Recent Researches in Health Sciences

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Edited by

Nelya Lukpanovna Shapekova,
Levent Ozdemir,
Bilal AK,
Vesile Şenol
and Hicran Yıldız

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PREFACE

The book is organized into 4 sections and 47 chapters. A brief description of each of the sections follows:

Section 1 identifies and discusses the general medicine issues including lymphedema rehabilitation, cerebrospinal fluid, chronic thromboembolic pulmonary hypertension, lung volume reduction treatments, personalized chemotherapy, preclinical applications, chronic pancreatitis, prevention of chronic diseases, developments in hemoglobinopathies, homeopathic approach to chronic diseases, obesity, and inflammation, rehabilitation after injuries, impact of microbiota on foetal life, multiple sclerosis, idiopathic pulmonary fibrosis, psoriasis vulgaris and neurotransmitters.

Section 2 examines some challenges on child health and child education. The section has 10 chapters including the effects of television on development of children, integration of global citizen education to early childhood education, social skills of the children, cyber bullying in the adolescence period, adolescent pregnancies, autism and sport, social work practices in schools, nutrition and obesity in children.

Section 3 has 4 chapters including diet, nutrition and non-communicable diseases, nutritional status according to anthropometric measurements in elderly, the effect of salt on health, the role of nutrition on health in the elderly.

Section 4 presents an analysis of issues and concerns in health management. This section has 10 chapters including violence in the health sector, health promotion and health literacy, health and mobbing, work study- ımprovement of business processes in healthcare, health of healthcare professionals, risk management in emergency healthcare services, characteristics of healthcare and hospital services, cyberloafing.

Contributions in each chapter are prepared by experts in the respective fields and mirror the advancement in the approach. This book contains important future tasks of the particular fields and supplies extensive bibliographies at the end of each chapter, as well as tables and figures that illustrate the research findings. All these make this book highly useful and a must read for students, researchers and professionals in health sciences.

We would like to express our gratitude to all contributors for bearing with us as the volume has taken time to come to fruition.

We particularly wish to express our thanks to the team at Cambridge Scholars Publishing for preparing the book for publication.

The Editors

MEDICINE AND GENERAL HEALTH SCIENCES

CHAPTER 1

LYMPHEDEMA REHABILITATION

SEVIL CEYHAN DOĞAN

Introduction

Lymphedema (LE) is a chronic, progressive disease disrupting the quality of life. It is a regional or diffuse accumulation of interstitial fluid high in protein content (1 g/1000 mL) in the skin and subcutaneous tissues. Lymphatic stasis induces the proliferation of adipose tissue and an inflammatory reaction that results in fibrosis. Although it often affects upper and lower extremities, it may also involve the head, trunk and genital region (Alper, 2016; Morgan et al., 2005; Yüksel et al., 2016). The clinical presentation may vary from a mild to extremely severe disease in LE. A sensation of heaviness in the arms or stiffness of the skin may develop if it is not diagnosed or if left untreated (Bakar et al., 2017). In LE, heaviness, stiffness, swelling, pain, cosmetic concerns and functional loss can lead to psychological disorders and impairment in the family-, work-, social- and sexual life-related quality of life (Delialioğlu et al., 2010; Fu et al., 2011).

Breast cancer is the most commonly seen cancer in women based on data from the American Cancer Society, representing 15% of all cancer-related deaths. The American Cancer Society estimated that there will be 232,340 new cases with breast cancer in 2013 and that 2.9 million patients with breast cancer will have a lifetime risk for LE in the United States. In a previous study, more than one-half of breast cancer survivors reported the serious concern regarding the risk for LE (Fu et al., 2013). LE develops following breast cancer in 6-30% of patients (Petrek et al., 2001). In addition, LE incidence is estimated as 26% in patients with breast cancer (Dominick et al., 2014). In a study, it was suggested that LE symptoms may onset immediately after surgery or many years after surgery (Geller et al., 2003). Again, in a single-centre study, patients underwent mastectomy and total axillary dissection was followed for 20 years. It was reported that

breast cancer-related lymphedema (BCRL) developed within the first 3 years in 77% of patients and those remaining patients had an annual risk by 1% for LE development (Petrek et al., 2001).

Lymphedema Classification

In general, LE is classified as primary or secondary based on aetiology. Primary LE is a genetic disorder due to lymphatic aplasia, hypoplasia or hyperplasia. Secondary LE is seen as a common complication of cancers such as breast cancer or gynaecological cancers and/or cancer therapy; however, it may also develop due to trauma, phlebo-lymphostatic edema caused by chronic venous insufficiency, individual factors such as obesity and other causes such as infection. Secondary LE is the most common cause in LE, which is mainly seen in association with cancer and cancer treatment (Alper, S., 2016; Morgan et al., 2005; Yüksel et al., 2016; Bakar et al., 2014).

Survival has been increased in cancer patients by the improved likelihood of early diagnosis due to screening programs and advanced diagnostic methods and advancements in cancer treatment. However, improved survival in cancer patients also increases the risk for long-term complications of therapy such as BRCL (Smile et al., 2016). BRCL is in 21% of patients with breast cancer on average, ranging from 5% to 60% (Smile et al., 2016; Shah et al., 2011; DiSipio et al., 2013).

In a meta-analysis, it was reported that the risk for BRCL is markedly higher in patients undergoing regional node irradiation than whole-breast irradiation (Shaitelman et al., 2017).

Lymphedema Staging

Clinically, LE is classified into 4 stages according to the International Society of Lymphology (ISL) (Dirican et al., 2011):

Stage 0 (latent, subclinical LE): Lymphatic vessels are injured in some extent and lymphatic drainage capacity is sufficient. No lymphedema is present clinically. In this stage, patients may experience heaviness or are totally asymptomatic. Stage 0 is critically important to prevent overt LE.

Stage 1 (acute phase; spontaneously reversible LE): There is a soft, pitting edema which can be reversed by extremity elevation. No fibrotic change is present. The extremity is generally normal early in the morning and almost at normal size.

Stage 2 (chronic phase; spontaneously irreversible LE): Reversibility is decreased. There are fibrosclerotic changes and the extremity is

enlarged with stiffness. Stemmer's sign is positive. In this stage, skin infections are common due to the dysfunctional immune system.

Stage 3 (lymphostatic elephantiasis): Swelling is irreversible and the extremity is extremely enlarged in this stage. The tissue is stiff, namely fibrotic. The severity of papilloma, fistula, and hyperkeratosis is markedly increased. There is pitting with pressure but it disappears immediately. There is a decrease in function and fine skills.

Stewart Treves syndrome (lymphangiosarcoma): There is increased pigmentation, large vesicles, and keratotic lesions. It is fatal with the marked loss in functionality. It is generally seen in patients with breast cancer undergoing mastectomy, mainly in women. The syndrome is considered as stage 4 LE by some authors whereas a rare complication of chronic LE by others (Petrek et al., 2001, Berebichez-Fridman et al., 2016, Krich et al., 2016).

The severity of LE is rated in 4 categories by comparing with the healthy extremity (Dirican et al., 2011; Gonzalez et al., 2014):

Grade 1: Mild. Asymptomatic. No swelling, compression or sensation of heaviness in extremities. It is generally seen in distal parts of the extremity. Circumferential difference is <4 cm.

Grade 2: Moderate. Intermittent swelling in the extremity but no increase in the highest diameter and stockings are still fitting. The circumferential difference is >4 cm and <6 cm.

Grade 3a: Severe oedema. Swelling and the sensation of heaviness in the fixed arm. Stockings do not fit. Oedema is physically disturbing but does not cause functional loss. Infection is common since the risk for interruption of skin integrity is increased but the patient experiences fewer than 4 infections per year.

Grade 3b: Massive oedema. The sensation of heaviness, disability, decreased functionality and severe swelling in the fixed arm. Similar symptoms as grade 3a but involves more than one extremity.

Grade 4: Gigantic oedema. Elephantiasis. Serious and irreversible edema. Oedema may involve head and neck region. Infections are frequent and patient generally experiences more than 4 infections per year.

Diagnostic Evaluation in Lymphedema

LE is a progressive disease. Diagnosis should be made as early as possible for control by an effective treatment. Differential diagnosis of other disorders that may cause swelling such as deep vein thrombosis, heart failure, liver failure or renal failure is critical for accurate diagnosis. In routine clinical practice, the LE diagnosis is primarily made by physical

examination and the measurement of circumference in the extremity if the underlying cause is known (Özdemir, 2016). In general, swelling that has ≥2 cm increase in circumference or a circumferential difference of 2 cm or >200 mL volume difference between extremities or an increased volume by 10% in the extremity is sufficient for LE diagnosis. Although such parameters are frequently used, they are unable to distinguish extracellular fluid or lymph fluid from muscle, fat, bone or other soft tissues; thus, they may cause misdiagnosis of LE (Fu et al., 2013). Classical methods used in LE diagnosis fail to aid in the diagnosis of subclinical disease, resulting in the delay in treatment. Bioelectrical impedance analysis (BIA) is a method that may be used in the diagnosis of subclinical LE. The BIA determines the extracellular fluid difference between extremities by measuring tissue resistance against the flow of varying electric currents. The progression to clinically overt LE can be prevented by recognizing subclinical LE and taking appropriate measures, education and timely management (Erdogan Iyigun et al., 2017).

The LE diagnosis is generally made based on history and characteristic findings on physical examination. However, recent technological advances focus on novel methods and their use for imaging lymphatics in the diagnosis of LE (O'Donnell Jr. et al., 2017).

History and Physical Examination

In LE, history must include time of onset, localization of onset, the triggering factor, the medical and/or surgical history, the number of lymph nodes excised, the sensation of heaviness and whether there is a decrease in oedema in the morning. For other disorders that may cause oedema including cardiac, renal, hepatic diseases and thyroid disorders, travel and history of infection in the extremity involved should have to be questioned. In addition, family history should be taken for primary lymphedema or inherited disorders (Bakar et al., 2014; Özdemir, 2016; Cerrahoglu et al., 2015).

Inspection: Skin colour, scar tissues and posture of the patient should be observed (Bakar et al., 2014, Cerrahoglu et al., 2015). Skin colour is important regarding erysipelas and cellulitis. Hyper-keratotic and hyper-pigmented appearance may develop in advanced stages. In addition, definitive localization of oedema should be identified, which is critical for manual lymphatic drainage. If scar tissue is present, localization should be established (Akalın, 2016). Low-intensity laser therapy should be applied in treatment.

Palpation: Skin temperature, tissue stiffness and the presence or absence of pitting are examined. Pitting indicates increased fluid at an interstitial space. Pitting can be seen by stage 1 oedema. It is marked in stage 2; however, pitting can be either present or lacking in further stages due to tissue fibrosis. No pitting is present in stage 3 since tissue stiffness is extreme due to fibrosis.

In clinical examination, Stemmer's sign is assessed. It was first defined by Robert Stemmer in 1976. There is an attempt to pinch and lift the skinfold at the base of the second or middle finger (on the hand or foot). Failure to lift the skin is considered as positive, indicating thickened skin. This sign is pathognomonic for LE. Stemmer's sign is negative in lipoedema which generally involves the lower extremities. Physical examination is completed by the range of motion measurements and a motor and sensorial examination (Bakar et al., 2014; Özdemir, 2016; Akalın, 2016).

Current Measurements in Lymphedema

Extremity volume measurements are performed by several methods used in the management of LE. These methods include circumference measurements, bioimpedance spectroscopy, volumetric measurement, perometry, tonometry, lymphoscintigraphy, Kuhnke's disc method, Frunstrum formula, lymphography, magnetic resonance imaging and sonography (Bakar et al., 2014).

Circumference measurements: These are performed at standard landmarks defined by the clinician with the use of a tape measure. Circumference is measured at certain distances (4, 5, 10 cm) from fixed landmarks such as the ulnar styloid or medial malleolus (Özdemir, 2016). Data obtained can be used to calculate volume with a mathematical formula (Akalın, 2016). Measurements should be performed from both extremities at the same position and repeated measurements should be made by the same observer if possible. This method is practical, rapid and inexpensive but cannot detect subclinical LE and may be subjected to inter-observer variation (Földi et al., 2006).

Kuhnke's disk method: The circumference of the extremity is measured from distal to proximal by 4-cm intervals (Bakar et al., 2014).

Frunstrum method: Circumference measurement is performed at the thickest and thinnest segment of the extremity. Volume is calculated by measuring the distance between the thickest and thinnest segment and employing the distance measured in a mathematical formula (Bakar et al., 2014).

Volumetric measurement: The water displacement method relies on calculating the volume of the affected limb by immersing in special water tanks and determining volume difference from the contralateral extremity. This method is developed based on Archimedes' principle suggesting that the volume of water displaced is equal to the volume of the object (Özdemir, 2016; Akalın, 2016). This method is accepted as the gold standard for the measurement of extremity volume (Armer et al., 2013). It has some disadvantages including the need for litres of water, being a time-consuming method, the need for the individual preparation of each patient, hygiene problems and inability for use in patients with open wounds (Akalın, 2016).

Perometry

Perometry is an infrared optical electronic scanner with high reliability in volume calculations. In recent years, it has been introduced in LE trials. The extremity is placed in a frame that sends the infrared beam via sensors. Volume is calculated by measuring extremity circumference by 4-mm intervals. This method has become the novel gold standard for volume calculation; however, it is an expensive device, which can perform measurements only at the upper and lower extremity; in addition, the device is not portable and cannot assess whole extremity (Özdemir, 2016; Akalın, 2016; Johnson et al., 2014).

Tonometry

This method measures tissue tone, namely, tissue stress, while most methods measure volume. It assesses the amount of fibrotic induration and skin compliance by measuring tissue resistance against compression and tissue stress (Johnson et al., 2014).

Bioimpedance Spectroscopy

Bioimpedance spectroscopy (BIS) is generally defined as a novel technology; however, it was first used to measure body fluid in 1969 and it was first reported that lower extremity oedema following lymphatic obstruction was measured in 1989 (Seward et al., 2016). It is a non-invasive method. Alternate current and resistance against current are measured across the extremity by cutaneous electrodes (Johnson et al., 2014). Resistance to electric current depends on the conductivity of various tissues. Bone and adipose tissues are isolators, namely insulator,

and will have high impedance. On the other hand, interstitial fluid and muscle tissues are conductive. Thus, higher fluid content in the extremity will lead to less impedance or resistance to electric current. This enables the selective measurement of fluid content by a device without measuring the amount of adipose and fibrous tissues (Seward et al., 2016). Its reliability and validity were shown in the diagnosis of lymphedema at upper and lower extremity. It may also be used to detect LE in hands and it has a strong correlation with perometry in the measurement of hand LE (Özdemir, 2016). In a prospective study, in patients with breast cancer undergoing surgery, bioimpedance measurements were performed before surgery, on month one after surgery and every 2 months for 2 years thereafter. Clinical LE was developed in 20 of 102 patients who were at risk for LE and subclinical LE was diagnosed by BIS ten months before clinical diagnosis (Cornish et al., 2001). In another study, 186 patients undergoing axillary lymph node dissection with a diagnosis of breast cancer were recruited in a monitorization program. In these patients, measurements were performed at baseline and by 3- or 6-month intervals after dissection over 5 years by using BIS. During follow-up, short-term LE rehabilitation, LE compression sleeves, exercise, arm elevation and infection measures as well as education about body mass index and hand use were provided to the patients diagnosed as subclinical LE. The control group included patients who had a baseline measurement but no follow-up measurement due to insurance issues or those who presented at the postoperative period. In these patients, arm circumference was monitored. Subclinical LE was detected in 33% of patients by BIS and the treatment was planned promptly. On follow-up, clinical LE was developed in 4.4% of patient groups whereas in 36.4% of controls. Periodical follow-up by BIS is recommended, particularly in patients at high risk for LE, since it allows early diagnosis and timely intervention. This may have positive effects on both quality of life and health care expenses (Soran et al., 2014). This method diagnoses LE by comparing the normal extremity; thus, the comparison is impossible in patients with bilateral LE. Normalization of extracellular fluid elevation against intracellular fluid volume and normalization against the uninvolved extremity (arm in bilateral lower extremity oedema and leg in bilateral upper extremity oedema) are used to solve this issue. It is promising to assess bilateral LE semi-quantitatively by using BIS (Ward et al., 2011).

Lymphography

It provides detailed anatomic data; however, it has disadvantages such

as allergic reaction, wound site infection and exposure to ionizing radiation. Today, it is not preferred (Özdemir, 2016).

Genetic assays

Gene mutations related to some types of lymphedema: Restricted gene domains such as VEGFR-3 (Milroy disease), FOXC2 or SOX18 (hypotrichosis, LE, telangiectasia) can be tested. In addition, there are ongoing research efforts about potential genetic disorders that are thought to increase risk for secondary LE (The Diagnosis and Treatment… 2013).

Current Approaches to Lymphedema Management

Since LE is a progressive disorder, treatment should be planned as soon as possible after diagnosis. Early diagnosis and treatment may slow disease progression, prevent complications, improve the quality of life and save treatment expenses (Bakar et al., 2014; Özdemir, 2016; Soran et al., 2014).

Treatment is considered as conservative (non-operative) and surgical (operative) in peripheral LE. Skin hygiene and care (cleaning, low pH lotions) are critical in the success of all treatment modalities. A simple range of motion exercises, external compression and extremity elevation aid in all patients (Anonymous, 2013).

Conservative (Non-operative) Management
Complex decongestive treatment

Although larger studies have been conducted regarding LE treatment, complex decongestive treatment (CDT) is still considered as the most effective treatment modality, representing the gold standard in LE management (Cerrahoğlu et al., 2015; Angooti Oshnari et al., 2016). CDT is a treatment approach combining several modalities; however, it has 4 components accepted by the Medicare Evidence Development and Coverage Advisory Committee: 1) Manual lymphatic drainage; 2) Compression garments and/or sleeves; 3) Exercise; 4) Skin care; and 5) Pneumatic compression pump (Armer et al., 2016). Other modalities used in CDT include; patient education, kinesiological taping, and laser therapy (Özcan et al., 2016). CDT has 2 phases. Phase I (treatment phase) includes intensive therapy aiming to reduce oedema as possible. Phase I involves sessions on 3 or 5 days per week over 2-4 weeks. In this phase, treatment modalities are selected based on the patient's status. Then, therapy

proceeds to phase II (maintenance phase) which aims at the exacerbation of oedema and continues for a lifetime (Angooti Oshnari et al., 2016). In phase II, custom-made or ready-to-wear garments (LE compression garments) are used. The compression garments have several types. For instance, there are sleeves with a silicone band extending to the shoulder, those with shoulder straps, and those with gauntlets or gloves alone for upper extremity LE. Similarly, there are knee-high, thigh-high or pantyhose compression garments, open- or closed-toe garments and unilateral or bilateral garments. The selection of compression garments is made based on the localization, type, and amount of oedema in the patient. The CDT does not only reduce oedema but it also relieves pain effectively (Angooti Oshnari et al., 2016; Hamner et al., 2007; Mondry et al., 2004).

Manual lymphatic drainage

Manual lymphatic drainage (MLD) was developed by Vodder in 1932. It is a specific technique of manual therapy and massage using 4 primary movements of Vodder (stationary cycle, pump, rotary, and scoop) (Bakar et al., 2014; Özcan et al., 2016). It is thought that specific light touches improve lymphatic drainage by contracting superficial lymphatics. Diaphragmatic breathing before and after MLD enhance the effects of MLD (Bakar et al., 2014). One MLD session generally takes 45 minutes but it may vary based on the severity of oedema and the region involved. The MLD is contraindicated in case of active cellulitis, uncontrolled infection, moderate-to-severe heart failure and acute deep vein thrombosis. Relative contraindications include renal failure, diabetes mellitus, uncontrolled hypertension, acute bronchitis, asthma, pregnancy, severe atherosclerosis, arrhythmia and acute inflammatory bowel disease (Özcan et al., 2016). It has been reported that MLD is more effective than the intermittent pneumatic pump and that it softens fibrosis (Bakar et al., 2014).

Compression bandaging

There is resting and working pressure features in compression bandaging. Bandaging with low resting and high working pressure is employed in LE. Multi-layer short-stretch bandaging is used (Badger et al., 2000). Thus, opposite forces by muscle and bandaging during exercise create a pump effect for lymph drainage (Cerrahoğlu et al., 2015). Bandaging involves a special technique. The number of layers is higher at distal in order to create a pressure gradient favouring proximal flow.

Padding can be used at sites with fibrosis. Inappropriate application of compression bandaging may lead to increased oedema or no effect. Thus, bandaging should be performed by trained professionals (Anonymous, 2013; Özcan et al., 2016).

Compression garments

Compression garments are used to maintain reduction and to prevent the increase in oedema in phase II. In addition, they protect skin with decreased elasticity (Cerrahoğlu et al., 2015). To achieve the best outcome, size measurements should be taken by trained individuals and garments have to be used regularly on a daily basis. Since these are custom-made products, it is important to follow instructions for use and cleaning. Compression garments will wear with decreased effectiveness in time as they are used and cleaned regularly. Thus, it is recommended they are changed at 6-month intervals (Bakar et al., 2014).

The pressure and type of compression garment are selected by considering stage and localization and the patient's preference.

Exercise

Exercise enhances lymphatic venous return via musculoskeletal pumping. In LE, exercise should be an integral part of life. Previously, it was thought that resistance exercises increase LE. However, many randomized-controlled studies demonstrated that progressive resistance exercises are safe (Sagen et al., 2009; Irdesel et al., 2007; Aras et al., 2016; Kilbreath et al., 2006). Rehabilitation and exercise interventions have been found beneficial in LE patients. However, it is recommended that exercise programs should be safe; that patients should be closely monitored for standardization and that exercises should be modified according to patient status, skills and exercise capacity (Armer et al., 2016). Exercises should be performed with the compression bandage or garments (Aras et al., 2016).

Skin care

In LE, it is crucial to protect skin integrity and hygiene since the risk for infection is increased in the involved extremity. The skin should be humidified regularly since dryness facilitates the invasion of bacteria and fungi. The extremity should be washed with soaps with neutral pH and humidified with ointments with low pH. The patient should be informed

regarding skin care (Bakar et al., 2014; Cerrahoğlu et al., 2015; Aras et al., 2016).

Intermittent pneumatic compression therapy

Intermittent pneumatic compression (IPC) devices have been used since the 1950s. These devices with different types of technological equipment are currently used in LE treatment. There are no established data regarding duration and pressure. Treatment duration may vary from 30 minutes to several hours. The pressure applied is critical to avoid injury of superficial lymphatics; thus, the pressure is set as 30-60 mmHg since it is proposed that pressure >60 mmHg results in the collapse of lymphatic vessels. Studies showed that multi-chamber devices act more rapidly (Bakar et al., 2014; Cerrahoğlu et al., 2015; Aras et al., 2016).

The IPC device alone is not effective in LE and may even cause LE in the genital region or trunk. Thus, it should be used as part of CDT (Bakar et al., 2014).

It is suggested that novel IPC devices act as MLD; however, there is no sufficient study in this context (Anonymous, 2013; Aras et al., 2016). The compression/decompression cycle is rapid in these devices, which is thought to improve lymphatic drainage (Bakar et al., 2014).

Patient education

Since LE is a lifetime chronic disorder, the patient and their relatives should be informed (Cerrahoğlu et al., 2015). The patients at risk for LE should be informed of risk factors, preventive measures, and disease. The involved extremity should be protected against trauma. One should avoid blood sampling or blood pressure measurements at the involved site. It is recommended to use the involved extremity during long journeys and flights. Excessive or forceful use should be avoided in the involved extremity. The patient should be informed that extreme heat or cold, tight garments and weight gain will negatively affect edema (Aras et al., 2016).

Low-intensity laser therapy

Low-intensity laser therapy (LILT) has been long used in LE treatment and was approved by the Food and Drug Administration (FDA) in 2007. It is thought that LILT is associated to anti-inflammatory and phagocytic effects and positive effects on wound healing, neuronal regeneration and skin infections (Omar et al., 2012; Lievens, 1991). In a rat study on wound

healing, it was suggested that laser therapy facilitates regeneration in both venous and lymphatic vessels. It is also reported that laser therapy provided a reduction in oedema volume and a decrease in pain, as well as improvement in scar mobility and movements of the shoulder (Aras et al., 2016). LILT is used at various doses and protocols; however, the protocol consisting of 2 periods is recommended in general. In the first period, LILT is applied in 3 sessions per week (over 3 weeks). The second period is given 8 weeks after the first period with the same regimen (3 sessions per week over 3 weeks). It is generally applied to the axilla, the surgical scar or the origin of oedema or fibrosis in the upper extremity. It is applied to 17 points (one minute each) by 2-cm intervals. In a study from the USA, it was reported that LILT added to standard treatment is associated with beneficial effects including reduction in LE and pain, improved ROM, and mobility of scar tissue (Dirican et al., 2011).

Kinesiological taping

In LE, kinesiological taping primarily aims to relieve circulation by reducing compression on lymphatic vessels at the tissue level (Çeliker et al., 2011). After the application of kinesiological tape, the space between skin and muscles is increased at the area where taping is applied (Tsai et al., 2009). Blood and lymphatic fluid flow are increased after the elevation of skin. Thus, lymph fluid moves towards lymphatics and lymph nodes. In addition, the spasm is relieved by the effects of taping on muscles, allowing the maximum contraction and relaxation of muscles. This massage-like effect regulates circulation. The patients must be evaluated for deep vein thrombosis and peripheral artery disease and a trial should be performed in a small area in patients with allergic or sensitive skin. The tape is sliced into 4-6 strips without cutting 2-3 cm at the base. The base is placed close to the lymph node in accordance with the direction of lymphatic flow, meaning that the base is placed proximal and the strips are plastered toward the distal part of the extremity. No stretching is applied to the base while strips are plastered with no or mild stretch. By taking the direction of lymphatic flow, separate applications should be performed at proximal and distal regions (Çeliker et al., 2011). A meta-analysis investigated the safety and effectiveness of kinesiological taping in LE. Although no significant difference was found in the reduction in extremity volume between the compression bandage and kinesiological taping, the extent of reduction was higher in the compression bandage group. In addition, no significant difference was shown in subjective experience although it is commonly thought that kinesiological taping is more

comfortable than the compression bandage. In addition, skin complications related to kinesiological taping were reported in 10-21% of patients. In conclusion, based on available evidence, it is recommended to use kinesiological taping carefully in cases where the compression bandage is not feasible (Gatt et al., 2016).

Herbal products and medical therapy

Selenium, horse chestnut, vitamin E and gamma benzopyrones have been investigated in LE treatment. The level of evidence is weak since the study design and sample are limited to these products. There are a limited number of randomized-controlled studies. In conclusion, there is no sufficient evidence supporting the use of herbal products and medical therapies in LE (Denert et al., 2006; Poage et al., 2015; Gothard et al., 2004; Barton et al., 2006; Badger et al., 2004).

Surgical (operative) Management

Surgical intervention could be considered if there is no response to conservative management or if there is extremity dysfunction. The surgical success rate is decreased since fibrosis in the subcutaneous tissue will further disrupt lymphatic return (Aras et al., 2016). In surgery, the risk-benefit ratio should be assessed according to the patient's requirements (Cerrahoğlu et al., 2015). Surgical techniques employed in LE include lymphaticovenous anastomosis, liposuction, excisional interventions, and vascularized lymph node transfer. The outcomes are assessed by volumetric extremity measurements and lymphoscintigraphy. Lymphaticovenous anastomosis and/or lymphaticovenous implantation can be a beneficial treatment option, particularly at the early stages, in LE treatment (Demirtaş et al., 2016).

Surgery is not recommended alone and should be supported by a rehabilitation program. In selected patients, it may function as a part of CDT. Micro-surgery should be performed by surgeons trained in both micro-surgery and lymphology (Anonymous, 2013).

Conclusion

In recent years, survival from cancer is prolonged by rapid advances in the diagnosis and treatment of cancer; thus, the incidence of complications related to cancer and its treatment is increased by prolonging survival. Secondary LE is one of these complications. The incidence of secondary

LE is increasing since the most common cause is cancer and cancer treatment.

Prevention of LE is far better than treatment after the onset of disease. Thus, patients at risk for LE should be referred to Physical Medicine and Rehabilitation clinics and patients should be informed and educated regarding LE. Appropriate treatments should be arranged by physiatrists. The ISL recommends CDT as the first-line therapy in LE.

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