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BREAST CANCER-RELATED LYMPHEDEMA: RISK FACTORS, DIAGNOSIS, MANAGEMENT, PREVENTION

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Keywords: breast cancer-related lymphedema (BCRL), upper limb lymphedema, risk factors, lymphedema diagnosis, lymphedema prevention, lymphedema management.

Summary

Breast cancer-related lymphedema (BCRL) is a negative outcome of breast cancer or its treatment, which affects 1 of every 5 patients. Disruption of the lymph flow results in its accumulation in the tissues with resulting edema. Diagnosis is based on the presence of symptoms such as progressive upper extremity swelling, limb pain and discomfort, skin changes, restricted range of motion, and the measurement of the extremity girth. First-line treatment is nonivasive, which includes compressions or physiotherapy. Prevention strategy focuses on compression therapy or exercises, however, limiting the extent of lymph node removal is the only measure shown to reduce the incidence of BCRL.

Introduction

Breast cancer-related lymphedema (BCRL) is a chronic condition characterized by an abnormal accumulation of protein-rich fluid in tissues of the upper limb or trunk due to disruption of lymphatic flow in the background of invasive breast cancer or as an outcome of its treatment [1, 2]. The overall estimated incidence of chronic arm edema after breast cancer is found to be 21.4%, indicating that BCRL is a widespread problem affecting 1 in every 5 patients following breast cancer treatment [2, 3].

The aim: to overview the risk factors, diagnosis, prevention, and management of breast cancer-related lymphedema.

Methods and materials

The search was conducted in PubMed and Google Scholar databases. A total of 9 publications in English were selected and analyzed. Keywords were utilized to identify the proper articles as follow: BRCL, BCRL risk factors, upper limb lymphedema, lymphedema diagnosis, lymphedema management, lymphedema prevention.

Results

Risk factors. The factors that are implicated in the etiology of BCRL are divided into beast cancer treatment-related and non-treatment related. Treatment-related risk factors include axillary lymph node dissection (ALND) and regional lymph node radiation (RLNR) [2, 4]. The ALND results in great lymphatic disruption and therefore is the primary cause of lymphedema in patients with breast cancer [3-5]. Studies show, the incidence of lymphedema raises with an increasing number of axillary nodes removed or disrupted during ALND. Radiation therapy can affect the lymphatic system by inhibiting lymphatic proliferation and promoting fibrous tissue formation resulting in blocked lymphatic flow, therefore RLNR of breast, axilla, and/or supraclavicular regions may contribute to the risk of developing BCRL. Early-onset lymphedema (<12 months postoperatively) is prone to manifest after ALND, while late-onset lymphedema (>12 months postoperatively) is associated with RLNR [2, 3, 5]. Well-established non-treatment-related risk factors for BCRL are body mass index (BMI) at time of diagnosis, subclinical edema, and cellulitis [2, 3]. Patients with a pre-operative BMI ≥ 30 and those who experience large weight fluctuations during and after treatment for breast cancer should be considered at higher risk for lymphedema [6]. Subclinical edema is also related to the progression of BCRL. Patients with small increases in arm volume with relative volume changes (RVC) ≥3% but <5% as well as larger increases in arm volume with RVC ≥3% but <10% within 3 months of surgery or increases in arm volume with RVC ≥5% but <10% from baseline at any point after surgery were more likely to progress to BCRL [1, 4, 6]. The pathophysiologic relationship between cellulitis and BRCL remains unclear, however, it exacerbates preexisting BCRL, leading to a recurrent cellulitis-BCRL flare cycle [2].

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Diagnosis. Diagnosis of BCRL can be fairly done only 1-month post-operation based on the symptoms and physical examination [3, 7]. The accumulation of excess lymphatic fluid mostly occurs in the upper limb, however, it can also involve the breast or trunk on the ipsilateral side of the breast cancer. Patients usually report symptoms such as progressive upper extremity swelling, limb pain and discomfort, skin changes, and restricted range of motion. In addition, the affected extremity is a subject for infection [2-4]. Measurement of the extremity girth is widely used to evaluate and classify lymphedema. The circumferences of both affected and non-affected limbs are measured with a non-stretch tape. The measurement sites are hand proximal to the metacarpals, wrist, and then every 4 or 10 centimeters from the wrist to the axilla [1, 3, 4]. The most common criterion for diagnosis has been a finding of ≥ 2 centimeters or ≥ 200 mL difference in limb volume as compared to the non-affected limb or 5% or 10% volume difference in the affected limb [1, 8]. The International Society of Lymphology (ISL) proposed staging of lymphedema based on the examination of the upper extremity and the volume difference between the extremities as stage 0 through stage III as shown in Table 1 [1, 9].

For advanced evaluation of lymphedema may be utilized lymphoscintigraphy, which uses radioactive material, computed tomography (CT) scans, or magnetic resonance imaging (MRI), however, these modalities are not routinely involved into BCRL diagnostics [3].

Management. The management of BCRL focuses on minimizing the degree of edema, slowing the rate of lymphedema progression, and preventing complication [2]. First-line treatment for BCRL is conservative. Compression therapy uses multilayered padding materials and short-stretch bandages. Manual lymphatic drainage (MLD) is a massage-like technique that belongs to physiotherapy. The combination of these two latter methods is preferred for patients with mild lymphedema (ISL stage I). A multicomponent technique known as complete decongestive therapy (CDT) is suggested for the management of moderate-to-severe lymphedema (ISL stages II to III). Intermittent pneumatic compression (IPC) is another method of compression therapy that stimulates lymph flow in the right direction. Patients with severe lymphedema (ISL stage III) may also benefit from IPC in addition to CDT [3, 4, 9]. While non-invasive treatment remains the standard of care for BCRL, surgical management is another avenue to treat persistent lymphedema, particularly for patients who do not respond to non-invasive treatments [2, 3, 9].

Table 1. The staging system for lymphedema.

Stage 0	Refer to a subclinical state where swelling is not yet evident despite impaired lymph transport and subtle changes in tissue fluid. May be present for months or years before overt edema occurs (Stages I-III).
Stage I	A visible swelling that subsides with limb elevation. Pitting may occur**.**
Stage II	Signifies that limb elevation alone rarely reduces tissue swelling and pitting is present. Late in Stage II, the limb may not pit as excess subcutaneous fat and fibrosis supervene.
Stage III	The tissue is fibrotic and pitting is absent. Skin changes such as thickening, hyperpigmentation, increased skin folds, fat deposits develop.

Prevention. Primary prevention strategies aim to avoid the occurrence of lymphedema and promote patient well-being [2]. Non-invasive methods such as range of motion exercises and compression sleeves may be beneficial if implemented early, however, it has not definitively been shown to prevent the occurrence of lymphedema at a later timeframe. For women with breast cancer, the only measure that effectively reduces the risk of developing lymphedema involves using sentinel lymph node biopsy for axillary lymph node staging rather than ALND [3,8]. Massachusetts General Hospital has successfully established one prospective BCRL screening program, however, further investigation and stardatization is needed [2].

Conclusions

1. The treatment-related risk factors are ALND and RNRT, non-treatment-related are BMI ≥ 30, subclinical edema, and cellulitis. The main risk factor overall is the ALND due to great lymphatic disruption.

2. Diagnosis is made on the symptoms and physical examination. Symptoms include progressive upper limb swelling, skin changes, discomfort, and limited range of motion. The measurement of the extremity girth is the key method used during physical examination.

3. Conservative methods are preferred for BCRL management. The combination of different conservative methods depends on the lymphedema staged based on ISL classification.

4. For prevention the physical exercise or compression therapy may be used, however, the fundamental priciple is limiting the extent of lymph node dissection during ALND.

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SU KRŪTIES VĖŽIU SUSIJUSI LIMFEDEMA: RIZIKOS VEIKSNIAI, DIAGNOSTIKA, VALDYMAS, PREVENCIJA

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Raktažodžiai: su krūties vėžiu susijusi limfedema, viršutinės galūnės limfedema, rizikos veiksniai, limfedemos diagnostika, limfedemos prevencija, limfedemos gydymas.

Santrauka

Su krūties vėžiu susijusi limfedema yra neigiama krūties vėžio ar jo gydymo baigtis, kuri pasireiškia 1 iš 5 pacienčių. Sutrikus limfos tekėjimui, ji kaupiasi audiniuose ir atsiranda edema. Diagnozė formuojama remiantis tokiais simptomais kaip progresuojantis viršutinių galūnių patinimas, skausmas ir diskomfortas, odos pokyčiai, ribotas judesių diapazonas. Remiamasi viršutinių galūnių apimties matavimų rezultatais. Pagrindiniai gydymo metodai yra neinvaziniai, tokie kaip kompresija ar fizioterapija. Prevencijai galima taikyti kompresinę terapiją arba fizinius pratimus, tačiau limfmazgių pašalinimo masto ribojimas yra vienintelė priemonė, mažinanti su krūties vėžiu susijusios limfedemos dažnį.

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