconstructive surgery. Before the delayed surgery, the management depends on the local state after mastectomy and the expected method of reconstruction. The main aim of physiotherapy in this period is to lead to the elasticity of the scar, which is achieved by the use of massage, mobilisation of the scar, and iodine iontophoresis, as well as the maintenance or improvement of the movement ranges of the

arm through participation in kinesitherapy. Adequate preparation of the uptake site before surgery with the use of the TRAM flap relies on strengthening the abdominal muscles, and with the LD flap – the dorsal muscles. The postoperative procedure after implantation of expander-prosthesis or expander, after healing the wound, requires massage to prevent shrinkage of the connective-tissue capsule around the prosthesis, the creation of which worsens the cosmetic effect of the reconstructed breast. Physical exercises of the shoulder girdle in full range are recommended 1 month after the operation. In the earlier period – limiting the range of motion of the limb to 90° to prevent movement of the implant in an undesired direction beyond the natural space of the breast, and exercises of the shoulder girdle without excessive work of the greater pectoral muscle. It is also recommended to apply specialised belts above the reconstructed breast for the whole period of completing the expander [38].

In the early period and for further 3–4 weeks after TRAM surgery, in which the patient's own tissues have been used, flexion position of the trunk and lower limbs (cradle position) is ensured in order to relax the abdominal muscles. Then breathing exercises along the thoracic track, with the assistance of the treatment places, with the use of training simulators for practicing forced expiration, and antithrombotic exercises are introduced. On the successive days, the patient sits down with lower limbs lowered and walks with a walker with a bent position of the trunk and starts active exercises of the upper limbs. In the postoperative period, patients should wear underwear modelling the reconstructed breast and do breathing exercises through diaphragmatic route, and broaden the scope and time of active exercises of the upper and lower limbs. In the conditions of ambulatory rehabilitation, a slow return of the trunk to the upright position takes place, but then it is necessary to provide an elastic belt for prevention of abdominal hernia. It is also necessary to introduce exercises stretching the chest, reinforcing the strength of the dorsal muscles and lower and upper limbs muscles, and after 2–3 months the walking distance should be lengthened. After 3 months, exercises developing general condition are done, gradually and carefully isometric exercises of the abdominal muscles without the participation of the abdominal pressure (with bent hip joints) are introduced, and after healing the wounds – massage of the area around scars. After the reconstruction of the flap from LD, during the early hospital period, a semi-sitting position is taken, and the range of exercise includes: breathing exercises, which stretch the muscles of the chest, without exceeding the limit of pain (up to 90° of the bending angle in the shoulder joint). In the period 6–10 days after the surgery, slow active exercises of upper limbs and exercises relaxing dorsal muscles can be done. After these surgeries it is

also recommended to wear special bras which maintain the correct shape of the reconstructed breast. Breathing exercises, active exercises of dorsal muscles, and exercises stretching the chest are done after three months, and after healing the wound – massage and mobilisation of the scar and the reconstructed breast. Throughout the period of improvement, it is necessary to follow the rules of antioedema prophylaxis [38].

After immediate breast reconstruction surgery, similar principles of rehabilitation, as after the delayed one, apply. Diagnosis of cancer is one of the most important factors impairing the quality of life. Immediate hospitalisation is associated with tremendous stress, a sense of loss of control, and difficulty in adaptation to a new role and social situation, regardless of the type of the applied treatment (mastectomy or conserving surgery). At each stage of the treatment, patients need holistic care, which also takes into account psychological aspects. But the diagnosis and treatment of breast cancer may also cause positive changes in the lives of women. These transformations relate to paying more attention to family and friends, greater acceptance and verification of purposes in life. Thanks to the disease, patients adapt well to deal with the specific requirements of the stressful situation. This commitment creates a sense of regaining control and improvement of self-esteem, provided that the patient is aware of the benefits resulting from the participation in meetings with a psychologist and is willing to be subject to such a form of therapy [39].

After finishing oncological treatment, women should continue taking care of the acquired physical fitness. In the late period of physiotherapy, it is recommended that they take an active part in activities organised by clubs of Amazons and to benefit from rehabilitation in conditions of sanatorium treatment. The task of women associated with the clubs is to provide support and find motivation to return to health, to achieve the best possible quality of life and to educate the public on the prevention, early detection, and treatment of breast cancer [40].

Good methods of maintaining physical activity are: swimming, walking, Nordic walking, yoga, tai chi, and running [21, 25, 40]. March training of a Nordic walking nature has a positive impact on the quality of life of patients after breast cancer treatment by reducing anxiety and depression, and improving functioning in the psychological and social spheres [40].

Systematic improvement and physical activity contribute to the improvement of movement ranges of the upper limb joints, effectively prevent an increase in lymphatic oedema and obesity, but also prevent the recurrence of the disease and increased mortality [26].

Today, women can freely participate in treatment during their stay in a sanatorium. They get a request to such treatment a minimum of 12 months after

completing the anticancer therapy. It is significant in the comprehensive rehabilitation because of climatic benefits, the possibility of mental rest from everyday responsibilities and worries, and the opportunity to benefit from exercises in water or practicing sports safe for them [21, 40].

Conclusions

In Poland increasingly better access to minimally invasive surgical methods and techniques of oncological surgery used in the treatment of breast cancer are observed. Modern treatment of breast cancer is based on collaboration of surgeons, oncologists, radiotherapists, physiotherapists, and psychologists in order to provide the fewest possible number of complications and dysfunctions of the limb, until a complete recovery. Early introduction of post-operative physiotherapy and its continuation later during the whole period of convalescence maintains physical efficiency and mental balance. The authors have obtained written consent from the subjects and the head of the clinic to use the images for publication.

Conflict of interest

The authors declare no conflict of interest.

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