



The Effect of Complex Decongestive Therapy on Sleep Quality and Quality of Life in Patients with Secondary Lymphedema After Cancer Surgery

Kanser Cerrahisi Sonrası Sekonder Lenfödemli Hastalarda Kompleks Dekonjestif Tedavinin Uyku Kalitesi ve Yaşam Kalitesi Üzerine Etkisi

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Abstract

Objective: It has been frequently observed that patients with lymphedema experience problems that impair quality of life (QoL), such as pain, edema and sleep disturbances. The positive effects of complex decongestive therapy (CDT) on pain, extremity volume and QoL have been reported in the literature. The aim of this study was to investigate the effects on sleep quality, pain, extremity volume, and QoL of the first phase of CDT applied to patients who developed lymphedema after cancer surgery.

Materials and Methods: The study included a total of 48 female patients with unilateral lymphedema (23 breast cancer and 25 urogynaecological cancer) who developed upper or lower extremity lymphedema after cancer surgery. The patients were questioned about QoL, pain, extremity volume, medical history, and demographic data before starting treatment. Then CDT was applied five days a week for three weeks, as a total of 15 sessions, after which the patients were re-evaluated. Pain severity was evaluated using a visual analog scale, sleep quality with the Pittsburgh sleep quality index, QoL with the lymphedema QoL questionnaire, and extremity volume was measured and calculated using the Frustum formula.

Results: A significant improvement was detected in pain ($p<0.001$), extremity volume ($p=0.015$), sleep quality ($p<0.001$) and overall QoL score ($p=0.012$) in the group that developed lymphedema in the upper extremity after treatment. A significant improvement was achieved in pain ($p<0.001$), extremity volume ($p<0.001$), sleep quality ($p<0.001$) and overall QoL score ($p<0.001$) in the group that developed lymphedema in the lower extremity.

Conclusion: This study is the first to demonstrate the effects of CDT on sleep quality while confirming its therapeutic effects on pain, extremity volume and QoL in patients who developed lymphedema after cancer surgery. When treating sleep disturbances in lymphedema patients, it is important to consider the therapeutic benefits of CDT on sleep quality.

Keywords: Lymphedema, complex decongestive therapy, sleep, quality of life

Öz

Amaç: Lenfödem hastalarında ağrı, ödem, uyku bozuklukları gibi hastanın yaşam kalitesini (QoL) bozan sorunlar sıklıkla görülmektedir. Daha önce kompleks dekonjestif tedavinin (KDT) ağrı, ekstremitte hacmi ve QoL üzerindeki olumlu etkileri zaten bildirilmişti. Bu çalışmanın amacı, kanser cerrahisi sonrası lenfödem gelişen hastalara uygulanan KDT'nin birinci fazının ağrı, ekstremitte hacmi, QoL gibi diğer semptomların yanı sıra uyku kalitesi üzerine etkilerini araştırmaktır.

Gereç ve Yöntem: Çalışmaya, kanser ameliyatı sonrasında üst veya alt ekstremitte lenfödem gelişen toplam 48 kadın hasta (23 meme kanseri ve 25 ürojinekolojik kanser) dahil edildi. Hastalar tedaviye başlamadan önce QoL, ağrı, ekstremitte hacmi, tıbbi geçmiş ve demografik veriler açısından sorgulandı. Ardından, üç hafta boyunca haftada beş gün olmak üzere toplam 15 seans KDT uygulandı ve hastalar yeniden değerlendirildi. Ağrı şiddeti görsel analog skala ile, uyku kalitesi Pittsburgh uyku kalitesi indeksi ile, yaşam kalitesi lenfödem QoL anketi ile değerlendirildi ve ekstremitte hacmi frustum formülü kullanılarak ölçüldü ve hesaplandı.

Bulgular: Tedavi sonrasında üst ekstremitesinde lenfödem gelişen grubun ağrı ($p<0,001$), ekstremitte hacmi ($p=0,015$), uyku kalitesi ($p<0,001$) ve genel QoL skorunda ($p=0,012$) anlamlı iyileşme saptandı. Bununla beraber alt ekstremitesinde lenfödem gelişen grubun ağrı ($p<0,001$), ekstremitte hacmi ($p<0,001$), uyku kalitesi ($p<0,001$) ve genel QoL skorunda da ($p<0,001$) anlamlı iyileşme elde edildi.

Sonuç: Bu çalışma, kanser cerrahisi sonrası lenfödem gelişen hastalarda KDT'nin uyku kalitesi üzerindeki etkilerini ortaya koyan ve ağrı, ekstremitte hacmi ve QoL üzerindeki terapötik etkilerini doğrulayan ilk çalışmadır. Lenfödem hastalarında uyku bozukluklarının tedavi sürecinde KDT'nin uyku kalitesi üzerindeki terapötik faydalarının dikkate alınması önemlidir.

Anahtar Kelimeler: Lenfödem, kompleks dekonjestif terapi, uyku, yaşam kalitesi

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Introduction

With the advances made in diagnosis and treatment methods, approximately 70% of cancer patients can now live for five years or more after diagnosis.¹ After the primary treatment of cancer is completed, patients face long-term problems due to the disease itself or treatment attempts. The main problems experienced are pain, fatigue, psychological problems, and sleep disorders.^{2,3} Sleep disturbance is quite common in cancer patients and has serious adverse effects^{4,5}, leading to deterioration of the general health status and a decrease in the quality of life (QoL). Insomnia, sleep-related respiratory disorders, and obstructive sleep apnea syndrome are the most common sleep disorders in cancer patients.

The incidence of cancer-related insomnia is almost three times that seen in the general population.^{4,5} According to the literature, the incidence of sleep disorders is 9-33% in the general population, while it ranges from 30-93.1% in cancer patients. It has been reported that 63% of women with metastatic breast cancer have sleep disorders and 37% use sleeping pills.⁶ Cancer symptoms and problems related to cancer treatment also contribute to sleep disturbance. Shoulder-arm pain and limitation of movement after breast cancer have been found to be associated with sleep disturbance, causing sleep disorders, fatigue, excessive daytime sleepiness and a decrease in the functions of daily living activities. In addition, it is associated with pain, depression, anxiety, and a decrease in QoL.⁷ Therefore, it is necessary to comprehensively evaluate cancer patients in terms of sleep disorders and sleep quality.

Lymphedema, a chronic and progressive disorder encountered after cancer surgery that develops due to impaired lymphatic drainage, is one of the problems that negatively affect the sleep quality of patients and is thought to contribute to the development of sleep disorders.⁸⁻¹¹ In developed countries, the most common cause of lymphedema is cancer surgery. Cancer-associated lymphedema is common, especially in some specific cancer types. After breast cancer surgery, lymphedema can be seen in the upper extremities, in the lower extremities in genitourinary and gynecological cancers, and in the upper or lower extremities depending on the localization of the tumor in melanoma.¹² Lymphedema in the upper and lower extremities following cancer treatment can develop for a variety of reasons, including infection, inactivity, and the use of chemotherapy or radiation therapy following surgery.^{13,14} If lymphedema is not completely cured it can seriously impair the physical and mental health and QoL of patients. Swelling and pain in the affected extremity cause a decrease in mobility and activities of daily living. The disproportion in body shape can lead to deterioration in body image and psychological problems such as depression and anxiety.¹⁵ In advanced stages of cancer-associated lymphedema, the sleep quality and QoL of patients are more severely impaired.¹⁰

Complex decongestive therapy (CDT) is currently accepted as the gold standard in the treatment of lymphedema.¹⁶ It consists of two phases: the first phase of CDT includes manual lymphatic drainage (MLD), skin care, compression therapy and

exercises performed by a therapist, while the second phase of CDT includes self-lymphatic massage, exercises, and the use of a compression garment, which the patient continues in daily life after the first phase is completed. It has been reported that CDT has positive effects on mobility and balance in patients who develop lymphedema after cancer surgery. It has also been shown to improve extremity functions, independence in activities of daily living, and QoL.^{16,17} However, from a scan of the relevant literature, only 1 case control study was found.¹⁸ The aim of this study was to investigate the effects on sleep quality and QoL of the first phase of CDT applied to patients who developed extremity lymphedema after cancer surgery.

Materials and Methods

Study Design

This cohort study was conducted in Ankara Bilkent City Hospital-Physical Medicine and Rehabilitation Hospital. Approval for the study was granted by the Clinical Research Ethics Committee of Ankara City Hospital (decision number: E2-21-505, date: 18.05.2021) and the study was conducted within the framework of the Helsinki Declaration principles. All participants provided written informed consent prior to study entry.

Participants

A total of 62 patients who developed unilateral lymphedema in the lower or upper extremities after cancer surgery were contacted and invited to participate in the study. Of these, 14 were excluded from the study for various reasons (8 patients had primary lymphedema, 2 did not meet the inclusion criteria, 2 discontinued the intervention, and 1 had an infection). The consolidated standards of reporting trails flow diagram is shown in Figure 1. No adverse events were reported during the training sessions. The study inclusion criteria were defined as age 18-65 years, the development of unilateral lymphedema in the lower or upper extremities after cancer surgery, and voluntary participation in the study. The study exclusion criteria were defined as unwillingness to participate in the study, the development of lymphedema due to primary causes, the presence of bilateral lymphedema, active infection, or mental or cognitive disorders, inability to communicate and cooperate, or the use of sleeping pills or antidepressants.

At stage 0, the lymph system is at a level that can handle lymph flow and no swelling is observed in the extremities. Therefore, stage 0 patients were also excluded from the study.

Outcome Measures

Before starting treatment, the patients were evaluated in respect of QoL, pain, extremity volume, medical history, and demographic data. A total of 15 sessions of CDT were then applied five days a week for three weeks, after which the patients were re-evaluated. Demographic information, physical features, and medical history were recorded using a standardized questionnaire. The lymphedema stages were determined according to the International Society of Lymphology criteria by a specialist doctor.¹⁹ All procedures were carried out by the same consultant.

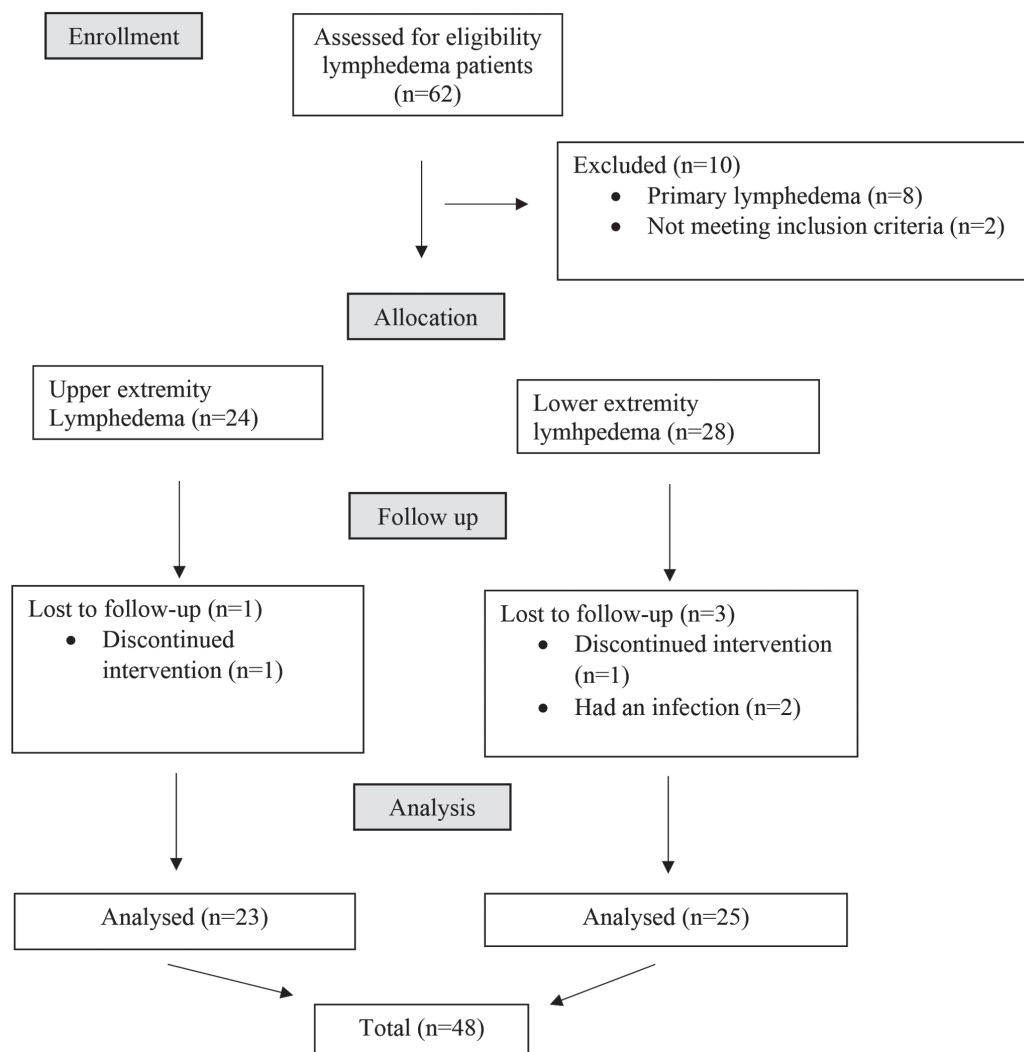


Figure 1. CONSORT flow diagram
CONSORT: Consolidated standards of reporting trails

Pain

Resting pain was evaluated using a visual analogue scale (VAS). The VAS is a straight line 10 centimetres (cm) long with no numbers. The patients were informed that the beginning of the line indicates no pain and the end of the line indicates unbearable pain, and were then instructed to mark the line at the point reflecting the level of pain felt in the affected extremity. The marked value was then measured with a tape measure and recorded in cm.²⁰

Extremity Volume

The Frustum formula $[V = (h \times [R1^2 + R1.R2 + R2^2]) / (12 \times \pi)]$ was used to calculate the volume of the affected extremity. Starting from the ulna/malleolus of the affected extremity, measurements were made with a tape measure up to the axilla/groin at 4 cm intervals. The extremity volume was calculated by entering the measured values into the formula and recorded in cm³.²¹

Sleep Quality

Sleep quality was assessed using the Pittsburgh sleep quality index. This scale consists of 24 questions, the first 19 of which are answered by the subject, and the last 5 by the bed partner, but the answers given by the bed partner are not included in the calculation. Each question is scored from 0 (no distress) to 3 (severe distress), under 7 sub-headings, providing a total score in the range of 0 to 21. A total score of ≤ 6 is evaluated as good sleep.²²

QoL

The lymphedema QoL questionnaire has a separate form for the lower and upper extremities, each of which has sub-headings of function, appearance, physical symptoms, and emotional state. The first 20 questions are scored from 1 (not at all) to 4 (a lot) points, and the last question evaluating the general QoL is scored between 0 and 10. The score for each sub-parameter is calculated according to the arithmetic mean, with higher scores indicating a poor QoL.²³

Intervention

After the initial evaluation of the patients, the first phase of CDT was administered by a professional and experienced lymphoedema therapist for 3 weeks/5 days a week (15 sessions). This phase consists of MLD, skin care, compression therapy and exercises. MLD was applied first to the neck and then to the abdominal region. Lymphatic anastomoses at dorsal and ventral sides of the body were treated and MLD was performed on the affected extremity. Skin care was applied after the MLD, and the extremity was moisturised with a neutral pH water-based moisturizer. A compression bandage was applied after skin care. The compression bandage consisted of a stockinette dressing, finger bandages, cotton, sponges, and short stretch bandaging applied from the toes to the groin. Skin care and remedial exercises were applied, respectively.¹¹

Statistical Analysis

Data obtained in the study were analyzed statistically using IBM SPSS Statistics vn. 24.0 software (IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY, USA). Conformity of the variables to normal distribution was examined with analytical (Shapiro-Wilk test) and visual (histogram and probability graphs) methods. The paired samples t-test and the Wilcoxon signed-rank test were used to compare the mean values. A value of $p < 0.05$ was accepted as statistically significant.

Results

A total of 48 female patients completed the study, of which 23 had upper extremity lymphedema following breast cancer

surgery and 25 had lower extremity lymphedema following urogynaecological cancer surgery.

The demographic characteristics of the patients and comorbidities are summarized in Table 1. Lymphedema history following surgery and other cancer treatments are shown in Table 2. The majority of the patients (52.1%) were in stage 2 (Table 2).

A significant improvement was detected in pain ($p < 0.001$), extremity volume ($p = 0.015$), sleep quality ($p < 0.001$) and overall QoL score ($p = 0.012$) in the group that developed lymphedema in the upper extremity after treatment. A significant improvement was achieved in pain ($p < 0.001$), extremity volume ($p < 0.001$), sleep quality ($p < 0.001$) and overall QoL score ($p < 0.001$) in the group that developed lymphedema in the lower extremity (Tables 3 and 4).

Discussion

This prospective cohort study is the first to have demonstrated that CDT applied 5 days a week for 3 weeks (15 sessions) was effective in improving sleep quality in patients who developed lymphedema in upper or lower extremities after cancer surgery, while confirming its therapeutic effects on pain, extremity volume and QoL.

CDT is known to be the gold standard in the treatment of lymphedema, and previous studies have shown its positive effects on QoL and that it reduces pain and extremity volume.¹⁹ In a study by Abakay et al.²⁴, a total of 20 sessions of CDT were applied to 20 patients who developed secondary lymphedema in the lower extremities. Extremity volume and

Table 1. Demographic characteristics and medical history of the patients

Characteristics		Upper extremity	Lower extremity	Total
		(n=23)	(n=25)	(n=48)
Age (year, mean \pm SD)		50.43 \pm 9.94	50.04 \pm 12.78	50.22 \pm 11.39
BMI (kg/m ² , mean \pm SD)		32.31 \pm 5.64	35.68 \pm 6.12	34.06 \pm 6.08
Education, n (%)	Illiterate	1 (4.3%)	2 (8%)	3 (6.3%)
	Primary school	10 (43.5%)	8 (32%)	18 (37.5%)
	High school	8 (34.8%)	10 (40%)	18 (37.5%)
	University	4 (17.4%)	5 (20%)	9 (18.7%)
Medical history, n (%)	1 Medical history	7 (30.3%)	11 (44%)	18 (37.5%)
	Diabetes mellitus	1 (4.3%)	1 (4%)	2 (4.2%)
	Hypertension	3 (13%)	7 (28%)	10 (20.8%)
	Hypothyroid	3 (13%)	3 (12%)	6 (12.5%)
	2 Medical history	1 (4.3%)	2 (8%)	3 (6.3%)
	Hypertension + hypothyroid	0	2 (8%)	2 (4.2%)
	Hypertension + diabetes mellitus	1 (4.3%)	0	1 (2.1%)
	3 Medical history	15 (65.2%)	12 (48%)	27 (56.3%)
	Hypertension + diabetes mellitus + hypothyroid	1 (4.3%)	0	1 (2.1%)
	None	14 (60.9%)	12 (48%)	26 (54.2%)

SD: Standard deviation, BMI: Body mass index

Table 2. Postoperative lymphedema history

		Upper extremity (n=23)	Lower extremity (n=25)	Total (n=48)
Postoperative time (year, mean ± SD)		4.39±4.15	4.12±2.71	4.25±3.44
Lymphedema duration (months, mean ± SD)		37.56±36.19	54.24±44.34	46.25±41.08
Chemotherapy, n (%)		12.69±8.47	10.80±5.31	11.70±6.99
Radiotherapy, n (%)		21.34±9.49	23.36±7.68	22.39±8.56
Affected side, n (%)	Right	11 (47.8%)	9 (36%)	20 (41.7%)
	Left	12 (52.2%)	16 (64%)	28 (58.3%)
Lymphedema stage, n (%)	1	8 (34.8%)	4 (16%)	12 (25%)
	2	14 (60.9%)	11 (44%)	25 (52.1%)
	3	1 (4.3%)	10 (40%)	11 (22.9%)

SD: Standard deviation

Table 3. Pain, extremity volume and sleep quality results

	Upper extremity		Lower extremity		Total	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Pain (mean ± SD)	5±1.88	3.06±1.03	4.19±2.25	3.06±1.92	4.58±2.10	3.06±1.54
	t=6.592; p<0.001*		t=7.801; p<0.001*		t=9.008; p<0.001*	
Sleep quality median; (min-max)	7; (5-16)	5; (2-13)	8; (4-16)	5; (3-13)	8; (4-16)	5; (2-13)
	Z=-3.832; p<0.001*		Z=-4.308; p<0.001*		Z=-5.729; p<0.001*	
Extremity volume (mL) median; (min-max)	2911; (2027-8704)	2880; (2104-8693)	14823; (7978-29506)	10977; (7740-22221)	8386; (2027-29506)	7976.50; (2104-22221)
	Z=2.626; p=0.015*		Z=-4.373; p<0.001*		Z=-5.518; p<0.001*	

t: Paired samples t-test, Z: Wilcoxon test
*p<0.05
SD: Standard deviation, min-max: Minimum-maximum

Table 4. Quality of life results

	Upper extremity		Lower extremity		Total	
	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Function median; (min-max)	2.10 (1-3.20)	1.37 (1-3.70)	2.20 (1.38-4)	2 (1-3)	2.11 (1-4)	1.50 (1-3.70)
	Z=-2.714; p=0.007*		Z=-3.381; p<0.001*		Z=-4.187; p<0.001*	
Appearance median; (min-max)	2; (1.20-4)	1.80; (1-3.80)	2.70; (1.80-4)	2.28; (1-4.80)	2.46; (1.20-4)	2.10; (1-4.80)
	Z=2.090; p=0.037*		Z=2.160; p=0.041*		Z=-2.660; p<0.001*	
Physical symptoms (mean ± SD)	2.41±0.92	1.96±0.96	2.60±0.63	1.91±0.54	2.51±0.78	1.93±0.76
	t=2.560; p=0.018*		t=8.422; p<0.001*		t=-6.025; p<0.001*	
Emotional status median; (min-max)	2.33; (1.33-3.66)	1.66; (1-3.50)	2; (1-3.50)	1.60; (1-2.60)	2.13; (1-3.66)	1.66; (1-3.50)
	Z=-2.801; p=0.005*		Z=-3.209; p=0.001*		Z=-4.159; p<0.001*	
Overall score median; (min-max)	6; (4-8)	7; (5-8)	6; (2-8)	7; (5-9)	6; (2-8)	7; (5-9)
	Z=-2.501; p=0.012*		Z=-3.666; p<0.001*		Z=-4.421; p<0.001*	

t: Paired samples t-test, Z: Wilcoxon test
*p<0.05
SD: Standard deviation, min-max: Minimum-maximum

QoL improved after CDT.²⁴ Sezgin Ozcan et al.²⁵ applied CDT treatment to patients who developed lymphedema after breast cancer surgery for 5 days a week for 3 weeks, and at the end of 3 weeks, significant reductions in extremity volume, pain and heaviness sensation, and significant improvements in QoL were obtained.²⁵ In another study, it was found that

CDT applied for 5 days a week for 4 weeks to patients who developed lymphedema after breast cancer surgery resulted in a decrease in extremity volume, and a positive improvement in the function and general health sub-parameters of QoL.²⁶ The results of this study have confirmed the current knowledge that CDT is effective on pain, extremity volume, and QoL in

patients who developed lymphedema in both the upper or lower extremities.

There has been shown to be a 10% decrease in the joint range of motion of patients due to lymphedema developing after cancer surgery. The development of lymphedema in the affected arm/leg together with the decreased range of motion may cause a decrease in the functional levels of the patients, which can explain the deterioration in the QoL.²⁷

Sleep problems can be seen intensely and for a long time in cancer patients. While sleep problems can be seen in approximately 30% of newly diagnosed patients, this rate increases at advanced stages of cancer.²⁸ In addition, the development of lymphedema in patients after cancer surgery may adversely affect the sleep. Lymphedema symptoms such as an increase in volume, pain, numbness, and tingling in the extremity are among the factors that negatively affect sleep.²⁹ A previous study reported that obstructive sleep apnea was determined in 74% of 43 lymphedema patients admitted for CDT. Especially in patients with lower extremity lymphedema, sleep problems are more common, which has been attributed to the correlation between lower extremity volume and the prevalence of obstructive sleep apnea.⁹ In addition, the increase in peripheral edema is among the other factors thought to cause obstructive sleep apnea by reducing the upper airway and increasing the upper airway resistance.³⁰ Roux et al.⁹ applied 12 sessions of CDT to patients who developed obstructive sleep apnea due to lymphedema, and reported no significant change in sleep apnea following the treatment. This was thought to be due to the masking of the effect of CDT by obstructive sleep apnea during treatment.⁹ In a case study by Janavlekar et al.¹⁸, CDT was applied to a patient who developed lymphedema in the upper extremity after breast cancer surgery. As a result of the treatment, it was concluded that CDT played an important role in reducing lymphedema and improving sleep quality and QoL in metastatic breast cancer patients.¹⁸

The results of the current study showed a significant improvement in the sleep quality of patients with upper or lower extremity lymphedema. Decreased pain and extremity volume, which are among the factors affecting sleep, may be the reason for this change.

Study Limitations

The strength of this study was that it is the first in literature to have revealed the efficacy of CDT on sleep quality in patients who developed lymphedema. However, the results of this study only reflect phase 1 of CDT. There is a need for further studies with long-term follow-up, including the second phase of CDT. Moreover, due to the small number of participants, the patients could not be classified according to clinical stages.

Conclusion

Sleep is essential for healing and QoL, especially for postoperative cancer patients who face numerous physical and environmental obstacles to uninterrupted sleep. As a lack of sleep can result in pain, depression and anxiety, patients who get enough sleep tend to have better moods and experience fewer anxiety

or depressive episodes.³¹ The impact of poor sleep quality on outcomes and patient QoL demonstrates the need for new therapeutic options with few side-effects. As a result of this study, it was concluded that CDT, which is known as the gold standard for reducing extremity volume in lymphedema patients, improved sleep quality in patients who developed secondary lymphedema in both upper and lower extremities. It can be suggested that clinicians should consider the efficacy of CDT on sleep quality in the management process of sleep disturbances of lymphedema patients.

Ethics

Ethical Approval: Approval for the study was granted by the Clinical Research Ethics Committee of Ankara City Hospital (decision number: E2-21-505, date: 18.05.2021) and the study was conducted within the framework of the Helsinki Declaration principles.

Informed Consent: All participants provided written informed consent prior to study entry.

Authorship Contributions

Surgical and Medical Practices: C.Ş.P., M.E.Y., M.D., P.B., Concept: C.Ş.P., M.E.Y., E.E.Ö., M.D., Design: C.Ş.P., M.E.Y., Data Collection or Processing: C.Ş.P., E.E.Ö., M.D., P.B., Analysis or Interpretation: C.Ş.P., M.E.Y., E.E.Ö., Literature Search: C.Ş.P., M.E.Y., Writing: C.Ş.P., M.E.Y., E.E.Ö., M.D., P.B.

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