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Complications of Surgical Treatment of Breast Cancer

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Abstract

Introduction: *Breast cancer is a serious medical problem. Surgical treatment is often the basis of breast cancer treatment. However, it is associated with numerous complications that both patients and doctors should be aware of.*

Results: *Complications of surgical treatment of breast cancer are very diverse and may appear both during surgery and months after surgery. Intraoperative complications include vascular or nerve damage, whereas hematoma and postoperative wound infection may appear in the early postoperative period. An important and relatively safe procedure during surgical treatment of breast cancer is sentinel node biopsy. If lymph node metastases are confirmed, lymphadenectomy is required. It is associated with many short- and long-term complications and the most dangerous and most difficult complication to treat is lymphoedema. Complex Decongestive Physical Therapy (CDPT) is considered the most effective form of lymphoedema treatment. Axillary Web Syndrome is also a specific complication after breast cancer treatment. Breast loss is also associated with many adverse changes in the mental sphere of patients. Breast reconstruction has become an important part of treatment in breast cancer. Despite its numerous advantages, it also leads to serious complications such as capsular contracture, breast deformation and fat necrosis. Their occurrence varies depending on the reconstruction method used, the time it was carried out and the use of radiation therapy.*

Conclusion: *Surgical treatment of breast cancer has many complications, but surgery is a rapidly growing field, so there is a chance that the quality of life of patients after surgery will improve in the future.*

Key words: *breast cancer, surgery, complications.*

Introduction

Breast cancers are the most common cancers in the developed countries. In Poland, they are responsible for about one-fourth of cancer cases. This disease is a serious problem especially among older women [1].

The way of treatment depends on the patient's clinical and histopathological situation [2]. In general lobular carcinoma in situ does not require local and systemic therapies, but patients should be offered information about chemoprevention with selective estrogen receptor modulators and should undergo rigorous breast cancer surveillance. Ductal carcinoma in situ is treated with breast-conserving surgery and radiation therapy because it can progress to invasive cancer. It does not require further lymph node dissection or systemic therapy. Stage I and II breast cancers are usually treated with breast-conserving surgery, radiation therapy and adjuvant systemic therapy that depends on lymph node involvement, hormone receptor status, ERBB2 (formerly HER2 or HER2/neu) overexpression, and patient age and menopausal status. Stage III breast cancer depending on the situation first requires chemotherapy induction, followed by breast-conserving surgery, or the mastectomy as well as axillary lymph node dissection and chest wall radiation. In stage IV the prognosis is usually poor and often the treatment is palliative [3].

Surgical treatment of breast cancer provides the best chance of recovery. However, at the same time, it creates the possibility of serious complications not related directly to the course of the disease but the treatment used. Complications may occur both during and immediately after surgery, but they can also appear many years after surgucal treatment [4]. Therefore, both doctors and patients must be aware of possible complications and risk factors that increase the rate of these.

Early postoperative complications

Intraoperatively, there is a risk of an accidental damage to blood vessels including the axillary vein, as well as cutting or nerve damage leading to

sensory disorders and motor defects [5]. Among patients subjected to modified radical mastectomy, those who were smokers, diabetics and persons subjected to past chest irradiation, were more likely to encounter complications during an operation [6]. Other complications also include hematoma or surgery site infection [7]. In the case of mastectomy with immediate reconstruction, postoperative wound complications can accelerate implant loss and affect the cosmetic result [8]. After surgery, the range of motion in the upper limb may decrease [9]. Shoulder dysfunctions that are a complication of surgical treatment of breast cancer are believed to be a predisposing factor for rotator ring disorders [10]. Other complications include chronic postoperative pain occurring after both lumpectomy and mastectomy, and its frequency varies from 25 to 60% [11]. It is often associated with damage to the intercostal nerve [12]. Discomfort applies not only to the breast, but also to the armpit or shoulder area and may last up to 2–3 years after surgery. In addition to physical ailments, pain is also associated with increased levels of mental stress, anxiety and even depression. Treatment methods include analgesic pharmacotherapy, physical therapy, and mind-body exercises that also reduce stress and fatigue [13].

Research indicates that up to 20–33% of women report lymphoedema and other dysfunctions within the shoulder, arm or breast for at least a year after treatment [10]. The risk factor for edema is overweight and obesity [13]. If lymphoedema occurs in the breast, it is recommended to use properly fitted, seamless underwear that supports the breast well [14]. As a result of the accumulation of lymph fluid or blood plasma, seroma may form [15]. According to the available data, it appears in 15 to 85% of patients causing pain and reduced movement [16]. The presence of seroma results in an increased risk of infection, skin flap necrosis, delayed wound healing, reduced comfort, as well as delayed implementation of adjuvant therapy [15,16]. It seems that closing the dead space after mastectomy using a variety of techniques with the use of tissue adhesives or suction drainage may be important in avoiding the formation of seroma [15,17]. The presence of this complication depends on many variables.

Risk factors after modified radical mastectomy include breast volume, obesity, hypertension, and tamoxifen and heparin [6]. The conclusions of another study show that when comparing modified radical mastectomy and broad local excision, the only predictor is the type of surgery, whereas age, number of axillary lymph nodes removed, or neoadjuvant chemotherapy are not significant [17].

The type of surgery and technique used also play an important role. It has been proved that the volume and time of outflow of serous fluid is smaller after complete mastectomy with only sentinel node taken compared to axillary lymph node excision [18]. However, the use of electrocoagulation increases the risk of seroma formation [17]. The use of this technique causes thermal tissue damage initiating an inflammatory reaction leading to disturbance of lymphatic flow. However, it is used during breast resection because blood loss is less compared to using a conventional scalpel [16]. However, the use of a harmonic scalpel reduces the chance of seroma formation, while reducing intraoperative blood loss [17,16].

Complications of surgical removal of axillary lymph nodes

Axillary lymph nodes dissection (ALND) is indicated in the case of confirmed lymph node metastases [19]. This procedure affects systemic therapy planning and the provision of prognostic information. Moreover, evidence suggests that patients who have no axillary lymph nodes removed at all are at increased risk of locoregional recurrence, which means regrowth of cancer in the breast, mastectomy scar area or underarm glands. However, surgical removal of axillary lymph nodes can lead to short-term surgical complications and long-term problems. Short-term adverse events include acute local surgical complications, such as hematoma, infection, delayed healing, brachial plexus injury and acute systemic complications, such as chest infection, deep venous thrombosis, pulmonary embolism, cardiac failure, cardiac ischemia and cerebrovascular accident. Long-term complications of surgical removal of axillary lymph

nodes are lymphoedema, shoulder stiffness, arm or shoulder movement impairment, loss of functional capacity, paresthesia, numbness, pain, winging of the scapula and wound contracture or scarring [20].

If the patient has clinically negative lymph nodes, intraoperative sentinel lymph node (SLN) biopsy should be performed [19]. This procedure is safe, has high sensitivity and the results show the current state of the lymph nodes [21]. The American College of Surgeons Oncology Group trial Z001 has confirmed the hypothesis that "Sentinel Lymph Node Dissection (SLND) results in fewer postsurgical complications overall than using SLND and ALND. Approximately 75% of the ALND patients had a complication, compared with 25% of the SLND patients" [22].

It is revealed that ALND is a significant predictor for developing a wound infection and axillary seroma. Also, it is a risk factor for axillary paresthesias at 30 days, probably because intercostobrachial nerve rupture is more likely during this procedure. Also, the number of nodes removed is a significant predictor for the development of paresthesia for ALND arm. The risk factor for developing seroma after ALND is older age, while a greater BMI predisposes to wound infections that appear to be unaffected by the age and number of nodes removed [22].

One of the most severe and difficult-to-treat complications of surgical treatment is breast-cancer related arm-lymphedema (BCRL). It is defined as a chronic swelling of the arm and sometimes concomitantly of the breast or trunk. This is caused by an accumulation of protein-rich interstitial fluid, which leads to chronic inflammation with later fibrosis. The symptoms of BCRL include not only abnormal swelling but also pain in the affected arm, skin fibrosis, arm heaviness and impaired shoulder or arm movement. These lymphedema-associated symptoms were found to be significant for the detection of BCRL because objective assessments, such as limb volume change measurement, might not detect all grades of BCRL [23]. There are also blood flow disorders and neurological complications observed. Increased susceptibility of the skin to injuries may result in the discharge of the lymph and recurring infections. All this results in aesthetic problems which often cause stress and emotional problems [24].

Approximately one in five patients after breast cancer treatment will develop BCRL. Although the data concerning the occurrence of lymphoedema following mastectomy is diversified and ranges from 5.5 to 80% of all cases. That may be related to the method of measurement, length of follow up and type of treatment. Almost 90% of BCRL appears within the first two years after treatment, however in some cases, fluid may accumulate for a much longer period, although at a slower rate [23,24].

There are risk factors associated with more frequent lymphoedema. A lot of research has been done to identify the most important, but the results are inconclusive. Some studies report that significant risk factors for the occurrence of BCRL are adjuvant chemotherapy, postoperative complications, and nodal stage [23]. According to another study, adjuvant chemotherapy and neoadjuvant chemotherapy with a taxane, ALND, supraclavicular radiation therapy, the number of dissected axillary lymph nodes over 10 and the advanced stage at diagnosis are identified as independent risk factors for lymphedema. Factors not significantly associated with lymphedema included age and BMI. Chronic arm swelling also showed no association with the type of surgery [25]. But other studies maintain that high BMI is one of the most important risk factors of lymphoedema and the type of therapy, lateralization of cancer, stage and the number of metastatic lymph nodes do not increase substantially the risk of lymphoedema [26]. According to trial Z0011 having had an ALND was not a significant predictor of lymphedema at 6 months, but it was significant at 1 year and afterward. That is why doctors may overestimate the incidence of lymphedema after ALND and underestimate it for SLND [22].

The lack of proper treatment leads to the progression of the lymphedema and that is why the therapy of the patients with BCRL must be started as early as possible [24]. Conservative treatment, such as physiotherapy and pharmacotherapy and surgical treatment, is used to reduce lymphedema. Among the operations performed on patients with lymphoedema, two large groups can be distinguished: reducing operations and reconstruction operations. Reducing operations involve the excision of

swollen fibrotic subcutaneous tissue of the limb and sometimes also the skin, while the reconstruction operations are lymphatic-venous anastomosis and lymphatic transplants [27]. However, nowadays Complex Decongestive Physical Therapy (CDPT) is considered to be the most effective form of conservative treatment. It consists of two phases: intensive edema reduction and maintaining the result achieved and prevention of the recurrence of edema [28]. Patients are also encouraged to take care of the skin, place their limb in a special sling above the level of the chest throughout the night and do the exercises adjusted individually [24].

To prevent complications it is recommended to avoid the trauma, prevent the infection and apply closed suction drainage after ALND. Patients should be encouraged to exercise the limb to minimize stiffness and frozen shoulder. Surgeons should preserve the intercostobrachial nerve whenever possible to minimize the risk of numbness or paresthesia of the arm. And of course the most important in the prevention of that harmful complications is early diagnosis and sentinel lymph node procedures [29].

Axillary web syndrome

A fairly specific complication of the surgical treatment of breast cancer is the axillary web syndrome also called the axillary cording [30]. There have been some cases reported in which AWS occurred in patients without breast cancer – one was secondary to axillary folliculitis and the other occurred after sentinel node biopsy in the course of melanoma diagnosis [31]. This syndrome usually develops within a few weeks after surgery, however, in some cases it manifests later than in the early postoperative period, and also persists up to 18 months after surgery or is recurrent. Clinically it manifests as one or more stringy resistance within the armpit, visible or palpable only [32]. The fibrous strands can extend all the way to the elbow bottom and even to the palm surface of the wrist. Cords cause limitation of shoulder movement and pain in abduction [9,13,33,34].

There are various determinants that increase the risk of this disorder. Among them there are: more radical procedures such as contralateral prophylactic mastectomy, a greater number of lymph nodes removed, younger age and the use of complementary chemotherapy or radiation therapy [9,13,32,33]. Lower BMI is also predisposed to occurrence of axillary web syndrome [13,32,33]. The correlation between AWS and body weight is not fully understood. It is suggested that obese women experience diagnostic difficulties because the fibrous bands are hidden under a layer of excessively developed adipose tissue [33]. Another hypothesis assumes that the formation of this syndrome is part of the body's physiological response to damage to lymphatic vessels and in women with high BMI this response is suppressed because obesity adversely affects wound healing [32].

It is suspected that iatrogenic damage to the lymphatic or venous system leading to local stasis, hypercoagulability, and consequently inflammation within the affected vein or lymphatic vessel is involved in pathogenesis. It was also considered whether AWS is a variant of Mondor's disease, or superficial thrombophlebitis, including the pectoral veins or the dorsal vein of the penis [32,35]. However, recent studies exclude this hypothesis. Another concept assumes that after damage to the lymphatic system, vessels attempt to recanalize and connect to existing vessels to remove excess lymph and restore flow. By mistake, instead of attaching to a vessel, they can connect with the subcutaneous tissue and thus form cords [32].

Axillary web syndrome has been identified as a risk factor for long-term impairment of the function of the affected limb and for changes in the movement pattern, which is why early implementation of appropriate therapy plays an important role [9,32,33]. For this purpose, physical therapy is used, i.e. massage, lymphatic drainage, tissue stretching and pharmacotherapy in the form of nonsteroidal anti-inflammatory drugs and opioids [9,14,34]. The use of thermotherapy remains a debatable issue, as the heat makes collagen more elastic, which improves the range of motion of the limb, but on the other hand high temperature dilates the vessels, thereby increasing the chance of lymphoedema [34].

Psychological complications

Breast loss is a traumatic experience in a woman's life. After treatment, patients often feel anxiety associated with the risk of recurrence, metastasis and, consequently, death. It is paired with traumatic memories related to the fight against illness. In conjunction with chronic fatigue and abandoning previous passions, it can contribute to depression and even the appearance of suicidal thoughts [36]. Some studies have noted that the symptoms of mental disorders after surgical treatment of breast cancer show some similarity to those of post-traumatic stress disorder [37].

Breast amputation has the strongest effect on how one's body is viewed, because this particular part of it is identified with the symbol of femininity and motherhood [36,38]. The change in appearance means that women often do not feel attractive and confident. This negatively affects their interpersonal relationships, often causing them to withdraw from social and even family life. Satisfaction with the sexual activity plays an important role in assessing the quality of life after mastectomy [36]. Studies show that the level of satisfaction with intercourse is higher in married women than unmarried women [39]. Negative self-assessment after mastectomy is also prevented by a high level of general mental resistance [37].

Physical activity plays a significant role in returning to mental well-being. Regular exercises improve the functioning of the limb, which in turn translates into more efficient performance of daily activities [36]. Movement has a positive effect on the quality of life, reduces fatigue and improves sexual functioning [40]. An important role during the convalescence also play associations such as Amazons, where women can exchange their experiences and be a source of motivation for one another, among others to maintain an adequate level of physical activity [36]. In the recovery process, the patient's age and the support of relatives also play an important role, as shown by studies in which it has been proven that older people living together with family members experience greater satisfaction with social life [39].

Complications connected with breast reconstruction after mastectomy

Breast reconstruction following mastectomy has become an integral part of the comprehensive treatment in breast cancer [41]. The operative breast reconstruction aims to achieve satisfactory aesthetic effects, to prevent negative psychological effects, improve the quality-of-life and, interestingly, the reconstruction also affects the maintenance of correct body posture. Patients undergoing radical mastectomy have got static disorders of the trunk and they tended more to lean forward, while the posture of women after immediate reconstruction is comparable to the posture of healthy women [42]. Despite these advantages, breast reconstruction surgery is associated with many complications, which vary depending on the method of reconstruction, the time of its implementation and the use of postmastectomy radiation therapy [43].

There are complications common to every type of breast reconstruction such as wound dehiscence, infection or systemic blood circulation disorders. There are also specific complications observed depends on reconstructive techniques [44].

Implant-based breast reconstruction is one of the oldest but also the quickest, relatively the easiest and the most popular method of breast reconstruction. This technique provides an excellent aesthetic result, but common local complications include capsular contracture and implant rupture, which is caused by a thin layer of skin remaining after mastectomy and not providing reliable coverage of the implant. That is why often before inserting the implant the expander-based breast reconstruction technique is used. The main drawback of skin expansion is frequent outpatient visits, for example, to gradually fill the expander or remove it which is associated with an increased incidence of complications. After the implant-based reconstruction breasts can look unnatural and asymmetrical because the implant is always more or less fixed to the patient's chest and therefore often requires adaptive surgery of the contralateral breast to achieve symmetry. The formation of a capsular contracture enhances breast deformation [45]. The placement of the implant in the context of

complications is also important. Placing the implant behind the pectoralis major muscle provides a better aesthetic appearance and the lowest incidence of capsular contracture. However, that technique is associated with pain and functional impairment of pectoralis major muscle and rarer complications such as necrosis, seromas and implant loss [46]. Prepectoral breast reconstruction is recommended for those whose lifestyle requires extensive use of the pectoralis major muscle. In addition to various reconstruction techniques, to prevent postoperative complications and to achieve a better cosmetic effect, implants are improved and acellular dermal matrices are used [47].

Another method of breast reconstruction is autologous breast reconstruction that has the advantage of providing superior long-term aesthetic results. This method also has many variations, mainly regarding the donor site. Option using the latissimus dorsi muscle transferred from the back can be associated with highly visible scars, contour deformity, backache and atrophy of the muscle, which almost always requires an implant to restore volume, which exposes the patients to an accumulation of the two technique's morbidities. Abdominally-based flaps seem to be a preferred option for breast reconstruction, but it is not free from defects. That method is also technically more demanding and special infrastructure is needed, as compared to implant-based breast reconstruction [45]. Abdominal donor-site complications included hematoma, wound dehiscence, wound infection, donor site necrosis, chronic fat necrosis, seroma, abdominal wall bulge, laxity or hernia, muscle weakness, contour deformity and hypertrophic or keloid scarring. Breast complications include hematoma, wound dehiscence, wound infection, mastectomy skin flap necrosis, partial or total flap loss, chronic fat necrosis, seroma, and hypertrophic or keloid scarring [48].

Autologous fat grafting using non-vascularized lipoaspirate fat has recently become a more and more popular method of breast reconstruction and correct post-surgical irregularities. It is less invasive than other methods, it does not induce foreign body reaction and allows for excellent aesthetic effects. Researchers assure the safety of this method, but

common complications associated with that method include cyst formation, fat necrosis, infection, microcalcifications, which may be difficult to distinguish from breast cancer in imaging tests, sometimes there are also breast cancer recurrences and the need for reoperation. Future studies are still needed to evaluate the safety, effectiveness, and efficiency of autologous fat grafting procedures to the breast [45,49].

Patients undergoing any breast reconstruction method are more likely to develop complications than those receiving mastectomy without reconstruction but autologous reconstruction seems to be a more intensive surgical procedure that requires longer initial hospitalization and more frequent rehospitalization than others [50].

Also, the time of reconstruction surgery contributes significantly to a different number of complications. Immediate breast reconstruction is currently increasingly preferred because of reducing the total number of surgical procedures, lower costs as well as significant psychological effects and a neutral impact on the further therapeutic decision. However, regardless of the method used, it is associated with increased frequency of complications such as wound contracture and reconstituted deformation breasts, which requires additional treatments and increases the costs compared with delayed breast reconstruction [44]. Some studies report that "complications after immediate implant-based breast reconstruction are higher than recommended by national standards" [51].

Based on the research, whose results nevertheless often differ from each other, there are identified risk factors for complications regardless of the method used such as smoking, increased BMI, time operation, and the experience of the surgeon performing the procedure [45,52]. Also, radiation therapy seems to be an important factor in increasing the risk of complications. It increases the frequency of infection in all patients after breast reconstruction as well as the complications specific to each method [50].

All in all, there is no single right choice and indication for breast reconstruction. Decision making should take into account the quality of life, surgical outcomes, radiotherapy history, cosmetic results, and life expec-

tancy. That is why breast reconstruction should be personalized at its best and doctors should help patients to be aware of their decision [43].

Discussion

The purpose of this article was to present the complications of surgical treatment of breast cancer, including reconstructive procedures. Complete recovery is most likely by means of surgical techniques, but they carry the risk of various complications both during surgery, in the early postoperative period and many years after treatment [4]. Their occurrence depends on the coexistence of many different variables, depending on the type of intervention and also on the individual conditions of the patients. Among other things, the impact of BMI on the risk of developing lymphoedema of the upper limb remains debatable – according to one study it is not a statistically significant factor [25,26]. Also, the relationship between the BMI value and the occurrence of axillary web syndrome is not clear. Perhaps it results from diagnostic difficulties caused by excessively developed adipose tissue or from suppression of physiological healing reaction in obese people [32,33]. Some scientific reviews report that ALND is associated with increased survival among patients compared to those who did not undergo this procedure [20]. However, other sources maintain that ALND does not affect patients' survival, but only allows assessment of cancer stage and regional control of the disease [19]. It is uncertain whether no axillary surgery increased the risk of distant metastasis compared with ALND [20].

Further research also requires fat tissue transplantation used during autologous fat grafting breast reconstruction, as it has been noticed that with residual glandular tissue – as in the case of BCT – the presence of progenitor cells within adipose tissue can accelerate disease progression and increase the risk of spreading the cancer [45]. It is necessary to conduct further research in order to improve existing techniques, including those used during reconstruction, as well as to develop new schemes of surgical procedures to prevent and cover the treatment of these com-

plications. The review of the literature presented can also help medical staff postoperatively care for patients, thanks to expanding knowledge of complications, which will translate into their faster diagnosis and early implementation of appropriate treatment. Better treatment of complications will also positively affect the quality of life of patients.

Conclusions

Breast cancer is a global problem because, according to data, it remains one of the most-diagnosed cancers in developing countries, and in Poland accounts for 25% of diagnosed cancers. The treatment regimen depends on the histopathological diagnosis as well as the patient's clinical situation. The use of surgical intervention creates the most certain possibility of cure, however, it is associated with numerous complications, which both doctors and patients should be aware of. During the procedure, blood or lymphatic vessels and nerves, especially the intercostal nerve, may be damaged. Many women also have chronic postoperative pain as well as lymphoedema and other dysfunctions in the upper limb and breast. Lymphoedema is one of the most severe complications after surgery to remove lymph nodes, occurring in every 5 patients within 2 years of surgery. It results from the accumulation of interstitial fluid, which in turn leads to the development of inflammation and subsequent fibrosis. BCRL definitely reduces the comfort of life by adversely affecting the aesthetic sphere and causing physical ailments. In its treatment, pharmacotherapy, physical methods, as well as limiting and reconstructive operations are used. However, acute complications after removal of lymph nodes include infection, hematoma, pulmonary embolism or stroke.

Another disorder within the upper limb may also be an axillary web syndrome manifested by the appearance of stringy resistance within the armpit, which can reach even to the wrist. The pathogenesis of this phenomenon has not yet been clearly explained. The occurrence of this syndrome predisposes to a chronic change in the movement pattern and impaired limb function.

The appearance of seroma predisposes to the occurrence of secondary complications such as skin flap necrosis or the development of infection. However, using a harmonic scalpel instead of a conventional one prevents the formation of seroma, while limiting intraoperative blood loss.

An important aspect that we should not forget is the impact of surgical treatment of breast cancer on the psyche of patients. Breast loss has a significant impact on the perception of one's body, often resulting in a lack of acceptance of a change in appearance, which adversely affects social ties, family relationships and sex life. Anxiety, depressive disorders and suicidal thoughts may also appear. That is why it is important for medical staff to encourage patients to take up physical activity, enroll to associations such as Amazons, and to use psychological help. Post-mastectomy breast reconstruction can also help to improve quality of life. However, it should be remembered that systemic circulatory disorders or infection may appear irrespective of the type of technique used, and there are also specific complications such as capsular contracture and implant rupture or fat necrosis and oil cysts after using non-vascularized lipoaspirate fat. Dynamic development in the field of surgery, brings hope that future treatments and surgical procedures will have a lower risk of developing complications than at present.

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