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MODERN CONCEPTS ABOUT POSTMASTECTOMIC LYMPHODEME, METHODS OF ITS TREATMENT AND PREVENTION

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Таянч сўзлар: лимфадема, постмастэктомик, сут бези раки.

The article presents data on postmastectomy lymphedema, the causes of its development, and the main directions and stages in the development of methods for conservative and surgical treatment of lymphedema of the upper extremities, both domestic and foreign authors. In particular, ways to prevent post-mastectomy lymphedema of the upper limb are presented.

ПОСТМАСТЭКТОМИК ЛИМФОДЕМА ҲАКИДАГИ ҲОЗИРГИ ЗАМОН КАРАШЛАРИ, ДАВОЛАШ УСУЛЛАРИ ВА ПРОФИЛАКТИКАСИ

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Ушбу мақолада постмастэктомик лимфодемалар ҳакидаги маълумотлар баён этилган, уни келиб чиқиш сабаблари, асосий йўналишлари ва ривожланиш босқичлари, лимфадемани консерватив ва хирургик даволаш борасида хорижий ва махаллий муаллифларнинг карашлари акс эттирилган. Шу жумладан кўлдаги постмастэктомик лимфадемани олдини олиш буйича профилактик чора – тадбирлар баён этилган.

СОВРЕМЕННЫЕ ПРЕДСТАВЛЕНИЯ О ПОСТМАСТЭКТОМИЧЕСКОЙ ЛИМФОДЕМЕ, МЕТОДАХ ЕЕ ЛЕЧЕНИЯ И ПРОФИЛАКТИКИ

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В статье представлены данные о постмастэктомической лимфедемы, причины ее развития и основные направления и этапы развития методов консервативного и хирургического лечения лимфедемы верхней конечностей, как отечественных, так и зарубежных авторов. В частности представлены пути профилактике постмастэктомической лимфедемы верхней конечности.

Breast cancer over the past 10-15 years has occupied the 1st place in the structure of oncological morbidity in women (Kaprin A.D. et al., 2015), and a significant part of them are women of working age. Thus, the problem of medical rehabilitation of this category of patients acquires a social aspect (Komova-Polevaya E.B., Chistyakov S.S., 2006; Puzin S.N. et al., 2010). Against the background of radical treatment of breast cancer, especially when it is accompanied by lymphodessection or radiation therapy, a complex of functional disorders occurs, in which the leading place belongs to lymphatic edema of the upper limb on the side of the operation or the so-called post-mastectomy lymphedema, the presence of which contributes to the disability of patients and this negatively affects their psychological state and thus worsening the quality of life. (Andronov O.V., 2007; Zerkalov V.N., 2009; Strozhev S.V., 2014; Grushina T.I. et al., 2016). Lymphatic edema of the upper limb is not an indispensable complication of radical treatment of breast cancer.

This is due to the fact that the lymphatic structures have sufficient regenerative capacity and in some patients new lymphatic collaterals are formed. In their absence or failure in the occurrence of lymphedema, various factors become important. Of the associated factors in the development of lymphatic edema of the upper limb, the leading one is regional lymphodessection, which is performed with various types of radical operations. Due to the fact that, until recently, radical mastectomy according to Halsted-Meyer, according to Patey, according to Madden, was performed in the

surgical treatment of breast cancer, doctors began to call the edema of the upper limb “post-mastectomy edema” or “post-mastectomy lymphedema”. The volume of lymphadenectomy performed directly affects the development of lymphedema. S. F. Senur et. al. (2005) [1], believes that removal of one sentinel lymph node reduces the likelihood of developing edema of the upper limb to approximately 3%. So, according to A.M.V. Ermoshchenkov et al. (2013) [2], the risk of developing lymphedema increases to 50% if the patient has 8-10 lymph nodes removed.

Analyzing the literature data M Goker et. al. (2013) [3] noted that the risk of developing lymphedema after surgery with the inclusion of lymphadenectomy is 30%. In the treatment of 681 patients with breast cancer, S. A. Norman et. al. (2010) [4], showed that the risk of developing lymphedema was increased by axillary lymphadenectomy followed by radiation therapy, this risk did not increase, but a combination of lymphadenectomy with adjuvant chemotherapy with the inclusion of anthracyclines led to a 4-5-fold increase in it. In contrast, S Allgra et. al. (2002) [5] report that with the combined use of surgical treatment and external beam radiation therapy, edema of the upper limb occurs in more than 70% of cases, while, as soon as after lymphodenectomy, in 20% [6].

N. Olszewski (2003) [7], gave such a definition of lymphedema - this is a pathological condition in which an increase in the mass of soft tissues of the limb occurs due to the accumulation of high-protein fluid in the intercellular space and lymphatic pathways, an increase in the number of keratinocytes, fibroblasts, as well as migrating immunocomponent cells and intercellular substance. V. Foldi (1994) [8], described lymphedema as follows - lymphedema is a chronic progressive disease characterized by swelling of one or more limbs due to the accumulation of fluid with a high protein content in the interstitial space, mainly in the subcutaneous fatty tissue, due to a violation of lymph transport along lymphatic vessel. There are common pathogenetic aspects characteristic of postmastectomy lymphedema. Removal of lymph nodes, transection of lymphatic tracts, and trauma to the vascular nerve bundle during surgery disrupt lymphodynamics in the upper limb at several levels of the lymphatic system, which leads to loss of the normal resorption capacity of the lymphatic capillaries [9]. According to the modern view on the structure and physiology of the lymphatic system, the area of the lymphatic vessel between the two valves is the lymphangion. Lymphangions are combined into a common circuit thanks to the "boundary valve".[10]. Thus, during contraction, the lymphangion pushes the lymph into the adjacent central lymphangion and thereby provides lymph flow. With the development of lymphedema, the vascular wall is affected, its muscular-elastic complex. This complex softens the pushes of the lymph to the valves [11]. L.V. Potashov et al. (2002) [12], notes that when networks and bundles of myocytes, as well as elastic fibers, are destroyed, they are replaced by growing collagen tissue. In this case, the contours are smoothed, and the segmental structure of the lymphatic vessel is lost (2010) [13].

N.A. Bubnov et al. On the basis of experiments and clinical data, they put forward a theory according to which the main etiological factor of lymphedema is the defeat of the contractile function of lymphangions. As a result of such processes, highly active proteins and products of protein metabolism accumulate in the intercellular space.

According to G.G. Karavanova et al. (1967) [14] - these are mainly albumins, while the amount of globulins in the lymph decreases. Protein binds acid mucopolysaccharides, which are plastic materials for the development of connective tissue [15]. G.G. Karavanov et al. (1967) [14] D.D. Zerbino (1974, 2008) [16,17], proved that the emerging morphological changes in the soft tissues of the limb, regardless of the etiopathogenesis of edema, lead to fibrosis [18]. This, in turn, impedes the circulation of fluid and protein through the membranes and contributes to further compression of the lymphatic vessels and an increase in the already existing edema [19.20].

According to T.I. Grushina (2006) [21], impaired lymphatic drainage after radical treatment of breast cancer is often combined with impaired venous outflow. These disorders lead to an increase in venous pressure, which increases the filtration of fluid in the tissue, increases extracellular pressure, and thereby leads to even greater difficulty in blood circulation in the upper limb.

The treatment of lymphedema is still a difficult task, for the solution of which the efforts of

many domestic and foreign specialists are being made (Vyrenkov Yu.E et al.) 2011; Klimovich Ya.K., 2012; Cormrier L. N. Et. al., Degtyareva A.A., 2013; Makorova V.S. 2014). [22] Believe that there is no radical treatment for lymphedema today, and the main rehabilitation measures can only be aimed at reducing edema. To resolve postmastectomy lymphedema, representatives of different scientific schools use conservative or surgical methods of treatment.

Conservative methods of treating mastectomy lymphedema include various medications, elastic and compression products, medical massage, therapeutic exercises, as well as the use of physical factors such as pneumatic compression, electrotherapy, shock wave, laser and phototherapy (Oremus M., 2012; Grushina T.I., 2014; Shao J .2014; Ezzo, 2015.

According to a number of domestic and foreign authors, conservative treatment of lymphedema is aimed at the main links in the violations of the lymphatic outflow [23]. This is provided for the purpose of improving the drainage function of the lymphatic system, strengthening the tone of the lymphatic vessels, increasing the speed of lymph outflow, normalizing the microcirculatory bed and redox processes of the interstitial tissue, increasing the compensatory adaptive mechanisms of the body. The International Society of Lymphologists has named complex physical therapy as the method of choice in the treatment of upper limb lymphedema. Complex physical therapy consists of a phased application of a number of conservative measures: manual lymphatic drainage, compression therapy, therapeutic exercises, oral lymphotonizing agents throughout the patient's life. The effectiveness of lymphatic drainage massage for all degrees of postmastectomy lymphedema ranges from 4.33 to 55.7%. When comparing the effectiveness of lymphatic drainage massage with standard anti-edematous therapy L. Andersen et al. (2000) [24] noted a reduction in edema in both cases, with a 12% greater reduction in edema due to the addition of lymphatic drainage massage. T.W. Huang et al. (2013) [25], and J. Ezzo et al. (2015) [26], in their randomized trials noted that lymphatic drainage massage is most effective in patients with initial and moderate manifestations of lymphedema.

Compression bandaging is used as an integral part of complex anti-edematous therapy and is performed after a session of manual lymphatic drainage. K. Didem et al. (2005) [27], and M.L. McNeely et al. (2004) [28], using bandaging, achieved a 36% reduction in edema. and by 38.6%.

The use of elastic compression products in the form of sleeves makes it possible to create selective pressure on the upper limb: maximum - in the distal, minimum - in the proximal sections, which contributes to the normalization of lymph flow, improvement of microcirculation [29,30,31]. Analyzing the literature A. Moseley et al. (2007) noted an 8% effectiveness of patients wearing elastic products.

Also, for the purpose of compression, a fairly new method of treatment is used - taping. To do this, latex-free fabric tapes are used, similar in elasticity to skin, on a hypoallergenic adhesive basis. With the help of a special adhesive layer, they provide muscle support, while maintaining the full mobility of the patient, improve blood circulation and lymph flow. H.J. Tsai et al. (2009) [32] note that tapes can serve as an alternative to bandaging in standard decongestant therapy.

D. Morris et al. (2013) and D. Melgaard (2016) compared the effectiveness of bandaging and kinesio taping for reducing lymphedema. The authors note the same effectiveness of both methods, but emphasize the economic benefits of using teips.

The method of intermittent multisectional pneumatic compression is based on the contraction of the smooth muscles of the walls of the lymphatic and blood vessels, the acceleration of venous and lymphatic outflow, the increase in fibrinolytic activity, and the regulation of neurohumoral mechanisms [33,34,35.]. The efficiency of this method ranges from 3 to 86%. Lydase electrophoresis, magnetotherapy, and laser therapy are also used to treat postmastectomy lymphedema.

Thus, the analysis of the literature showed that conservative rehabilitation measures play an important role in the treatment of postmastectomy lymphedema, improving lymphodynamics in the upper limb at several levels of the lymphatic system and interstitial exchange. However, they do not affect other known causes of lymphedema development, and therefore, their use alone does not solve the problem of medical rehabilitation of breast cancer patients with edema of the upper

limb on the side of the operation.

Surgical treatment of lymphedema is fundamentally divided into two main types - draining and resection operations, which differ from each other in the surgical principle of eliminating edema [36,37,38,39,40].

When performing draining operations, new ways of lymph outflow are created in various ways of own and intact lymphatic structures [41,42,43].

Depending on the general condition of the patient and the degree of edema, resection operations can be staged or one-stage. During resection operations, the subcutaneous tissue with fascia is removed and the subsequent wound surface is closed using reconstructive plastic surgery [44,45,46].

In 1908, for the first time, a draining operation for lymphedema of the limbs was performed by W. Sampson Handley. The author placed several sterile silk threads into the subcutaneous adipose tissue along the entire length of the upper limb. At the same time, it was assumed that the lymph can rise more proximally and then move along the collaterals to other lymphatic spaces. This operation was called "lymphangioplasty" [47]. D. Silver et al. (1976) [48], a Teflon thread was used for drainage and, at the same time, postoperative complications were not observed and edema was reduced in terms of up to 5 years. On the contrary, some authors have noted a short-term therapeutic effect during threading due to overgrowing with scar tissue. N.P. Shmatkov (2013) [49], returned to the development of passive lymph drainage in the 21st century.

So, with postmastectomy lymphedema, he suggested performing vertical, horizontal or combined tunneling and spiral drainage of subcutaneous or subcutaneous-muscular canals and collectors.

R. Baumeister (1990) [50], performed direct restoration of lymphatic outflow during autotransplantation of unchanged lymphatic vessels into the subcutaneous fat of the affected limb. A number of authors have suggested using an autovein for lymphatic shunting of the affected limb.

Thus, C. Campisi et al. (2006) [51], reported that when using an autovein and performing lymphovenous lymphoplasty, a “significant” objective decrease in edema was noted in 83% of patients, while the “average decrease” reached 67% of excess limb volume.

P. Trevidic et al. proposed free grafting on microvascular anastomoses to improve lymphatic drainage from the edematous limb of the axillary flap with lymphatic vessels and nodes.

Lymph-venous anastomosis for the treatment of lymphedema was first proposed by B.M O'Brien et al. The authors proved the regression of lymphatic edema from 42 to 83% in patients who underwent microsurgical operations.

In 1983 L.Nieuborg used direct lympho-venous shunting in patients with post-mastectomy edema and at the same time reduced edema by 47% after 6 months, and 57% after 12 months.

In 2003 M.S. Bardychev et al., using lympho-venous shunting, in 32% of cases recovered patients with complete reduction of edema, and in 43% of cases there was a significant reduction in edema of the upper limb. Yu.A. Abramov et al., combined the imposition of lymphovenous anastomoses with traditional bandaging and intermittent pneumocompression. Edema reduction was achieved in 14.5% of cases, a significant reduction in edema - in 61.8% of cases.

A.A. Malinin reported that when applying lymphovenous anastomoses for the treatment of postmastectomy lymphedema, good results were observed in 24.4% of patients, satisfactory - in 43% and unsatisfactory - in 32.6% of patients.

M.A. Smagin, combining the operation of applying lympho-venous anastomoses with injections of a drug mixture from solutions of marcaine and proserin into the region of the brachial plexus in the treatment of patients with breast cancer with stage II-III lymphedema, noted a decrease in the diameter of the edematous limb by 43.6%, an increase in lymphatic outflow by 66, 7%, decrease in the thickness of the subcutaneous fat of the limb by 41%.

There is evidence that after the normalization of pressure in the lymphatic system, most anastomoses are thrombosed. When analyzing the biopsy material, the patency of lymphovenous anastomoses up to 8 months was revealed in 53% of cases, and in the remaining 47% of cases, oc-

clusion of the anastomosis penetrating from the side of the vein was diagnosed.

Transplantation of vascularized tissue in the area of transplantation of microsurgical anastomosis. K. Becker et al. (2006) associated with the site of transplantation of inflammatory nodes in the armpit in 17 patients and in 7 patients - in the cubital fossa. Complete regression of lymphatic edema was achieved in 42% of patients, partial regression of edema was noted in 50% of patients.

Thus, it can be assumed that the use of drainage operations, including microsurgical ones, is advisable only with reversible changes and a compensated state of the lymphatic channel, i.e. with lymphedema I-II degree.

To date, a large number of different resection operations have been proposed, differing from each other in terms of the volume of excision of the affected tissues.

These operations were originally proposed for the treatment of lymphedema of the lower extremities, but subsequently they were used for lymphedema of the upper extremities. The main disadvantage of operations of this type is the development in the late postoperative period of a pronounced cicatricial process with limb deformity, which does not justify the hopes of patients and the efforts of surgeons.

At the end of the 80s of the last century, some authors suggested using liposuction not only in bariatric surgery, but also for the treatment of benign symmetrical lipomatosis, gynecomastia, gigantomastia, and also lymphedema of the extremities. This was due primarily to cosmetic considerations.

During liposuction, subcutaneous tissue is removed from a small incision using special instruments - a cannula and vacuum suction.

A.G. Warren et al. Based on the analysis of literature data, of all types of surgical interventions for lymphedema, liposuction is considered the most promising.

Currently, there are no unified approaches to the surgical treatment of postmastectomy lymphedema. The largest study in the post-Soviet space was carried out by M.O. Myasnikova at the St. Petersburg State Medical University. Academician I.P. Pavlov and summarized the analysis of data on 500 patients with varying degrees of severity of postmastectomy lymphedema treated since 1980. Despite the long follow-up period and a large sample of patients, data were presented on 47 patients who underwent lymphovenous bypass grafting and 16 patients who underwent resections. operations. Immediate and long-term results of surgical intervention were evaluated. The authors noted that directly satisfactory results of resection operations in half of the cases worsened after 2-5 years. By the end of the study (15 years of follow-up), no positive results were noted. In the long term, only 40% of patients were satisfied with the results of resection surgery. Out of 47 patients operated on with lymphovenous anastomoses, “good” (according to the terminology of the authors) results in the long-term period were transformed into satisfactory ones (67%), and in 29% of cases a poor long-term result was stated. It was also reported that the factors that worsened the long-term results in both groups of observation were recurrent erysipelas and patients who violated the frequency of conservative therapy or completely refused it.

It was noted that the decrease in the volume/circumference of the extremities varied from 2 to 50%, regardless of the type of surgical intervention, and persisted for 1 to 132 months. Thus, based on the review of the literature, it can be concluded that there is no unified approach to the surgical treatment of postmastectomy lymphedema. The very variety of proposed methods of surgical treatment of this pathology indicates their low efficiency. Any options for radical operations performed for the treatment of postmastectomy lymphedema have significant drawbacks and a relatively low percentage of long-term positive results.

The positive effect of radical resection operations for postmastectomy lymphedema in the long term is achieved in no more than 40% of cases. This type of operation is associated with high trauma and is characterized by a large number of postoperative complications. In contrast to the surgical practice of treating primary lymphedema, when planning resection interventions for postmastectomy edema, the question always arises of choosing unaltered tissues for closing the wound defect. In the previously performed complex treatment for locally advanced breast cancer, which

includes a component of radiation therapy, the collection of a sufficient volume of intact tissues to close the defect is always problematic. A high percentage of edema recurrence after resection-type operations necessitates repeated surgical interventions, each of which is associated with greater technical difficulties compared to the previous one.

Drainage-type operations in surgery for post-mastectomy lymphedema have a good result, provided that an adequate lymphovenous bypass anastomosis is created.

This is possible when using a variant of microsurgical technique, which requires large material costs, long-term surgical intervention, special equipment and trained personnel. The optimal and long-term positive effect with this treatment option is observed in the early stages of post-mastectomy lymphedema, in which the issue of improving the patient's quality of life can be resolved using less traumatic and financially costly measures. In general, the frequency of a persistent effect of drainage operations in this pathology does not exceed 60%. Regardless of whether a resection or drainage type of surgery is used, maintaining a long-term positive result requires patient motivation for repeated courses of conservative therapy, compliance with a number of physical activity restrictions, and prevention of inflammatory processes, which is not always achievable.

In recent years, research on the prevention of lymphedema has been actively conducted. In 2016, it was proposed to perform prophylactic lymphovenular anastomoses when removing small pelvic tumors, since, regardless of the degree of lymph node dissection in the small pelvis, most of these patients experience lymphostasis. A number of authors suggest using T-BAR and LYMPHA technology for primary prevention of lymphedema, as well as predicting the development of lymphedema depending on the number and groups of removed lymph nodes using various technologies (indocyanine green control, computer simulation).

The priority in creating artificial lymphovenous anastomoses belongs to N.I. Makhov (1950), who was the first to propose and implement the connection of the lymphatic collectors of the thigh with the saphenous vein by introducing a lymphatic vessel into the lumen of the vein, while he did not put sutures on the anastomosis, that is, he did not fix it. Subsequently, the technique of lymphovenous anastomoses was modified so that in their works the peripheral end of the transected lymphatic vessel was implanted into the lumen of the vein using a needle with a thread and fixed with one suture to the vein wall. The essence of the LVA technique is the creation of a path for the outflow of lymph into a venous vessel using an anastomosis. To detect the lymphatic duct, a contrast agent was injected - a 2% solution of methylene blue intradermally 2 cm away from the axillary region. Lymphatic vessels are visualized using a magnifier 40 times (microsurgical glasses). With the help of LVA, a visual assessment of the state of the lymphatic vessels was carried out in terms of their diameter and contractility. In accordance with these criteria, the most functional and active lymphatic vessel is selected for the formation of the LVA. End-to-end suturing of the lymphatic and venous vessel is performed. Simultaneous formation of lymphovenous anastomosis is a modern surgical approach for the prevention of lymphostasis in patients with breast cancer. Drainage of lymph into the venous bed leads to a shortening of the term of lymphorrhea and thereby eliminates the risk of lymphedema. This, in due time, restores working capacity and improves the quality of life of patients with breast cancer.

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