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Original Article

The impact of obesity on the outcomes of complex decongestive therapy among patients with breast cancer-related lymphedema

Aysegul Yaman[1], Pınar Borman[2], Funda Koç[3]

[1]Department of Physical Medicine and Rehabilitation, Ankara Etlik City Hospital, Physical Medicine and Rehabilitation Hospital, Ankara, Türkiye
[2]Department of Physical Medicine and Rehabilitation, Ankara Medipol University Faculty of Medicine, Ankara, Türkiye
[3]Department of Physical Medicine and Rehabilitation, Hacettepe University Faculty of Medicine, Ankara, Türkiye

ABSTRACT

Objectives: This study aims to evaluate the influence of complex decongestive therapy (CDT) on patients with breast cancer-related lymphedema (BCRL) in terms of reducing volume, improving functional capabilities, and enhancing the quality of life and analyze the effect of obesity on their recovery process.

Patients and methods: This retrospective study was conducted between January 2018 and March 2020. The investigation comprised individuals with unilateral BCRL who received CDT during the previous year. The participants were split into two classifications: those with a normal or overweight status (Group 1) and those classified as obese or morbidly obese (Group 2). Each participant engaged in CDT sessions five times weekly for three weeks. The groups were compared regarding their functional status and quality of life scores as measured by the Quick Disabilities of the Arm, Shoulder, and Hand and Lymphedema Quality of Life (LYMQOL)-Arm questionnaires.

Results: This study included 81 female patients (mean age: 53.6±10.4 years; range, 28 to 87 years) with BCRL. Half of the participants were identified as obese and the mean body mass index (BMI) was 30.32±4.63 kg/m^2. The median lymphedema duration was 12 months. After treatment, there was a notable reduction in both the mean initial limb volume and excess volumes (3183±681 cm^3 *vs.* 2912±599 cm^3 and 30.1% *vs.* 19.3%, respectively; p<0.001). Both groups showed substantial and similar enhancements in volumes, functional scores, and all subscores of the LYMQOL-Arm questionnaire following CDT. When the patients with a BMI below and above 30 were compared, the improvement in function and appearance scores of LYMQOL-Arm was substantially distinct between the two categories. We also indicated a substantial negative relationship between the enhancement of LYMQOL-Arm function and appearance subscores and BMI (p=0.005, r=−0.486 and p=0.042, r=−0.361).

Conclusion: The influence of CDT on decreasing volume and improving functionality was comparable between obese and nonobese patients with BCRL; however, obesity may negatively impact CDT outcomes concerning quality of life issues.

Keywords: Breast cancer-related lymphedema, complex decongestive therapy, obesity.

Lymphedema is an abnormal buildup of protein-rich fluid within the interstitial tissue resulting from diminished capacity for lymphatic drainage or elevated lymphatic load. Upper extremity lymphedema may manifest at any given time following surgery or radiation therapy for breast cancer. It is regarded as a severe and exhausting illness. In lymphedema, macromolecules, proteases, and proinflammatory molecules may result in chronic inflammation, fibrosis, adipose deposition, hardening of the skin, and increased susceptibility to infections. If left untreated, breast cancer-related lymphedema (BCRL) may bring about functional impairments, psychological challenges, and diminished quality of life (QoL).[1-12]

Several studies have evaluated the association between obesity and lymphedema, as well as the impact of dietary or exercise treatments.[6-17] Previous research has demonstrated that obesity may raise

Corresponding author: Ayşegül Yaman, MD. Ankara Etlik Şehir Hastanesi, Fiziksel Tıp ve Rehabilitasyon Kliniği, 06170 Yenimahalle, Ankara, Türkiye.
E-mail: aysegulyaman06@gmail.com

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the probability of BCRL.[1,6-15,17] Ridner et al.[15] found that patients whose body mass index (BMI) is greater than 30 kg/m^2 had approximately 3.6 times higher risk of experiencing BCRL six months or more after their diagnosis, in comparison to those with a BMI below 30 kg/m^2. Prior research has documented that people with a BMI over 30 kg/m^2 are 2.9 times more likely to develop upper extremity lymphedema than individuals with a BMI lower than 25 kg/m^2.[8] It has been reported that individuals suffering from lymphedema exhibit higher baseline and current BMI levels compared to those who do not have the condition, as evidenced by findings from another clinical trial.[14] However, they indicated that weight gain was not significantly associated with the emergence of lymphedema. Greene et al.[17] reported that obese individuals suffering from lymphedema had a greater risk of contracting infections, requiring hospitalization, and experiencing moderate to severe limb enlargement compared to those with a normal BMI. Some investigations have demonstrated that severe obesity may lead to marked impairment of lymphatic function and primary lymphedema.[6,16,18,19]

Complex decongestive therapy (CDT) is widely recognized as the recommended protocol for individuals diagnosed with lymphedema. Its efficacy and comprehensive approach make it a prominent treatment option in this field.[1-4,12,18,19] In practice, the effectiveness of CDT varies among patients. Research on the impact of obesity on CDT outcomes in BCRL cases is quite scarce.[3,9,20,21] These studies have concentrated on how obesity impacts only the volume reduction in the affected extremities. However, none have evaluated the influence of obesity on functional impairment and QoL following CDT. This investigation sought to analyze the impact of CDT in obese and nonobese patients with BCRL regarding the volume reduction, functional status, and QoL and investigate the effect of obesity on recovery.

PATIENTS AND METHODS

The study retrospectively gathered data from individuals diagnosed with unilateral BCRL who received CDT within the past 12 months at the Hacettepe University Faculty of Medicine, Department of Physical Medicine and Rehabilitation between January 2018 and March 2020. Patient records were examined to collect information on various demographic and clinical characteristics, such as age, BMI, educational background, marital situation, job, exercise routine, smoking habits, dominant hand, and location of the lesions. Information regarding breast cancer therapies, surgical methods, histopathological evaluations, stage of cancer, and adjuvant treatments, such as radiation, chemotherapy, or hormone therapy, was also recorded from the data. In our lymphedema unit, limb volume was routinely computed based on a simplified truncated cone formula, which depended on circumferential measurements of the limbs by 4-cm intervals. The presence and clinical diagnosis of lymphedema were routinely conducted by evaluating the volume difference between limbs and BCRL defined as an interlimb volume difference exceeding 10% or demonstrating an excess volume of more than 200 mL. We routinely used the International Society of Lymphology criteria to determine the stage of lymphedema and record the stages of the patients.[2] Within grades 1 to 3, the level of severity was determined by the differences in volume, categorized as mild (less than a 20% increase), moderate (a 20 to 40% increase), or severe (more than a 40% increase). The features of lymphedema encompassing its duration and the initial location on the limb (whether proximal or distal), which were all routinely recorded in patient files, were included in the data analysis. Written informed consent was obtained from all participants. The study protocol was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Committee (date: 05.11.2014, no: GO-14-554). The study was conducted in accordance with the principles of the Declaration of Helsinki.

The classification of BMI was divided into three ranges: normal (18.5 to 24.9 kg/m^2), overweight (25 to 29.9 kg/m^2), and obese, which encompassed both obese and morbidly obese individuals (30 kg/m^2 or higher). Patients were categorized into two groups: Group 1 was normal/overweight, and Group 2 was obese/morbid obese. Due to the small number of participants with normal weight and morbid obesity, the effect of obesity severity on volume reduction and other treatment outcomes was evaluated by grouping participants as either normal/overweight or obese/morbidly obese. All data were obtained from patients participating in the combined phase 1 CDT. This phase included a comprehensive program comprising skin care, manual lymphatic drainage, multilayer bandaging, and supervised exercises, conducted five times each week for three weeks, amounting to 15 sessions in total. Excess limb volumes were assessed using

serial circumference measurements obtained at the baseline and the conclusion of the third week. The enhancement in functionality and QoL scores, assessed through the Quick Disabilities of the Arm, Shoulder, and Hand (Q-DASH) and the Lymphedema Quality of Life Questionnaire (LYMQOL)-Arm questionnaires, was compared across the groups based on routine documentation in the

TABLE 1
The demographic and clinical variables of the patients (n=81)

	n	%	Mean±SD	Median
Age (year)			53.6±10.4	
Body mass index (kg/m^2)			30.32±4.63	
Education				
Illiterate	1	1.2		
Primary school	40	49.4		
High school	20	24.7		
University	20	24.7		
Marital status				
Married	68	84		
Single	8	9.9		
Widow	5	6.1		
Occupation				
Housewife	47	58		
Officer	12	14.8		
Retired	22	27.2		
Exercise habit				
Yes	23	28.4		
No	58	71.6		
Smoke				
Yes	9	11.1		
No	72	88.9		
Type of surgery				
Radical mastectomy	1	1.2		
Modified radical mastectomy	68	83.9		
Lumpectomy	12	14.8		
Breast cancer stage				
1	9	11.1		
2	42	51.9		
3	22	27.2		
4	1	1.2		
Histopathologic diagnosis				
Infiltrative ductal	58	71.6		
Infiltrative lobular	7	8.6		
Others	16	19.8		
Adjunctive therapies				
Chemotherapy	71	87.7		
Radiation therapy	57	70.4		
Hormonal therapy	57	70.4		
Duration of lymphedema (month)			31.84±40.98	12
Dominant side involvement	43	53.1		
Initial site of lymphedema				
Proximal	29	35.8		
Distal	52	64.2		
Stemmer sign				
Positive	51	63		
Negative	30	37		
Stage of lymphedema				
1	28	34.6		
2	53	65.4		

SD: Standard deviation.

TABLE 2
The outcome measures before and after the phase 1 CDT and the difference of the groups in regard to the improvements in outcome measures

	Before therapy	After therapy	
	Mean±SD	Mean±SD	*p*
Volumes (cm^3)			
Group 1	3066±669.8	2759±537.7	<0.001[a]
Group 2	3276±683.9	2979±609.6	<0.001[a]
Excess volume (%)			
Group 1	31.48±14.36	18.66±10.11	<0.001[a]
Group 2	28.98±12.77	18.07±8.13	<0.001[a]
Q-DASH			
Group 1	40.34±18.24	34.32±18.64	0.043[a]
Group 2	44.54±22.15	37.34±20.62	0.008[a]
LYMQOL-Arm			
Function			
Group 1	1.88±0.62	1.53±0.67	0.002[a]
Group 2	2.30±0.71	1.66±0.64	<0.001[a]
Appearance			
Group 1	2.47±0.73	1.75±0.73	<0.001[a]
Group 2	2.69±0.97	1.78±0.74	<0.001[a]
Symptom			
Group 1	2.11±0.58	1.56±0.53	0.001[a]
Group 2	2.30±0.87	1.81±0.68	0.001[a]
Group 2 emotion			
Group 1	1.89±0.70	1.47±0.53	0.008[a]
Group 2	1.97±0.74	1.63±0.54	0.037[a]
Overall			
Group 1	6.50±1.62	7.92±1.24	<0.001[a]
Group 2	5.25±2.07	7.65±1.35	<0.001[a]
Improvement detected in volumes (cm^3)			0.865[b]
Group 1	307±237		
Group 2	297±185		
Improvement detected in excess volumes (%)			0.337[b]
Group 1	12.82±7.62		
Group 2	10.91±7.32		
Improvement detected in Q-DASH			0.664[b]
Group 1	-6.02±22.29		
Group 2	-7.2±20.49		
Improvement detected in LYMQOL-arm function			0.025[b]
Group 1	-0.35±0.16		
Group 2	-0.64±0.16		
Improvement detected in LYMQOL-arm appearance			0.032[b]
Group 1	-0.72±0.19		
Group 2	-0.91±0.13		
Improvement detected in LYMQOL-arm symptom			0.650[b]
Group 1	-0.55±0.15		
Group 2	-0.49±0.21		
Improvement detected in LYMQOL-arm emotion			0.055[b]
Group 1	-0.42±0.18		
Group 2	-0.34±0.53		
Improvement detected in LYMQOL-arm overall			0.732[b]
Group 1	1.42±0.22		
Group 2	2.4±0.58		

CDT: Complex-decongestive therapy; SD: Standard deviation; Q-DASH: Quick Disabilities of the Arm, Shoulder and Hand; LYMQOL: Arm Lymphedema QoL-Questionnaire-Arm; [a]: paired sample t-test; [b]: independent samples t-test.

files.[22,23] The Turkish LYMQOL-Arm questionnaire demonstrated good internal consistency and reliability, with Cronbach's alpha values between 0.88 and 0.90 and a test-retest intraclass correlation coefficient ranging from 0.45 to 0.71.[23]

Statistical analysis

Statistical analysis was conducted using IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Continuous variables were represented using the mean ± standard deviation (SD) or median, whereas categorical variables were presented in frequency and percentage. A normal distribution was analyzed with the utilization of the Kolmogorov-Smirnov test. Repeated measurements of outcome variables were analyzed using paired sample t-test. The detected improvements were compared with the independent samples t-test. The relationship between variables was assessed using Pearson's correlation. A p-value <0.05 was considered statistically significant.

RESULTS

The study encompassed 81 female participants (mean age: 53.6±10.4 years; range, 28 to 87 years), with 36 in Group 1 and 45 in Group 2. Table 1 displays the patient's demographic and clinical features. The lymphedema duration was detected to be approximately 12 months. A total of 28 individuals were in Stage 1, while 53 patients were in Stage 2. Table 1 also illustrates the patients' lymphedema features. The mean age, median lymphedema duration, and distribution of participants according to lymphedema stage revealed no statistically significant differences among the groups. Table 2 compares the outcome data collected before the CDT was implemented with the results observed afterward. We observed a substantial decrease in volumes (3183±681.6 cm^3 *vs.* 2912±599.9 cm^3, p<0.001) and excess volume (30.1±13.5% *vs.* 19.31±9.42% p<0.001) in all patients after the CDT. Furthermore, all patients showed improvement in functional scores and all subscores of LYMQOL-Arm questionnaires following CDT. Both groups demonstrated notable enhancement following CDT in several key areas, including limb volumes (Group 1, 3066±669 cm^3 *vs.* 2759±537 cm^3; Group 2, 3276±683 cm^3 *vs.* 2979±609 cm^3; p<0.001), functional assessments (Group 1, 40.34 *vs.* 34.32; Group 2, 44.54 *vs.* 37.34; p<0.05) and LYMQOL-Arm questionnaire subscores (overall QoL; Group 1, 6.5±1.6 *vs.* 7.9±1.2; Group 2, 5.3±2.1 *vs.* 7.7±1.3; p<0.001). The improvement in both categories was comparable to excess volumes and functional status; however, the functional and appearance subscores of LYMQOL-Arm were statistically better in Group 1 than in Group 2, indicating that obesity negatively affected QoL (Table 2).

A substantial negative correlation was identified between the enhancement of function and appearance subscores of LYMQOL-Arm and BMI (p=0.005, r=–0.486 and p=0.042, r=–0.361; Table 3). These results demonstrated that obesity had a detrimental effect on QoL, independent of volume reduction and disability.

DISCUSSION

Lymphedema, characterized by abnormal gathering of fluid high in protein content in the interstitial areas, is a complication following breast cancer treatment. It may cause physical and psychological morbidity and impair QoL.[1-12] The gold standard treatment of lymphedema is CDT, with robust scientific evidence.[1-5,12,18,19,24-26] A meta-analysis conducted by Shamoun and Ahmad[24] concluded that patients should have CDT to enhance their upper extremity function, QoL, and reduce pain and edema volume. In a review, Donahue et al.[25] indicated that evidence supporting the efficacy of CDT varied. Another systematic review emphasized the improvement of QoL subscales with CDT in BCRL patients.[26]

In our study, we observed substantial enhancements in extremity volumes, functional scores, and QoL subscores after CDT within both patient groups. While the enhancements in volume reduction and functional status showed no significant difference for obese and nonobese patients, the LYMQOL-Arm scores related to functionality and appearance were statistically lower in obese individuals. This indicates that obesity negatively impacts CDT outcomes. Additionally, our analysis revealed a notable inverse relationship between BMI and the improvement of the LYMQOL-Arm function and appearance subscores, underscoring the negative implications of obesity on CDT concerning QoL issues.

Previous studies have established a connection between obesity and an increase in the risk of BCRL.[1,6-15,17] Body mass index, at the moment of being diagnosed with breast cancer, appears to be a more important risk element for the onset of

TABLE 3
The correlation coefficients between demographic variables and the improvements in outcome measures

	Improvement detected in volumes	Improvement detected in excess volumes	Improvement detected in LYMQOL-Arm function	Improvement detected in LYMQOL-Arm appearance
Age				
r	NS	NS	NS	NS
p	NS	NS	NS	NS
Body mass index				
r	NS	NS	−0.486	−0.361
p	NS	NS	0.005	0.042
Stage of lymphedema				
r	NS	0.303	NS	NS
p	NS	0.006	NS	NS
Duration of lymphedema				
r	NS	NS	NS	NS
p	NS	NS	NS	NS
Improvement detected in Q-DASH				
r	NS	NS	NS	NS
p	NS	NS	NS	NS
Improvement detected in LYMQOL-Arm function				
r	−0.387	NS	-	0.398
p	0.029	NS	-	0.024
Improvement detected in LYMQOL-Arm appearance				
r	NS	NS	0.398	-
p	NS	NS	0.024	-
Improvement detected in LYMQOL-Arm symptom				
r	NS	NS	NS	NS
p	NS	NS	NS	NS
Improvement detected in LYMQOL-Arm emotion				
r	NS	NS	NS	NS
p	NS	NS	NS	NS
Improvement detected in LYMQOL-Arm overall				
r	NS	NS	NS	NS
p	NS	NS	NS	NS

LYMQOL-Arm:Lymphedema QoL-Questionnaire-Arm; Q-DASH: Quick Disabilities of the Arm, Shoulder and Hand; NS: Not statistically significant (p>0.05).

lymphedema compared to weight gain occurring after therapy.[11,13] Patients with obesity might have limited lymphatic capacity prior to receiving treatment for breast cancer, and this could result in CDT not being as effective as in nonobese patients. Chronic interstitial fluid accumulation results in fibrosis, persistent inflammation, and adipose tissue deposition, reducing the potential for response to therapies.[6] The prediction of improvement after CDT is difficult due to unknown affecting factors. In a retrospective study involving 107 patients with BCRL, Liao et al.[3] noted that the severity of lymphedema at baseline was the most crucial predictor of the effectiveness of CDT. Duyur Cakit et al.[9] carried out a prospective clinical trial comparing CDT's long-term effectiveness in obese and nonobese patients with BCRL. They found that while CDT effectively reduced volume

in both groups, its efficacy was lower in obese patients. After one year, the extremity volumes in the obese group returned to their initial levels, whereas the nonobese group maintained their volume reduction. Eyigör et al.[20] reported a notable negative association between the posttreatment arm volume affected by lymphedema and the weight gain observed after the surgical procedure. According to Vignes et al.,[21] two factors that predict an absolute reduction of lymphedema volume following CDT were lymphedema duration and BMI. None of these previous studies considered the effect of obesity beyond extremity volume as an outcome measure. We investigated the effects of obesity not only on volume reduction but also on functional disability and QoL. In our study both obese and nonobese patients had comparable improvement in volume and functional disability. However, the scores in the appearance and functional subgroups of the specific QoL instrument were lower in nonobese patients with BCRL, indicating a better QoL compared to obese patients. It is important to emphasize that obesity negatively impacts QoL, regardless of volume reduction and functional improvement. The findings highlight the significant impact of obesity, which may be greater than previously thought.

This study's limitations include its retrospective design and the short-term evaluation of outcome measures. Additionally, we were unable to assess patients' weight changes at the time of cancer diagnosis and during the treatment process, which may be another limitation. However, the relatively large study group, the homogeneity of the included patients (Stage 1 and 2), and the detailed demographic and clinical features, along with specific functional and QoL assessments routinely recorded in patient files, add value to this study and contribute to the literature on QoL issues in obese BCRL patients. We included the total scores of the subgroups in the LYMQOL-Arm dataset. Consequently, we could not calculate the internal consistency of the LYMQOL-Arm for each new sample.

In conclusion, the impact of CDT on volume reduction and functional improvement was comparable between obese and nonobese patients with BCRL. However, obesity may negatively impact CDT outcomes concerning QoL issues. We recommend that healthcare providers be conscious of this condition and emphasize the importance of weight control education to improve the QoL in managing BCRL.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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