

Mini Review**Breast Cancer Related Lymphedema- Brief Review****Takalkar Unmesh Vidyadhar^{1*} and Advani Suresh¹**¹*United CIIGMA Hospital, Aurangabad, India***Abstract**

Breast cancer related lymphedema is a progressive and often debilitating condition frequently observed after surgical and radiation treatment of breast cancer. Patients with breast cancer may develop lymphedema within few days to up to decades after treatment. It causes cosmetic deformity, continuous pain and psychological strain affecting quality of life. Lymphedema of arm has received significant attention because of its challenging management. Mastectomy, extent of axillary dissection, radiation therapy, age, wound infection, stage of the disease, and presence of positive lymph nodes are risk factors. Numerous methods have been described in literature for the assessment of lymphedema like volumetric methods (water displacement), serial circumferential measurements, tonometry, tissue dielectric constants, MRI and bioelectrical impedance. The complexity of breast cancer related lymphedema needs multidisciplinary therapeutic approach including surgical and non-surgical approaches.

Introduction

Breast cancer related lymphedema is a progressive and often debilitating condition frequently observed after surgical and radiation treatment of breast cancer. It is a significant potential long-term morbidity that can appear in some people during the months or even years after treatment ends in the arms and hands. But sometimes it may affect breast, underarm, chest, trunk and back also. Around 20% of the women experience arm swelling following axillary node dissection. The incidence of upper limb lymphedema varies from 2-40% in breast cancer women treated with surgery, radiation therapy or both [1]. There is a wide variation in the range of incidence of lymphedema among breast cancer survivors. It may be due to lack of consensus regarding clinical criteria, methods and timings of assessment for lymphedema [2]. Also 3.5% of the patients who underwent sentinel lymph node biopsy reported lymphedema [3].

In lymphedema, chronic tissue swelling is due to the damage to lymph nodes and vessels. Abnormal accumulation of proteins in the interstitial space occurs due to interruption of normal lymphatic drainage system [4]. Lymphedema progresses from acute phase of subclinical

edema to mild swelling and lastly to chronic swelling with irreversible changes. In initial phase there is collection of excess fluid in subcutaneous tissue that manifest as pitting edema. Later on inflammatory fluid with fibrocytes and adipocytes leads to deposition of fat in subcutaneous tissue those results in non-pitting type of edema, solid phase of lymphedema. Further it progresses to fibrosis, impairment of lymphatics, and decreased distensibility around joints that restricts joints mobility [5]. Sometimes such chronic debilitating condition needs lifelong management. Concerns with breast cancer lymphedema are the functional disability and disfigured body image due to swelling. It is one of the most troubling complications causing physical as well as psychological strain to the patients. Hence it is a great challenge for the breast cancer survivors, their family and treating physicians.

Lymphedema among breast cancer women present with swelling, heaviness, tightness, pain, numbness followed by stiffness and limited range of movements in arms. On clinical examination, cutaneous and subcutaneous fibrosis, peau d'orange skin can be observed. In addition to physical features, psychological burden causes anxiety, frustration, distress, depression not only among patients, but family members also suffer adjustment problems affecting quality of life [6]. Also social health gets compromised due to lack of social support, pain and disability [7]. Patients with breast cancer may develop lymphedema within few days to up to decades after treatment. It has been reported that 75% of the cases present within first year after surgery and 90% within 3 years [5].

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As overall survival of breast cancer is improving with advanced therapeutic modalities, incidence of long-term complications is rising. Lymphedema of arm has received significant attention because of its challenging management. Hence identification of risk factors for lymphedema and implementation of prevention strategies is vital among breast cancer survivors. Mastectomy, extent of axillary dissection, radiation therapy, age, wound infection, stage of the disease, and presence of positive lymph nodes are risk factors. One of the meta-analysis that included 98 independent studies reported relative risk (RR) of arm lymphedema increased after mastectomy compared to lumpectomy alone (RR 1.42; 95% confidence interval (CI) 1.15-1.76), axillary dissection compared to no axillary dissection (RR 3.47; 95% CI 1.32-1.80), axillary dissection compared with sentinel node biopsy (RR = 3.07; 95% CI 2.20-4.29), radiation therapy (RR = 1.92; 95% CI 1.61-2.28), and positive axillary nodes (RR = 1.54; 95% CI 1.32-1.80) [8].

Post mastectomy radiation therapy (PMRT) is one of significant risk factor for lymphedema. Lymphedema secondary to PMRT has been reported to occur with incidence of 0%-54%. C.S.Hinrichs et al revealed significant association of lymphedema with total dose of the radiation therapy and posterior axillary boost, overlapping technique and years of radiotherapy. Technique of radiation delivery affects the incidence of lymphedema [6]. Deo S V and colleagues evaluated retrospectively 300 treated breast cancer patients for one year. They reported prevalence of lymphedema 13.4% in patients who received only surgical treatment, while 42.5% in patients treated with surgery and radiotherapy. They observed stage of the disease, body surface area > 1.5m², presence of co-morbid conditions, post-operative radiation therapy and Anthracycline based chemotherapy as significant risk factors on univariate analysis and presence of co-morbid conditions and axillary irradiation as independent risk factors [2].

Assessment of lymphedema

Numerous methods have been described in literature for the assessment of lymphedema like volumetric methods (water displacement), serial circumferential measurements, tonometry, tissue dielectric constants, MRI and bioelectrical impedance. Objective assessment of lymphedema can done by measuring limb volume using multiple circumference measurements of the upper limb and by water displacement volumetry. In circumference measurement method, divide the upper limb into four segments. The upper limit of measurement, known as the 65% point, marks a point on the upper arm, which is 65% of the distance from the olecranon to the acromion tip. The four segments: (i) Wrist (at the level of ulnar styloid) to mid forearm, (ii) Mid forearm to elbow (at the level of olecranon), (iii) Elbow to mid arm and (iv) Mid arm to the 65% point. Assume each of these segments to be a truncated cone (frustum). As the shape of upper limb is

not exactly cylindrical, studies have shown that calculations using the frustum assumption produce the least standard error of measurement. The volume of each segment can be calculated using the formula, $h(C_1^2 + C_2^2 + C_1C_2) / 12\pi$, where h is the length of each segment, C₁ and C₂ are the circumference of each segment at both ends. The sum of these volumes gives the volume of the limb [9]. In the primary care settings, circumferential measurements are the most practical as no special equipment or skill is needed. Any change in arm circumference by 2 cm or more between affected and unaffected limb is diagnosed as lymphedema.

In water displacement volumetry, the patient's upper limb is immersed in a graduated steel cylinder up to the 65% point. The volume of water displaced is calculated using the formula $\pi r^2 h$; where r is the radius of the cylinder and h is the height of water displaced. With the help of high frequency ultrasound probes, skin, subcutis, thickness of the upper limb are measured sonographically. Water displacement method is the most sensitive method to assess changes in limb volume. But it is contraindicated in patients with wounds, skin ulcers or cellulitis [10].

Management of Postmastectomy Lymphedema

International Society of Lymphology suggests complex physical therapy (CPT), a technique consisting of manual lymphatic drainage (MLD), functional compression wrapping, therapeutic exercises, and skin care, lymphatic self-massage and elastic wrap for physical management of lymphedema. Treatment is chiefly focused on reduction of edema and pain.

Comprehensive decongestive therapy (CDT) is a multimodal therapy comprised of manual lymphatic drainage (MLD), compression bandaging, and exercise, skin and nail care. It is effective to control post mastectomy lymphedema by promoting acute limb volume reduction. CDT is recommended as the primary evidence based therapy. There are two phases of CDT- initial phase is intensive one. It is a reductive phase in which patients receive CDT everyday for 3-8 weeks. Second phase is maintenance, which is individualized according to response. Patient education plays very important role. Randheer S et al observed beneficial therapeutic responses in terms of maximum limb volume reduction in 25 patients who received CDT in intensive phase from trained physiotherapist [11].

High-voltage electrical stimulation (HVES) is used for the relief of lymphedema. It reduces microcirculation permeability; decreases size of capillary pores and restrains movement of proteins to the interstitial space [12]. In one of the study, protocol included HVES with self-massage, therapeutic exercise, limb care was found to be effective to treat the post mastectomy lymphedema. Effect of the protocol was assessed by perimetry, calculation of volume difference between the limbs and

calculation of the volume increase percentage of the affected limb compared to contralateral limb [13].

Surgical options for lymphedema are more efficient including physiological methods. Autologous LN transplantation, recent microsurgical technique seems to have favorable persistent improvement during the treatment of post mastectomy lymphedema. Becker C et al observed LN transplantation as a safe modality with good long-term results among post mastectomy lymphedema patients especially in the early stages of the disease. In their study, 24 breast cancer females with lymphedema of duration more than 5 years and resistant to physiotherapy underwent microsurgical LN transplantation from femoral to axillary region [14]. Anne M Saaristo and colleagues' demonstrated improvement in lymphatic drainage on simultaneous combination of LN transfer with standard breast reconstruction procedure among post mastectomy lymphedema cases [15]. Microvascular LN transfer is emerging as novel ideal option for patients with lymphedema. An algorithmic approach to simultaneous VLNT with microvascular breast reconstruction demonstrated promising results among 29 patients with refractory lymphedema secondary to breast cancer treatment [16].

Apart from these therapeutic approaches, some newer techniques are being used like manual lymph drainage, stellate ganglion block, acupuncture, low level laser therapy, deep oscillation and pneumatic compression [17]. Hyperbaric oxygen chambers are also studied for its effectiveness for wound healing among lymphedema patients. Obesity has been identified as risk factor for breast cancer related lymphedema. Hence weight reduction also found to be useful for significant reduction of edema [18]. Lymphedema-related wounds and infections should be managed with antibiotics promptly to prevent further complications. Because of accumulation and stasis of fluid, cellulitis occur and if neglected progress to sepsis [19].

Conclusion

Lymphedema, post-treatment sequelae remain a prevalent and potentially incapacitating condition among breast cancer survivors. It causes cosmetic deformity, continuous pain and psychological strain affecting quality of life. The complexity of breast cancer related lymphedema needs multidisciplinary therapeutic approach including surgical and non-surgical approaches. Because of improved advanced therapy, more breast cancer becomes long term survivors. Psychological and social sequelae, unrecognized and neglected complication of breast cancer related lymphedema should be taken care of by the clinicians and caregivers.

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