J Surg Med. 2019;3(4):300-303.
DOI: 10.28982/josam.551125

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN: 2602-2079

Efficacy of complex decongestive therapy on breast cancer-related lymphedema: A cross-sectional study

Meme kanseri ilişkili lenfödem ve kompleks dekonjestif tedavisi etkinliği: Kesitsel çalışma

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Ethics Committee Approval: Ethical committee approval has been obtained from the ethical committee of Antalya Training and Research Hospital.
Etik Kurul Onayı: Etik kurul onayı Antalya Eğitim ve Araştırma Hastanesi etik kurulundan alınmıştır.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 4/17/2019
Yayın Tarihi: 17.04.2019

Abstract

Aim: Lymphedema is a protein-rich interstitial fluid accumulation which occurs as a result disruption of lymphatic circulation. Breast cancer is a major reason of secondary cancer lymphedema. Breast cancer related upper extremity lymphedema result from the obstruction or disruption of the lymphatic system due to axillary lymph node dissection and/or radiation therapy of axillary region. A variety of conservative therapies have been aimed to decrease the limb swelling and its associated problems have been developed. Conservative treatments are complex decongestive therapy (CDT). The aim of our study was to investigate efficacy of CDT on the occurrence of breast cancer related lymphedema.

Methods: Between 2009 and 2018, 47 consecutive patients with histologically proven breast cancer were first treated with breast surgery, axillary lymph node dissection and radiotherapy and/or chemotherapy. These were analyzed collectively with retrospective data of our medical records who had 15-30 set of CDT and who had complete assessments before and after the treatment. CDT consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises. Patients were treated with active therapy schedule (manual massage for lymphatic drainage and exercise therapy, 45-60 min per day) by the same trained physiotherapist. Volumetric quantification by circumference measurement of affected and healthy extremities was used for diagnosis and follow-up of lymphedema in all patients.

Results: The data of the 47 patients complying with the criteria specified in this retrospective study were evaluated. When the volumetric changes in the affected extremity were examined before and after lymphedema treatment, it was determined that the amount of lymphedema decreased after CDT (P=0.001). 31 (66%) patients received radiotherapy after mastectomy. When the patients were compared in terms of volumetric changes in extremities before and after CDT according to getting postoperative radiotherapy, it was determined that the changes in the patients who did not get radiotherapy were significantly higher than those getting radiotherapy (P=0.01).

Conclusion: Our study results show that CDT can be used for the management of breast cancer related lymphedema of limb. A thorough cost-effective analysis of protocol for CDT should be performed in a future study. In addition, as the factors underlying treatment delay were not included in this study, we believe future studies examining this area may be beneficial.

Keywords: Lymphedema, Complex decongestive therapy, Breast cancer

Öz

Amaç: Lenfödem lenfatik dolaşımının bozulması sonucu, proteinden zengin interstisiyel sıvının birikimiyle karakterize bir durumdur. Meme kanseri ilişkili lenfödem genellikle aksiller lenf nodu diseksiyonu ve/veya aksiller radyasyon sonucu üst ekstremitenin lenfatik drenajının bozulması nedeniyle oluşur. Tedavi yaklaşımları, ekstremitedeki şişliğin azaltılması, semptomların kontrolü ve komplikasyonların azaltılmasına yöneliktir. Bu çalışmadaki amacımız meme kanseri ilişkili lenfödem ve kompleks dekonjestif tedavisi (KDT) etkinliğini araştırmaktır.

Yöntemler: Meme kanserine bağlı olarak cerrahi müdahale, axiller lenf nodu diseksiyonu,radioterapi ve/veya kemoterapi almış ve üst ektremitede lenf ödem gelişen, 15-30 seans KDT uygulanan ve ayrıca rehabilitasyon öncesi ve sonrası değerlendirmeleri eksiksiz yapılan hastaların dosyaları değerlendirmeye alındı. Tüm hastaların lenfödemin tanı ve takibinde etkilenen ve sağlam ekstremitenin çevre ölçümleri aracılığıyla elde edilen volümetrik ölçümler kullanıldı. Hastaların tedavi öncesi ve sonrası sağlam ve etkilenen ekstremitelerinin çevre ölçümlerinden faydalanarak ekstremite volümleri hesaplandı ve kaydedildi.

Bulgular: Yapmış olduğumuz bu retrospektif araştırmada belirtilen kriterler ile uyumlu 47 hastanın verileri değerlendirmeye alındı. Lenfödem tedavisi öncesi ve sonrasındaki tutulan ekstremitedeki volüm değişimleri incelendiğinde ise KDT sonrasında lenfödem miktarının anlamlı derecede azalmış olduğu tespit edildi (P=0.001). Değerlendirmeye alınan hastalardan 31'i (%66) mastektomi sonrası radyoterapi almıştı. Hastalar postoperatif radyoterapi alma durumuna göre KDT öncesi ve sonrası ekstremitede meydana gelen volümetrik değişim açısından karşılaştırıldığında radyoterapi almayan hasta grubundaki değişimin radyoterapi alanlardan anlamlı derecede daha fazla olduğu belirlendi (P=0.01).

Sonuç: Çalışmamızın sonuçları KDT tedavisinin lenfödem tedavisinde etkin bir tedavi yöntemi olduğunu göstermiştir. Gelecek zamanda kompleks dekompresif tedavinin komponentlerinin etkinliğini değerlendirilebilmek için uzun takip süreli kontrollü çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Lenfödem, Kompleks dekompresif tedavi, Meme kanseri

How to cite / Atıf için: Karaman NS, Karataş Ö, Samur A, Çipli A, Balcı N. Efficacy of complex decongestive therapy on breast cancer-related lymphedema: A cross-sectional study. J Surg Med. 2019;3(4):300-303.

Introduction

Lymphedema is a protein-rich interstitial fluid accumulation which occurs as a result disruption of lymphatic circulation [1]. Breast cancer is a major reason of secondary cancer lymphedema. Breast cancer related upper extremity lymphedema result from the obstruction or disruption of the lymphatic system due to axillary lymph node dissection and/or radiation therapy of axillary region [2]. Breast cancer related lymphedema-associated symptoms are pain in the affected arm, skin fibrosis and impaired shoulder/arm movement altogether with worsening in their quality of life [3]. All patients with breast cancer who treated for lymph node dissection and radiation therapy has a risk of developing lymphedema, swelling of the upper extremity and concomitantly of the breast [4]. Additionally, there is a relationship between the risk of lymphedema, and treatment outcome according to the extent of lymph node dissection.

Lymphedema is considered irreversible condition. A variety of conservative therapies have been aimed to decrease the limb swelling and its associated problems have been developed. Conservative treatments are complex decongestive therapy (CDT), manual lymphatic drainage (MLD), self/partner massage, pneumatic pumps, oral pharmaceuticals and Low level laser therapy. Physical therapy treatment of patients with lymphedema is based on the principles of CDT which consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises [5]. There are two phase program with an initial phase can be allowed for the reduction of lymphedema. It is followed by a maintenance phase based on compression therapy with the aid of bandages, self-lymphatic massages with regular use compression garments, skin care and remedial exercises [6]. Lymphedema cannot be completely cured and when untreated conditions, the risk of increasing over of extremity volume which leads to chronic inflammation later then fibrosis. Therefore, effective treatment of lymphedema is important for improving quality of life.

The aim of our study was to investigate efficacy of CDT on the occurrence of breast cancer related lymphedema.

Materials and methods

Between 2009 and 2018, 47 consecutive patients with histologically proven breast cancer were first treated with breast surgery, axillary lymph node dissection and radiotherapy and/or chemotherapy. These were analyzed collectively with retrospective data of our medical records. Exclusion criteria were involvement of both side, recurrence, patients treated in another center before, patients who have not completed CDT and patients who had bone metastasis.

All patients were informed about lymphedema and the therapy in the first assessment. They were also given a schedule for home exercises and thought self-massage. Patients were treated with active therapy schedule (manual massage for lymphatic drainage and exercise therapy, 45-60 min per day) by the same trained physiotherapist. The same physiotherapist made multıple part-compressive bandage therapy at the end of the day. CDT was used for 15 to 30 sessions 5 days a week according to patients' condition.

Patients' ages, the extremity involved in lymphedema, dominant extremity in use, any surgical procedure, the duration since the beginning of CDT, the duration of CDT and any previous treatment involving radiotherapy and/or chemotherapy. Volumetric quantification by circumference measurement of affected and healthy extremities was used for diagnosis and follow-up of lymphedema in all patients. Circumference measurements of all patients' affected and healthy extremities were made symmetrically in 5 cm intervals from the ulnar styloid process to the axilla pre- and post-treatment. Both extremity circumference measurements of the patients assessed and recorded pre- and post-treatment.

Statistical analysis

Statistical analyses were performed with the SPSS Software Package (version 22.00; SPSS Inc., Chicago, USA). Descriptive statistic parameters, such as frequency distribution, mean and standard deviation, were used for characterizing the study group. Mean differences of two independent groups were determined using "Student t test" when parametric test assumptions were met, while mean differences of two dependent groups were determined using "paired difference test". Additionally, strength of association between continuous variables was assessed with Spearman's correlation coefficient, while that of between discrete variables was assessed with Pearson's correlation coefficient. During analysis, a confidence level of 95% (or tolerance level of α=0.05) was deemed a statistically significant difference.

Results

The data of the 47 patients complying with the criteria specified in this retrospective study were evaluated. The mean age of the patients were 55.63 (9.60) years (min 35 - max 74 years) and the period until CDT was started was 74.25 (39.55) months (min 18, max 168 months). 28 (%59.6) patients were operated for left and 19 (40.4%) patients were operated for right breast ca and the mean BMI values of the patients were 31.34 (5.22) kg/m2. When the patients on the scope of the study were examined for comorbid diseases, one or more comorbid factors were detected in 24 (60%) patients. The most common comorbid diseases are; endocrine diseases such as diabetes mellitus, hyperlipidemia and thyroid dysfunction in 17 (41.5%) patients, cardiovascular diseases especially hypertension in 12 (30.8%) patients and pulmonary diseases in 3 (7.3%) patients. Demographic and clinical characteristics of patients are shown in Table 1.

It was determined that the affected extremity volumetric values before treatment of patients who received CDT had significantly higher than the unaffected extremity, that this difference continues after treatment too (P=0.001). When the volumetric changes in the affected extremity were examined before and after lymphedema treatment, it was determined that the amount of lymphedema decreased significantly after CDT (P=0.001) (Figure 1).

When the patients were divided into two groups according to age of under 65 years of age (37 patients, 78.7%) and 65 years of age and above (10 patients, 21.3%), there was no difference between the groups according to the change in the amount of lymphedema before and after treatment (P=0.79). In

addition, no difference was found between the groups when the changes in the amount of lymphedema before and after treatment in terms of right or left extremity affected were compared (P=0.73, Table 2).

31 (66%) patients received radiotherapy after mastectomy. When the patients were compared in terms of volumetric changes in extremities before and after CDT according to getting postoperative radiotherapy, it was determined that the changes in the patients who did not get radiotherapy were significantly higher than those getting radiotherapy (P=0.01). When the patients were compared according to getting chemotherapy, there was no difference between the groups in terms of the change in the amount of lymphedema before and after treatment. In addition, when the patients were evaluated according to the presence of comorbid diseases, it was found that there was no significant change in the amount of lymphedema before and after CDT among the patients with one or more comorbid diseases and those without any comorbid disease (Table 2).

When the patients were evaluated in terms of risk factors, there was a statistically significant strong correlation between BMI and the amount of lymphedema before and after treatment (r=0.74 and r=0.73, P=0.04) (Figure 2, 3).

Table 1: Demographic and clinical characteristics of patients

	Patient group (n=47)
Age, years, mean (SD)	55.6 (9.6)
Affected side (right/left) mean (SD)	28 (59.6%) /19 (40.4%)
BMI kg/m^2, mean (SD)	31.34 (5.22) kg/m^2
CDT sessions, mean (SD)	16.80 (3.52) (min 15, max 30)
Length of time from diagnosis to CDT (months), mean (SD)	74.25 (39.55) months (min 18, max 168 months)
Post-operative chemotherapy (n, %)	36 (76.6)
Post-operative axillary radiotherapy (n, %)	31 (66)
Comorbid disease + (total)	24 (60)
Cardiovascular disease (n, %)	12 (30.8)
Endocrine disease (n, %)	17 (41.5)
Pulmonary disease (n, %)	3 (7.3)

SD: Standard deviation

Table 2: Clinical parameters associated with lymphedema volume comparison between pre-treatment and post-treatment

	Pre-treatment lymphedema limb volume mean (SD)	Post-treatment lymphedema limb volume mean (SD)	P-value
Age			
< 65 years (n=37, 78.7%)	3.30 (0.87)	2.87 (0.73)	0.79
≥ 65 years (n=10, 21.3%)	3.47 (0.63)	2.95 (0.48)	
Effected limb			
Right upper limb (n=19, 40.4%)	3.40 (0.87)	2.89 (0.64)	0.43
Left upper limb (n=28, 59.6%)	3.29 (0.80)	2.88 (0.72)	
Radiotherapy			
Yes (n=31, 66%)	3.43 (0.96)	2.96 (0.76)	0.01 ǂ
No (n=16, 34%)	3.16 (0.44)	2.74 (0.47)	
Chemotherapy			
Yes (n=36, 76.6%)	3.28 (0.86)	2.83 (0.67)	0.38
No (n=11, 23.4%)	3.52 (0.69)	3.06 (0.70)	
1 ≤ comorbid disease + (n=24, 60 %)	3.39 (0.83)	2.92 (0.69)	0.51
Comorbid disease - (n=23, 40 %)	3.07 (0.72)	2.68 (0.59)	

SD: Standard deviation, ǂ P<0.05

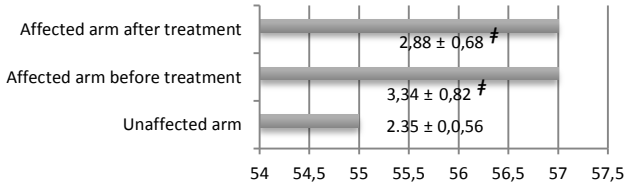

Figure 1: Comparison of affected and unaffected arm's volume between pre-CDT and post-CDT, ǂ P=0.001

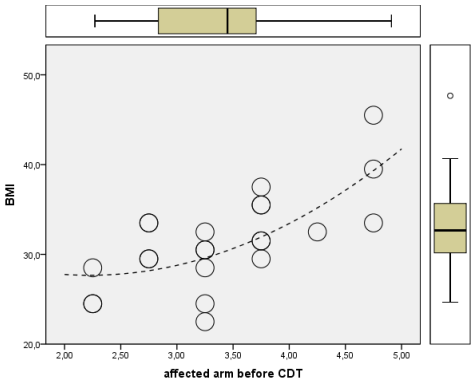

Figure 2: The relationship affected arm between BMI before CDT, ǂ (r=0.74, P=0.04)

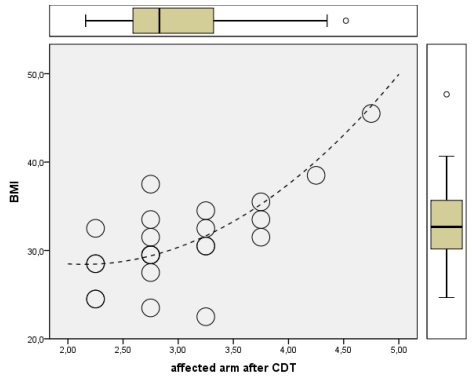

Figure 3: The relationship affected arm between BMI post CDT, ǂ (r=0.73, P=0.04)

Discussion

Lymphedema is important complications of breast cancer treatment. In the Arm lymphatic vessels were drained from the hand and forearm via superficial channels. There are also deep channels that drain via the occasional deep lymph node accompanying arteries in the forearm to the axillary nodes. Then lymph drains up the arm, passing through a few deep brachial and deltopectoral lymph nodes, before draining into the infraclavicular and axillary lymph nodes [7]. Lymphatic vessels remove circulating fluid and large molecules from the extracellular spaces and transport them to the lymph nodes. It is essential for maintain correct extracellular fluid balance and clearance of pathogenic elements. After then lymph is returned back systemic circulation via the vascular system. But in lymphedema, this normal way is impaired and excess protein rich fluid especially subcutaneous tissue. Some risk factors that may lead to developing lymphedema have been identified such as surgical removal of lymph nodes, radiotherapy to lymph node areas, obesity [8,9]. In our study, we also observed significant correlation between breast-cancer related lymphedema, and radiotherapy and obesity. Radiotherapy treatment is a risk factor of developing lymphedema; this condition may also be associated with some skin excoriation. This can decrease the transport capacity of the initial lymphatics but should slowly improve once the treatment has been completed [8]. Warren et al. [10] showed that radiotherapy to regional lymph nodes increase risk of developing lymphedema. Rupp et al. [3] collected from 385 patients data who underwent multimodal therapy for breast cancer, including breast conserving surgery, axillary dissection, and local radiotherapy and their aim is studied the effects of individual risk factors on the occurrence of breast cancer related lymphedema when breast cancer therapy included complete axillary lymph node dissection. As a result they found

association between chemotherapy and increase risk of breast-cancer related lymphedema like some studies [3,11]. Chemotherapy can lead to an enhancement of interstitial fluid filtration, capillary protein leakage and subsequently edema. In our study, this result is not in conformity with our study. We couldn't found significantly correlation between chemotherapy and lymphedema. This difference may be occurred because of our study include the relatively small and clinically diverse sample population.

As mentioned, there is no cure for lymphedema, and the aim of the treatment is to reduce the swelling and to decrease discomfort. CDT can be effective in reducing arm volume. CDT consists of the following components; skin care, manual lymphatic drainage, bandaging and exercises [12]. The treatment is based on manual lymphatic drainage 5 times weekly and each treatment takes 45-60 minutes. However, standardization between different treatment locations and among treating physiotherapists does not exist. Some studies demonstrated that a reduction in upper extremity volume can be done with CDT [13-15]. In our study, results suggest that decongestive phase of therapy is effective in the maintenance of volume reduction. CDT is a combined method of treatment, and the relative efficacy of each of the components of this comprehensive treatment program has been investigated in some studies [16]. There is a debate as to which components of CDT play the most crucial and whether bandages are more effective at reducing swelling than compression hosiery. Lack of experienced therapists and inadequate resources mean that standard treatment is likely to consist of compression hosiery with advice on skin care and exercise. In case manual lymphatic drainage is not accessible, patients are often taught to perform a simplified form known as self-administered massage, however, as to which of these methods is the more effective unknown yet. These questions are required to further research investigation able to answer. This is important how we can identify the most effective physical treatment and achieve the desired clinical benefit with patient comfortable.

The main limitation of this study was the small sample size which may restrict the generalization of the results. Another limitation was the lack of adequately designed randomized controlled trials. The other one, its retrospective design prevented uniform measurement of the arm volume. And also this study had no control group; we only aimed to compare pretreatment and posttreatment status. In addition, the factors underlying treatment delay were not documented in this study. Therefore, we believe future studies for this issue may be beneficial.

In conclusion, CDT can be effectively used for the management of breast cancer related lymphedema of the limb. A thorough cost-effective analysis of protocol for CDT should be performed in a future studies.

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The National Library of Medicine (NLM) citation style guide is used in this paper.
Suggested citation: Patrias K. Citing medicine: the NLM style guide for authors, editors, and publishers [Internet]. 2nd ed. Wendling DL, technical editor. Bethesda (MD): National Library of Medicine (US); 2007-[updated 2015 Oct 2; cited Year Month Day]. Available from: http://www.nlm.nih.gov/citingmedicine