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Complex Decongestive Therapy for Lower Extremity Lymphedema: Results from a Tertiary Care Center

Alt Ekstremite Lenfödem Tedavisinde Kompleks Dekonjestif Tedavi: Bir Üçüncü Basamak Merkezin Sonuçları

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Abstract

Objective: Complex decongestive therapy (CDT) is the gold standard of lymphedema treatment. In this retrospective study, we aimed to evaluate the effectiveness of CDT in patients with lower extremity lymphedema.

Materials and Methods: In this retrospective study, demographic data, disease characteristics, percentage of excess volume, and lymphedema volume to body mass index (LV/BMI) ratio of lower extremity lymphedema subjects were analyzed.

Results: Treatment outcomes of 198 extremities from 127 patients were analyzed. Pre- and post-treatment LV/BMI values were significantly higher in the venous insufficiency group. Lymphedema grade was found to have a positive and significant correlation with BMI (p<0.05). Post-treatment LV/BMI values showed a positive correlation with patients' activity levels and number of radiotherapy sessions (p<0.05).

Conclusion: We have observed that primary lymphedema responds equally well to CDT as does cancer-related lymphedema. We have also detected similar volume reduction values with CDT in patients with chronic venous insufficiency.

Keywords: Complex decongestive therapy, lymphedema, rehabilitation, venous insufficiency

Öz

Amaç: Kompleks dekonjestif tedavi (KDT), lenfödem tedavisinde altın standart olarak kabul edilmektedir. Bu retrospektif çalışmada, alt ekstremite lenfödem tedavisinde KDT'nin etkinliğini değerlendirmek amaçlanmıştır.

Gereç ve Yöntem: Bu retrospektif çalışma, üniversite hastanemizde alt ekstremite lenfödemine yönelik KDT uygulanmış olan hastaların, demografik özellikleri, hastalık özellikleri, volüm farkları, lenfödem volümünün vücut kitle endeksine (LV/VKİ) oranı değerleri incelenmiştir.

Bulgular: Toplam 127 hastaya ait 198 ekstremitenin tedavi sonuçları incelenmiştir. Venöz yetmezliğe bağlı alt ekstremite lenfödemi bulunan hastalarda, tedavi öncesi ve sonrası LV/VKİ oranları anlamlı olarak daha yüksek saptanmıştır. Lenfödem evresi ile VKİ arasında anlamlı bir pozitif ilişki saptanmıştır (p<0,05). Tedavi sonrası LV/VKİ oranı ile hastaların aktivite düzeyleri ve radyoterapi seans sayısı arasında da anlamlı ilişki bulunmuştur (p<0,05).

Sonuç: Sonuçlarımız, primer lenfödemin de, KDT'ye kansere bağlı lenfödem kadar iyi yanıt verdiğini desteklemektedir. Ayrıca, kronik venöz yetmezlik hastalarında da KDT ile benzer volüm azalması elde edildiği gözlenmiştir.

Anahtar kelimeler: Kompleks dekonjestif tedavi, lenfödem, rehabilitasyon, venöz yetmezlik

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Introduction

Lymphedema is defined as the accumulation of protein rich lymphatic fluid in the interstitial tissues as a result of congenital or acquired insufficiency of the lymphatic system, that results in the gradual swelling, inflammation, adipose hypertrophy and fibrosis in the affected body area (1). Limbs are most commonly affected but trunk, abdominal structures or head and neck may also be involved. Lymphedema can be classified as primary or secondary, according to the presence of a discernable precipitating injury to the lymphatic system. Cancer and cancer treatment is the most common cause of lymphedema in the developed world, followed by infections, chronic venous insufficiency, and congenital lymphatic obstruction. Surgery, lymph node dissection, metastasis and radiation therapy all play a role in the development of cancer related lymphedema.

In addition to local complications such as infection, pain and ulceration, lymphedema causes significant morbidity such as depression, anxiety and limitation of daily activities (2). Although lower extremity lymphedema is more common and its etiology more varied, breast cancer related upper extremity lymphedema is the most thoroughly researched subgroup of lymphedema. There is still no definite cure for lymphedema and all treatment strategies aim to manage the swelling and related complications. Complex decongestive therapy (CDT) is still the most effective treatment strategy in controlling symptoms, but results differ according to etiology, site and extent of involvement.

Most studies assessing the effectiveness and results of lymphedema treatment focus on upper extremity lymphedema, more specifically cancer related upper extremity lymphedema. But treatment results and related factors are not as thoroughly researched as upper extremity lymphedema. The evidence regarding the effectiveness of additional treatment methods such as low-level laser therapy or pneumatic compression devices is still lacking. For this reason, the aim of this study was to retrospectively document the characteristics and treatment results of lower extremity lymphedema patients treated in our tertiary lymphedema rehabilitation clinic.

Materials and Methods

We have reviewed and recorded data from the patient files of those patients that had received at least one cycle of treatment for lower extremity lymphedema in the lymphedema care and treatment unit of our university hospital. For this study, we included patient records of those subjects that received CDT and had control limb measurements in their files that were followed up between 2010-2021. Ethical approval was obtained from Ege University Faculty of Medicine Clinical Research Ethics Committee for this retrospective study (decision no: 15-1.1/1, date: 29.06.2015).

Only adult patients were included in the study. Subjects that did not have lower extremity lymphedema (including those that were referred to us prophylactically), pediatric patients and lower extremity swelling caused by other reasons (lipedema, tumors etc.) were excluded. Demographic characteristics including age, height, weight, body mass index (BMI) as well as disease characteristics such as cause of lymphedema, history of chemotherapy and radiotherapy, number of removed lymph nodes, duration of lymphedema, lymphedema grade, duration of time to initiation of therapy, number of treatment sessions, presence of fibrosis, and patients' activity level were recorded and presented in Table 1.

In our routine patient follow-up, we use the limb circumference method for the calculation of excess lymphedema volume (LV) and for comparison between both sides. In this method, lower extremity circumference is measured with a tape measure, starting from the 1st metacarpophalangeal joint, ankle joint and every 4 cm proximally. Extremity volumes are then calculated with the help of a spreadsheet formula, the truncated cone volumes calculated using limb circumference measurements (3). For unilateral lymphedema, percentage of excess volume was calculated using the excess volume reported by Forner-Cordero et al. (4). Since most patients had bilateral lower extremity lymphedema, absolute limb volume differences were not sufficient to assess treatment outcomes. For this purpose, we have used the LV to BMI ratio, which was previously found to correlate well with degree of excess LV and lymphedema arade (5).

In our routine patient care, each new patient presenting to our lymphedema unit goes through a detailed evaluation. Every patient receives education regarding lymphedema selfmanagement protocol (SMP) including education about risk factors, precipitating situations, hygiene, protection of extremity from trauma, moisturization and suitable exercises. Exercise not only increases lymph drainage but also helps prevent limitation of joint movement. Proper exercises including stretching, range of motion, pumping, aerobic and strengthening exercises are tailored according to patients' status and needs and are reassessed regularly (6). Each patient is informed about weight control and overweight and obese patients are referred to a dietician and receive recommendations regarding weight loss. SMP also includes manual lymph drainage (MLD) techniques. CDT remains to be the cornerstone of conservative management of lymphedema. First phase or intensive phase of CDT, in addition to SMP and MLD, consists of compression therapy, usually in the form of bandaging of the affected area to increase drainage and rapidly reduce LV by creating a pressure gradient. This phase may also include pneumatic compression therapy. Second phase or maintenance phase continues to employ skin care, exercise and if necessary, compression garments to sustain limb volumes (7). In our center, all patients that receive compression bandage therapy also receive lower extremity pneumatic compression treatment as part of the compression therapy (BioCompression systems SC-3008-DL, USA). In our study, no patient showed adverse reactions to pneumatic compression therapy. After the completion of the intensive phase of CDT, every patient receives a prescription for compression garments and is followed up regularly during the maintenance phase.

Kinesiotaping may be added to treatment programs and is applied once or twice weekly in patients receiving CDT. Similarly, patients with fibrotic thickening of the skin may receive extracorporeal shock wave therapy (ESWT) once a week during the intensive phase of CDT. These treatment options, if applied, were recorded. Most patients that have fibrosis in their affected extremity receive low-level laser therapy. Laser therapy is applied by a physical therapy technician before each bandaging session.

Statistical Analysis

Statistical analyses were carried out using statistical software package SPSS version 20.0 (International Business Machines Corp., Armonk, NY, USA). Demographic and clinical parameters were presented using descriptive statistics (frequency distributions, mean and standard deviation). Before and aftertreatment values for LV/BMI were compared using Paired Samples t-test. Before and after-treatment percentage of excess volume values were compared using Paired Samples t-test. Excess volume and LV/BMI values belonging to cancer and venous insufficiency patient subgroups, and values belonging to different treatment groups were compared with independent samples t-test. Correlations between patient parameters and treatment outcomes were assessed with Pearson's correlation analyses.

Results

Files belonging to 166 patients were assessed for inclusion in the study. Twenty-three patients had lipedema and were excluded. Twenty-six patients had no treatment records. After excluding these cases, a total of 127 patients were included in the study. All patients were of Caucasian ethnicity. Fifty-six patients had received treatment for unilateral lower extremity lymphedema while 71 had bilateral lower extremity lymphedema. Treatment outcomes of a total of 198 extremities were recorded and analyzed. Patient demographic and clinical characteristics are presented in Table 1.

Only 1 patient had grade 1 lymphedema, all remaining subjects had grade 2 or grade 3 lymphedema. The mean age of patients was 55.5±14.3 years. Seventy nine percent of subjects were female. Nearly half of subjects (44%) had cancer related lymphedema, followed by lymphedema related to venous insufficiency (23.6%). Other etiologies were far less common. Cancer related lymphedema patients had gained approximately 8.2±9.8 kg after surgery and most of them had received both chemotherapy and radiotherapy (59% and 66% respectively). Mean duration of time from the start of lymphedema related symptoms to the initiation of therapy was 75.8±107.6 months and mean duration of follow-up was 25.7±15.2 months. Almost one third of patients had had at least one episode of lymphangitis.

One hundred and ninety-eight extremities were included in the study and a majority (72.7%) of those had received kinesiotaping in addition to SMP and compression bandaging therapy. LV/ BMI ratio decreased significantly with CDT (p<0.05) and mean percentage of decreased volume was found to be 11.6%. When grouped according to treatment types, all patients regardless of group, showed statistically significant improvement after treatment (p<0.05).

Table 1. Demographic and clinical cha patients (n=127)	racteristics of				
Age, year, mean±SD	55.5±14.3				
Female sex, n (%)	101 (79.5)				
Extremity involvement, n (%)					
Unilateral lower extremity	56 (44.1)				
Bilateral lower extremity	71 (55.9)				
Lymphedema grade, n (%)					
Grade 1	1 (0.8)				
Grade 2	65 (51.2)				
Grade 3	61 (48.0)				
Grade 4	0				
BMI, kg/m ² , mean±SD	31.8±7.0				
Etiology, n (%)					
Cancer	56 (44.09)				
Endometrium	17 (13.4)				
Ovarian	10 (7.9)				
Cervix	9 (7.1)				
Prostate	4 (3.1)				
Malignant melanoma	3 (2.4)				
Other	13 (10.2)				
Venous insufficiency	30 (23.6)				
Surgical complication, other than cancer	12 (9.4)				
Primary lymphedema	27 (21.3)				
Infection	2 (1.6)				
Cancer grade, n (%)					
Cancer grade, n (%) Grade 1					
	10 (7.9) 25 (19.7)				
Grade 1	10 (7.9)				
Grade 1 Grade 2	10 (7.9) 25 (19.7)				
Grade 1 Grade 2 Grade 3	10 (7.9) 25 (19.7) 13 (10.2)				
Grade 1 Grade 2 Grade 3 Grade 4	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks Regular exercise	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9) 16 (12.6)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks Regular exercise Athlete Duration from first symptom until first	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9) 16 (12.6) 1 (0.8)				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks Regular exercise Athlete Duration from first symptom until first treatment (months), mean±SD	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9) 16 (12.6) 1 (0.8) 75.8±107.6				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks Regular exercise Athlete Duration from first symptom until first treatment (months), mean±SD Duration of follow-up, months, mean±SD Had at least one episode of lymphangitis, n (%)	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9) 16 (12.6) 1 (0.8) 75.8±107.6 25.7±15.2				
Grade 1 Grade 2 Grade 3 Grade 4 History of radiotherapy, n (%) History of chemotherapy, n (%) Number of removed lymph nodes, mean±SD Weight gained after surgery, kg, mean±SD Genital lymphedema present, n (%) Fibrosis is present, n (%) Stemmer sign positive, n (%) Physical activity level, n (%) Sedentary Leisure walks Regular exercise Athlete Duration from first symptom until first treatment (months), mean±SD Duration of follow-up, months, mean±SD Had at least one episode of lymphangitis, n	10 (7.9) 25 (19.7) 13 (10.2) 8 (6.3) 33 (26.0) 37 (29.1) 10.8±16.9 8.2±9.8 34 (26.8) 62 (48.8) 122 (96.1) 25 (19.7) 85 (66.9) 16 (12.6) 1 (0.8) 75.8±107.6 25.7±15.2 36 (28.3)				

Of the extremities included in our study, 53 had a history of lymphangitis. Limb volumes and percentage of decreased volumes according to a history of lymphangitis are presented in Table 2 and Table 3. Patients with or without a history of lymphangitis showed similar levels of treatment response.

Cancer related lymphedema patients were the majority in our patient cohort and a total of 77 extremities were treated with

CDT. The second most common group consisted of chronic venous insufficiency related lymphedema and a total of 53 extremities were included in the study. A comparison between the two groups is presented in Table 4. When we compared treatment results from these two groups, venous insufficiency group had significantly higher mean BMI values (p<0.05).

Table 2. Treatment characteristics and results of 198 extremities from 127 patients, with pre- and post-treatment limb volume differences

Treatment type, n (%)	Percentage of decreased volume, mean±SD	LV/BMI, pre-treatment, mL m²/kg, mean±SD	LV/BMI, post- treatment, mL m²/kg, mean±SD
SMP+compression bandaging+kinesiotape+pneumatic compression therapy, 144 (72.7)	11.4±8.9	151.9±32.3	134.5±26.2*
SMP+compression bandaging+ESWT+pneumatic compression therapy+LLLT, 31 (15.7)	12.1±10.0	162.7±53.1	143.8±58.5*
SMP+compression bandaging+ESWT+kinesiotape+pneumatic compression therapy+LLLT, 23 (11.7)	11.6±9.7	128.4±27.2	144.0±25.1*
All extremities, 198 (100)	11.6±9.2	152.7±35.8	135.2±33.5*

*Difference between pre-treatment and post-treatment values is significant; p<0.05; Paired samples t-test

SMP: Self-management protocol (patient education, exercise and manual lymph drainage), LV: Limb volume, BMI: Body mass index, ESWT: Extracorporeal shock wave therapy, LLLT: Low-level laser therapy, SD: Standard deviation

Table 3. Comparison of limb volumes and decrease in volumes between patients with or without a history of lymphangitis				
	Limbs with a history of lymphangitis (n=53)	Limbs without a history of lymphangitis (n=145)	p-value	
Percentage of decreased volume, mean±SD	10.0±8.7	12.1±9.2	0.2	
LV/BMI, pre-treatment, mL m ² /kg, mean±SD	154.7±34.8	151.9±36.3	0.6	
LV/BMI, post-treatment, mL m ² /kg, mean±SD	138.2±28.6	134.2±35.1	0.5	
IV: Limb volume RMI: Body mass index. SD: Standard deviation_independent samples t-test				

Table 4. Comparison of treatment outcomes between cancer related and venous insufficiency related lymphedema patients' extremities

	Cancer related lymphedema (n=77)	Venous insufficiency related lymphedema (n=53)	p-value
LV/BMI, pre-treatment, mL m ² /kg, mean±SD	155.3±43.1	137.1±17.0	0.00*
LV/BMI, post-treatment, mL m ² /kg, mean±SD	136.8±42.3	121.6±15.8	0.01*
Decreased volume, %, mean±SD	12.7±9.6	11.1±7.9	0.32
Lymphedema duration, months, mean±SD	70.4±53.2	89.3±82.0	0.1
BMI, kg/m ² , mean±SD	29.9±5.6	35.6±7.3	0.00*
	Cancer related lymphedema (n=77)	Primary lymphedema (n=42)	p-value
LV/BMI, pre-treatment, mL m ² /kg, mean±SD	155.3±43.1	165.4±34.0	0.2
LV/BMI, post-treatment, mL m ² /kg, mean±SD	136.8±42.3	149.7±27.4	0.08
Decreased volume, %, mean±SD	12.7±9.6	8.9±8.0	0.02*
Lymphedema duration, months, mean±SD	70.4±53.2	198.3±189.2	0.00*
BMI, kg/m², mean±SD	29.9±5.6	31.4±7.3	0.2
*Level of significance, p<0.05, independent samples t-test. n: D SD: Standard deviation, LV: Limb volume, BMI: Body mass index			

Table 5. Correlations between treatment parameters						
	Age	BMI	Activity level	Percentage of decreased volume	LV/BMI, pre- treatment	LV/BMI, post- treatment
	r	r	r	r	r	r
Age	1.0	0.2	-0.2	0.1	0	0.1
BMI	0.2	1	-0.1	0	0	0.1
Activity level	-0.2	-0.1	1	-0.2	0.1	0.31*
Removed lymph nodes, n	-0.5	-0.3*	0.1	0.1	0.1	0.1
CT cycles, n	-0.3	-0.2*	0	0.2	0.1	0
RT sessions, n	0	-0.3*	0.1	0	0.1	0.2*
Lymphedema grade	0.2*	-0.2*	-0.2	0.2	0	-0.1
Treatment duration (days)	0	0.1	-0.1	-0.1	0.1	0.1
*p<0.05 correlation is significant						

BMI: Body mass index, LV: Limb volume, SD: Standard deviation, CT: Chemotherapy, RT: Radiotherapy, r: Correlation coefficient

Other demographic factors were similar between the two groups (p>0.05). Pre- and post-treatment LV/BMI values were significantly higher in the venous insufficiency group, although comparison of decreased volume percentages between the two groups was found to be insignificant (p>0.05). When we compared cancer related lymphedema patients with primary lymphedema patients, the percentage of decreased volume was found to be significantly more in the cancer patient group (p<0.05), although pre- and post-treatment LV/BMI values did not differ significantly in the two groups (p>0.05).

Correlation analyses between demographic and clinical parameters are presented in Table 5. Lymphedema grade was found to have a positive and significant correlation with BMI (p<0.05). BMI was also positively correlated with the number of removed lymph nodes as well as number of chemotherapy cycles and radiotherapy sessions (p<0.05). Pre-treatment LV/BMI ratio was not found to correlate with any clinical parameters, but post-treatment LV/BMI values showed a positive correlation with patients' activity levels and number of radiotherapy sessions (p<0.05). Curiously, no disease parameters were found to be correlated with the percentage of decreased LV.

Discussion

In this study, we have observed that most patients with lower extremity lymphedema, regardless of etiology, respond well to CDT.

Cancer and cancer treatment has become the most common cause of lymphedema in the developed world. Nearly 30% of breast cancer survivors develop upper extremity lymphedema. Overall incidence of lymphedema after different types of cancer has been reported to be around 15% (8). Although in some sources, chronic venous insufficiency has been reported to be the most common precipitator of lymphedema, our patient population composed by 56% of cancer related lymphedema cases, followed by venous insufficiency in 30% of cases. Our being a tertiary lymphedema center with a majority of our patients referred to us from the oncology department may explain this predominance of cancer related lymphedema in our patients. It has also been reported that lymphedema resulting from chronic venous insufficiency often goes unnoticed and underdiagnosed until reaching higher volumes, and this may be the case in our center (9). Mean disease duration until referral to the lymphedema unit was found to be 7 years. In accordance with the literature, our patients were predominantly female (79.5%) (10). Studies reporting a higher proportion of venous insufficiency patients also report higher proportions of male lymphedema patients. Our percentages are in accordance with the previously reported numbers (9,10).

Obesity has previously been reported to be related to the development and progression of lymphedema (9). Seidel et al. (11) reported that obesity (BMI \geq 30.0) was significantly more frequent in patients with advanced chronic venous disease. Increased intrabdominal and venous pressure in obese individuals may explain this relationship (12). In addition, obesity has been linked to increased inflammation and inflammation in turn has been proposed as one of the risk factors for fibrosis and progression of lymphedema (11). In some cases, obesity has been reported as the sole precipitator of lymphedema and these cases have been named "obesity-induced lymphedema" (13). In patients with secondary lymphedema, higher BMI has been correlated with higher lymphedema grades (9).

Although there is no known cure for lymphedema and tissue fibrotic changes are for the most part irreversible, CDT remains the golden standard of lymphedema treatment (14). Its effectiveness in the management of cancer-related lymphedema has been proven although fewer studies assess its effectiveness in other subtypes of lymphedema. Compression therapy with short-stretch bandages is the cornerstone of the intensive phase. All patients in our study had received compression bandage therapy as part of the intensive phase of CDT. Some authors report that compression bandage application alone is enough to reduce LVs during the intensive phase and it yields similar results to a more complex CDT program (15). In our clinic, every patient receives lower extremity pneumatic compression therapy in addition to compression bandaging. All patient groups, regardless of addition of laser therapy, ESWT or kinesiotaping, showed significant reduction in extremity volumes (p<0.05).

Fibrosis in lymphedema has been linked to many factors. Protein rich fluid which is normally degraded by macrophages in the interstitium builds up and starts an inflammatory reaction. Minor trauma that may go unnoticed can result in a lymphangitis episode that may further worsen fibrosis and tissue swelling. We have found no difference in treatment outcomes between patients with or without a history of lymphanoitis. Primary lymphedema patients generally present with bilateral lower extremity lymphedema. Onset may be during childhood or early adulthood. In this study, we have included results from our adult primary lymphedema patients but did not include pediatric patients, since comparison between children and adults would be difficult and results could be misleading. Primary lymphedema patients had, as expected, longer disease durations but pre- and post-treatment LV/BMI values were similar in cancer patients and primary lymphedema patients. A small but statistically significant difference was detected when we compared the percentages of volume decrease between the two groups, with cancer-related lymphedema patients having higher reduction in LVs. This may be due to the more chronic nature of primary lymphedema and the relative increase in fibrotic tissues with longer disease duration. Fibroadipose proliferation has been presented as one of the factors contributing to the development of lymphedema after the initial lymphatic injury. Although we do not know why not all patients with lymph vessel or lymph node dissection develop lymphedema, fibrotic proliferation may be one of the aggravating factors (16).

Low-level laser treatment is a non-invasive treatment that has been proposed to reduce inflammation, induce lymph vessel regeneration and prevent tissue fibrosis (17). Although there are not large randomized controlled studies assessing the effects of laser therapy on lower extremity lymphedema, it has been shown to be effective in reducing limb volumes in breast cancer-related lymphedema patients (18,19). Its ease of use and relatively low cost makes low-level laser therapy a suitable addition to the treatment protocol, especially for those patients with fibrotic thickening of the skin.

Pre- and post-treatment LV/BMI values were significantly higher in the venous insufficiency group compared to the cancer related lymphedema group although percentage of volume decrease was similar both groups. Patients in the chronic venous insufficiency group had significantly higher BMI values. The use of LV/BMI ratio aims to decrease the effect of body mass and weight differences while comparing patients with different body compositions. Although LV/BMI ratio is used in order to decrease the effect of obesity on lymphedema measurements when comparing different patients, factors related to obesity such as decreased physical activity, co-morbidities and chronic inflammation may indirectly influence the results of treatment strategies. In rare cases, obesity has been reported to cause lymphedema without additional risk factors (20). CDT has also been reported to be helpful in healing of chronic venous ulcers (21). Use of pneumatic compression devices has also been shown to be beneficial for the treatment of phlebolymphedema (22). Each patient that is referred to our clinic and receives CDT receives, before compression bandaging, pneumatic compression treatment for 20 minutes. Pneumatic compression has been utilized extensively in the treatment of lymphedema and chronic venous insufficiency (23).

Evidence for the effectiveness of kinesiotape applications in the treatment of lymphedema is still scarce. However, it has been reported that kinesiotaping is well tolerated and may reduce LVs significantly (24). Some authors state that kinesiotape application may be as effective as compression bandaging in reducing excess volume in upper extremity lymphedema patients (25). It is important to note that some patients may not tolerate compression bandaging or pneumatic compression therapy well and kinesiotaping may play a supportive function as part of the larger CDT approach. We did not come across a study assessing the effectiveness of kinesiotaping in the management of lower extremity lymphedema but in light of upper extremity studies, we often add kinesiotaping to our routine patient care for its relative ease of application and low cost. None of the patients in our cohort had reported any adverse effects related to kinesiotaping.

ESWT is being more commonly employed as a component of lymphedema treatment as new data emerges regarding its effectiveness in the treatment of lymphedema. We employ ESWT as an adjunct to CDT, although it has been shown to reduce LVs by itself (26). It exerts beneficial effects on lymphedematous tissues by promoting lymphangiogenesis and increasing the density of lymphatic vessels (27). Fifty-four of the 198 lymphedematous extremities included in our study received ESWT treatment in addition to compression bandaging and/or kinesiotaping. Aside from mild discomfort during application, none of the patients reported severe discomfort or pain and no patients needed to quit ESWT treatment. We usually prescribe ESWT treatment for lower extremity lymphedema if there is prominent fibrosis, in order to stimulate circulation and lymphangiogenesis. We could not compare results between ESWT receiving and ESWT free groups because of the difference in patient numbers but both groups showed improvements in treatment outcomes.

Study Limitations

The main limitation of our study is its retrospective quality. Although prospective studies would certainly produce more accurate results, there are not many studies assessing treatment modalities and treatment results in lower extremity lymphedema. Most patients in our study (72.7%) received a combination of compression bandaging, SMP and kinesiotape application. A more limited number of patients received ESWT in addition to SMP and compression bandaging. Because numbers in kinesiotaping and ESWT groups were far from equal, we could not compare their outcomes statistically, although all groups showed significant improvement with treatment. The lack of results from the maintenance phase of the CDT program is another limitation of our study. After the completion of the intensive phase, all patients are continued to be followed up regularly but the heterogeneity in the number of control visits, number of measurements and follow-up intervals made it unfeasible to compare these data. We did not include the effect of treatment on quality of life because not all subjects in our patient group had been assessed regularly for changes in quality of life, which is another limitation of this study.

Conclusion

Although lower extremity lymphedema is more common than that of upper extremity, studies examining the effectiveness of treatment strategies focus more on upper extremity lymphedema, especially breast cancer related lymphedema. CDT has been proven to be effective in decreasing LVs in patients with cancer related lymphedema. In this retrospective analysis of treatment results from a tertiary lymphedema clinic, we have observed that primary lymphedema responds equally well to CDT as cancer related lymphedema. We have also detected similar volume reduction values with CDT in patients with chronic venous insufficiency, although differences in BMI and body composition may have an additional effect on treatment outcomes. Kinesiotaping is well tolerated and may be added to routine CDT program, but we did not have a large enough cohort to analyze its effectiveness in addition to compression bandaging.

Ethics

Ethics Committee Approval: Ethical approval was obtained from Ege University Faculty of Medicine Clinical Research Ethics Committee (decision no: 15-1.1/1, date: 29.06.2015).

Informed Consent: Since this study was retrospective, patient consent was not required.

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Authorship Contributions

Concept: E.Ç., S.E., Design: E.Ç., S.E., Data Collection or Processing: E.Ç., B.N.A., E.Y.G., Analysis or Interpretation: E.Ç., S.E., B.N.A., E.Y.G., Literature Search: E.Ç., E.Y.G., Writing: E.Ç.

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