Review Article

Physical rehabilitation after breast cancer

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Abstract: Improvement of overall survival in breast cancer patients has lead recently to an increased focus on prevention and management of breast cancer-related lymphedema (BCRL), a condition that deeply impacts function and quality of life (QoL) of cancer survivors. Current data still demonstrate BCRL rates ranging from 10% to 30% at 2 years, with a high heterogeneity of measurement methods and different incidence of the disease (from 5% after breast-conserving surgery to over 50% after mastectomy, radiation and chemotherapy). The present paper will describe the available data regarding the value of prevention and rehabilitation treatments of BCRL.

Keywords: Physical rehabilitation; lymphedema; mechanical assisted therapies; prehabilitation; breast cancer

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Assessment, prevention and early diagnosis of breast cancer-related lymphedema (BCRL)

Detection and management of early-stage BCRL may prevent progression to chronic disabling disease and may enable cost-effective conservative interventions (1). Lymphedema is a condition characterized by accumulation of protein-rich tissue fluid in extravascular interstitial spaces that causes edema, due to the impairment of lymphatic system, producing chronic inflammation with pain, tightness and heaviness in the arm. Patients at high-risk for BCRL have history of axillary lymph-node dissection (ALND), regional nodal irradiation, taxane-based chemotherapy, increased BMI, and cellulitis. Surveillance and regular follow up reduce BCRL risk in these patients (1). Pathophysiology of BCRL shows an acute and chronic phase with different stages (2):

- Stage 0 or latent stage of BCRL, the accumulation of fluid may not be evident with subclinical volume accumulation
- Stage I with clinically palpable lymphedema, that disappears with elevation of the limb and it is characterized by a lack of fibrosis. Subsequently, intradermal fibrosis is an irreversible and chronic phase of BCRL lasting more than 3 months.
- Stage II lymphedema no longer pits on pressure because of excess fat deposition and tissue fibrosis and no longer reverses with elevation.
- Stage III lymphedema has progressive swelling with trophic skin changes, including papules, warts, skin folds, tissue bulges, and often open draining wounds, leading to severe impairment in mobility and high risk of infection (3).

Diagnostic techniques for BCRL have developed with increased sensitivity, allowing for subclinical detection and early treatment (4). Pre and postoperative circumferential measurements of both arms should be taken at 4 points (the metacarpal-phalangeal joints, the wrists, 10 cm distal to the lateral epicondyles, and 12 cm proximal to the lateral epicondyles). A difference of more than 2.0 cm at any of the 4 measurement points means the needs of BCRL treatment. It is important to keep attention to symptoms of heaviness, tightness, or swelling in the affected arm.

"Gold standard" technique is considered water displacement, performed by inserting the arm into a plastic cylinder. The diagnostic cutoff for defining lymphedema is a volume increase of 10% or 200 mL compared to contralateral arm or to a baseline measurement for the affected arm.

Optoelectronic perometry is able to show subclinical stage of BCRL measuring limb volume with infrared light but it presents too much space requirements and difficulties associated with its use.

Dual-energy X-ray Absorptiometry is another instrument that can measure improved consistency of the arm but limited data are available because it exposes patients to radiation.

Bioelectrical impedance analysis (BIA) is a noninvasive and reproducible technique of body composition analysis that measures the extracellular space volume and total water content with remarkable sensitivity, compared with traditional techniques, even in subclinical phases of lymphedema (up to 10 months before the development of clinical symptoms in several studies) (5). The procedure consists in measuring the impedance (or resistance) to the flow of a small electric current passing through the body's water (both intracellular and extracellular water), including a phase angle that has recently been described as an independent prognostic factor. In a study on 259 breast cancer patients, with different stages of disease at diagnosis, the median phase angle score was 5.6 (range, 1.5–8.9). Patients with phase angle ≤5.6 had a median survival of 23.1 months (95% CI, 14.2–31.9; n=129), while those >5.6 had 49.9 months (95% CI: 35.6–77.8; n=130), the difference being statistically significant (P=0.031). Multivariate Cox modeling, after adjusting for stage at diagnosis and prior treatment history, found that every unit increased in phase angle score was associated with a relative risk of 0.82 (95% CI: 0.68–0.99, P=0.041) (6). Among all types of BIAs, multi frequencies BIA (MF-BIA) is more accurate and less biased for the prediction of extracellular water compared to single frequency BIA (7). The MF-BIA technique, used to monitor the efficacy of lymphedema treatment in patients following breast cancer surgery, seemed significantly more sensitive than circumferential measurements to detect very small differences in the arm extracellular volumes (8).

Correct counseling is key to prevent and monitoring BCRL. In 2015, the NCCN Breast Cancer Panel recommended "to educate, monitor, and refer for lymphedema management" as a standardized follow-up (9). Patient education in self-assessment and self-monitoring on the early signs of BCRL, is therefore crucial, in order to prevent or detect BCRL at an early stage, when the chances to slow progression are optimal (10). The preoperative assessment of breast cancer patients should comprehend upper extremity range of movement (ROM), pain, strength and volume. Clinicians have to evaluate anamnestic comorbidity and risk factors related to surgery like age and body mass index and have to educate to stop smoking and eat mindfully, according to the most updated guidelines against diabetes and hypertension. It is useful for patients to be informed about local effects after surgery and early post-operative exercise protocols as a sort of "prehabilitation" program before oncologic treatments.

The early postoperative rehabilitation evaluation should be considered at least two weeks after surgery and prior to starting adjuvant treatments, such as radiation therapy or chemotherapy, aimed at evaluating decreased ROM, axillar web syndrome, weakness, pain or other conditions requiring rehabilitation protocols. Moreover, this counseling provides a chance for the patient to ask questions and to clear doubts about post-operative behaviors, advices and risks. Rehabilitation starts the first day after surgery, and a mild range of motion exercises should be promoted during the first week. Active stretching exercises can begin 1 week after surgical procedure and should be continued until full range of motion is reached. Progressive resistive exercises and strengthening can start using mild weights (1–2 pounds) within 4 to 6 weeks after surgery on affected upper arm. Women have to learn to massage scar tissue. The need for ongoing rehabilitation surveillance should be tailored on the patient's needs and compliance, taking into account cancer treatment plans (chemotherapy or radiation therapy), clinical status, individual risk factors for morbidity. Since prevention, early diagnosis and BRLC management depend on self-monitoring and follow up should be done regularly up to 1 year after surgery. Beside this, counseling about hand and arm hygiene and care is extremely important in BCRL prevention; avoiding trauma to the operated arm such as injections and vaccinations, venipuncture is useful to reduce risks of infection and lymphedema; appropriate treatment of wound infection or seroma is important also for lymphedema prevention (11).

In Literature, "upper quarter dysfunction (UQD)" (12) include Mondor's disease, a thrombophlebitis of the subcutaneous veins that occurs below the breast on the anterolateral thoracoabdominal wall, following breast surgery or radiotherapy. It can cause limited arm and scapular mobility, pain, reduced shoulder motion and functional impairment. Axillary web syndrome, instead, presents as tight, fibrous cords in the axilla that can extend along the arm to the antecubital fossa and forearm; the exact pathogenesis is unknown, however there is histologic and radiographic

evidence of a lymphatic origin (13). The cumulative incidence at 18 months has been reported as 50% and is higher in patients who undergo axillary lymph node dissection (72–75%) versus sentinel node biopsy (20–41%) (14). Risk factors include younger age, low body mass index, and greater number of lymph nodes removed. UQD, which should be diagnosed immediately, generally is self-limiting within 2–8 weeks and may require specific exercises, lymphatic drainage and anti-inflammatory drugs (15).

Treatment and rehabilitation of BCRL

Management of BCRL remains a major challenge for health care professionals, in order to reduce swelling and risk for infection, prevent progression and alleviate symptoms. These strategies include complete decongestive therapy (CDT) as a **c**ombined physical therapy, which is the "gold standard" for lymphedema treatment (16). This approach includes different techniques, such as manual lymphatic drainage (MLD), external compression garments and bandages, skin care and exercises guided by specially trained therapists, and can achieve edema volume reduction from 21% to 56% as compared to standard physiotherapy (17).

MLD is a massage technique that stimulates lymphatic vessels to contract frequently and direct fluids toward adjacent lymphatic basins. The pressure must be applied gently and slowly, according to natural pulsation of lymphatic flow; in mild edema (stages I and II), a compression garment, tailored on the individual patient, may be used instead of bandages. A Cochrane Review published in 2016 concludes that MLD is safe and may offer several benefits to compression bandaging for swelling reduction, particularly in mild-to-moderate BCRL but these data are to be confirmed by randomized trials; findings were unclear for arm range of motion and unsatisfying for quality of life. Regarding pain and heaviness, 60% to 80% of patients reported improvement after rehabilitation (18).

The use of pneumatic compression therapy is discussed. It can reduce swelling and may be indicated as adjunctive therapy when self-MLD is hard for the patient. Shao et al in a meta-analysis showed no significant differences in the percent of volume reduction and subjective symptoms (heaviness, pain, paresthesia) adding Intermittent Pneumatic Compression Pump to usual care (19).

Exercise decreases postoperative side effects and improves quality of life; physicians who prescribe exercise can increase patients' motivation and adherence to oncologic treatment protocols (20). Some clinicians, mostly in the past, have recommended avoidance of any vigorous movements against resistance, without any sound scientific evidence in Literature. Mobilization stretches and exercises after breast surgery, under the supervision of a health care professional are effective to improve shoulder range of motion and decrease breast tightness and pain; usually, it is prescribed a moderate-intensity exercise, 3 to 5 days per week, 20 to 30 minutes per session. Remedial exercises with the garment or bandage facilitate lymphatic flow through repeated muscles contraction and relaxation. Shoulder flexion and abduction improves when starting exercises in an earlier period after breast surgery. The literature suggests that progressive resistance exercise does not increase the risk of BCRL Anyway, the Cochrane review about upper limb lymphedema refer high heterogeneity of papers with risk of bias and the results should be considered with caution (21).

The low-level laser therapy (LLLT) has been used in order to stimulate lymphangiogenesis, enhance lymphatic motility and reduce fibrosis; however, some uncertainty remain about safety and risks of metastasis or local relapse in the treated areas.

The low-level laser in the axillary region was studied in literature (22). The results showed a reduction in limb volume in the patients treated with low-power laser compared to other modalities, but more extensive comparative studies are still lacking.

Recent studies have demonstrated that extracorporeal shock wave therapy (ESWT), widely used in orthopaedics, helps angiogenesis and lymphangiogenesis and seems to be an effective treatment of stage 3 lymphedema after breast cancer treatments, with clinically favourable outcomes, even in a long term follow-up (23). As innovative and non-invasive method, ESWT seems to be a promising modality for treatment of chronic and progressive lymphedema.

Only a few studies have analyzed the effect of Kinesio Tex taping (KTT) on BCRL. Authors compared KTT and usual care to the standard short-stretch-bandage (SSB) and usual care, and showed no significant differences in limb volume, water composition of the upper-limb, lymphedema-related symptoms and health-related quality of life (24).

Among the physical therapies for rehabilitation after breast cancer surgery, a very promising tool is mechanical assisted (MA) therapy through a machine system involving two motorized, cylindrical structure skin rollers applied to the limb by a specialized therapist. The rollers pick up and massage the skin, attracted by a negative pressure generated by a vacuum pump, with different kind of programs, frequencies and intensities according to the types of treatment (scars, skin adherences and lymphedema). A randomized prospective study on twenty women showed that

MA technique can be a safe and effective tool for radiation-induced skin fibrosis in breast cancer patients following conservative surgery, including improvement of local pain, itching, skin dryness, erythema and induration (25). A single-blinded randomized study compared MA therapy with MLD, both combined with compression bandaging, to treat secondary arm lymphedema showed in both groups significant reductions in whole arm volume, arm fluid and truncal fluid. There were also significant improvements in subjective heaviness, tightness, limb size and ROM at the end of the study compared with the baseline (26).

Conclusions

Gold standard management of breast cancer related lymphedema involves a combined physical therapy with several techniques, but sound evidence in this field is still lacking and more scientific data and better clinical trials are needed. Clinical counseling, through careful listening to patient's reported outcomes, is a central issue in prevention and early detection of lymphedema; such a surveillance model enhances patients' empowerment and improves patient-clinician relationship. Prehabilitation, through lifestyle changes, preoperative exercise prescription and risk factors detection, and early rehabilitation following surgery or adjuvant treatments provide patients with a wide range of tools, in order to prevent or slow progression of BCRL. In any case, a tailored exercise program, based on individual's attitudes, improves fatigue, physical functioning and quality of life; although epidemiologic studies have documented a positive association between physical activity and survival in many cancer types, the mechanisms underlying this association remain uncertain. Exercise might inhibit cancer growth through effects on metabolism, hormonal balance, inflammation and immune surveillance. Nevertheless, the hypothesis that mechanical forces within the tissues during exercise could directly impact tumor growth has received little attention. Recent advances in cancer biology are underscoring the importance of connective tissue in cancer biology and local tumor environment; inflammation and fibrosis are well-recognized contributors to cancer, and connective tissue stiffness is emerging as a driving factor in tumor progression. We also know that many patients benefit from active and passive physical manipulation of connective tissue, and stretching may have local anti-inflammatory effects independent of vascular or other systemic factors, but it is not clear what happens at the cellular and molecular level when these manipulations occur. Since physical-based therapies have been shown to reduce inflammation and fibrosis, they could have beneficial effects on cancer spreading and metastasis, enhancing natural healing responses, by reducing tissue stiffness and improving mobility (27). Even if high quality basic and clinical research are needed in this brand new horizon of medicine, such a fascinating hypothesis may shed a new light on physical-based treatments and their potential role, currently overlooked, in cancer biology.

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Footnote

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