Effectiveness of Exercise and Compression Garments in the Treatment of Breast Cancer Related Lymphedema

Meme Kanseri ile İlişkili Lenfödem Tedavisinde Bası Giysileri ve Egzersizin Etkinliği

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Summary

Objective: Lymphedema (LE) is a long term and important complication observed in patients with breast cancer that causes functional impairment and affects the quality of life. Total recovery could not be reached by current treatments. Therapeutic efforts remain focused on minimizing the edema and on reversing and restoring the functional and cosmetic nature of the limb. There are a limited number of randomized, controlled studies looking for the effectiveness of treatments, either seperately or combined. This study was designed to investigate the effectiveness of exercise and compression garment in the treatment of breast cancer related LE.
Materials and Methods: Nineteen patients with breast cancer related LE were randomly assigned to receive exercises (n=9) or exercises and compression garment (n=10). The efficacy of treatment was evaluated by reduction in lymphedema volume which was determined by measurement of arm circumference and by improvement in shoulder range of motion and in symptoms potentially related to lymphedema such as pain and tender points.
Results: The patients were followed-up for a total of six months. Almost all parameters improved in the second group whereas no significant improvement was seen in the first group.
Conclusion: As a conclusion, it can be suggested that the combination of compression garments and exercise therapy is an effective and simple way of treating LE. Since none of the treatment methods offer full recovery, educating the patients about the formation and characteristics of LE and preventive measures are very important. *Turk J Phys Med Rehab 2007;53:16-21*
Key Words: Breast cancer, lymphedema, treatment, exercise, and compression garment

Özet

Amaç: Meme kanseri kadınlarda en sık görülen malignitedir. Meme kanserli hastalarda uzun süreli ve önemli bir komplikasyon olan üst ekstremite lenfödemi fonksiyonel kayıba neden olur ve yaşam kalitesini etkiler. Mevcut tedavilerle tam iyileşmeye ulaşılamaz. Tedavi girişimleri ödemi azaltmaya ve kolun fonksiyonel ve kozmetik görünümünü geriye döndürmeye yöneliktir. Tedavilerin tek başına ya da kombine olarak etkinliğini gösteren az sayıda randomize, kontrollü çalışma bulunmaktadır. Bu çalışmada lenfödemli hastalarda egzersiz ve bası giysisinin etkinliği araştırıldı.
Gereç ve Yöntem: Meme kanseri ile ilişkili lenfödem tanısı almış olan 19 hasta iki gruba randomize edildi. Birinci grup (n=9) sadece egzersizle tedavi edildi. İkinci grup (n=10) ise egzersiz ile birlikte bası giysisi ile tedavi edildi.
Hastalar ağrı, duyarlılık, omuz eklem hareket açıklığı ve her iki kolun çevre ölçümü yönünden değerlendirildiler.
Bulgular: Sonuçlarımız 6 aylık izlem sırasında ikinci grupta hemen tüm ölçümlerde iyileşme olduğunu gösterirken birinci grupta tedavide anlamlı iyileşme olmadığını göstermiştir.
Sonuç: Sonuç olarak bası giysisi ve egzersiz tedavisi kombinasyonunun lenfödem tedavisinde etkili ve basit bir yöntem olduğu sonucuna varılmıştır. Ancak bu yöntemlerle tam bir iyileşme sağlanamaması nedeniyle lenfödem oluşumu ve özellikleri konusunda hastaların eğitiminin sağlanması ve önleyici önlemlerin alınması çok önemlidir. *Türk Fiz Tıp Rehab Derg 2007;53:16-21*
Anahtar Kelimeler: Meme kanseri, lenfödem, tedavi, egzersiz, bası giysisi

Introduction

Breast cancer is the most commonly diagnosed cancer in women and is treated by surgery, chemotherapy, or radiation. As newer and more effective modes of treatment have become available, cancer survivorship has continued to increase. Although these treatments have improved patient outcomes, they have been associated with substantial adverse effects. The role of rehabilitation has also been recognized in this patient population. Not only can there be residual functional deficits from malignancies, but, more importantly, sequelae from therapeutic interventions can result in functional impairment and decreased quality of life. One of important side effects is secondary lymphedema (LE) and is a major source of morbidity for people living with cancer, either

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as a direct result of the tumor or as a side effect of treatment and it changes functional abilities and may affect a patient's psychosocial adjustment and overall quality of life (1-4).

LE is the accumulation of protein-rich interstitial fluid within the skin and subcutaneous tissue that causes chronic inflammation and reactive fibrosis of the affected tissues (5). All female patients whose lymph canals have been surgically removed carry the risk of LE formation. LE can result from tumor compression or lymphatic vessel obstruction but it is caused more commonly by breast cancer therapy such as surgery and radiotherapy (6). The risk of LE is higher in women treated with axillary dissection and adjuvan radiation to the axilla (7). Reports of incidence vary from 10% to 48% with axillary lymph node dissection (8-10). The incidence of LE is difficult to establish because the length of follow-up in research studies varies from 1 year to 20 years and surgical technique has changed over time. The incidence of LE is affected by the method of arm volume measurement, the follow-up period of the patient population, and the duration between the axillary dissection and the diagnosis of LE (11).

As in the area of assessment of LE, no consensus regarding standards for the treatment of LE exists. Management of LE in women with breast cancer has been a subject of debate for many years. There is currently no cure for LE. Therefore, all of the current studies are focus on minimizing the edema and reversing and restoring the functional and cosmetic nature of the limb. To address this issue, the International Society of Lymphology Executive Committee in 1995 developed a consensus document that offered an integrated view of the various approaches currently utilized for the treatment of LE (12).

Treatment options include elevation, exercise, massage, compression garments, pneumatic compression pumps and complex physical therapy (13). The literature is limited in regard to scientifically proven LE treatments because of the lack of prospective, randomized clinical trials that accurately control all variables and measure the amount of LE present (14).

Therapeutic exercises and compression garments are established treatment methods of LE. Therapeutic exercises include remedial exercises that aid lymph flow through repeated contraction and relaxation of muscles.

A case series published by Harris and Niesen-Vertommen in 2001 suggested that women who have undergone treatment for breast cancer could engage in upper extremity exercises without developing LE (15).

A compression sleeve may be used to reduce edema in mild cases or to maintain the reduction achieved by compression bandaging or other volume-reducing techniques. It is custom fitted to apply external pressure in the range of 20–60 mmHg. These garments typically cover the arm from wrist to mid-humerus and may be prescribed with an attached gauntlet or separate glove. They are usually removed overnight.

Pecking compared the use of a compression garment/elastic sleeve with no treatment. There was no significant difference in the rates of LE between the two groups (55% with compression garments versus 45% for no treatment) (16). Hornsby compared the use of a compression garment plus self-massage with self-massage alone in women. During the first 4 weeks of treatment, 12 of 14 women in the experimental group and 4 of 11 in the control group showed a reduction in swelling as measured by the amount of fluid displaced from an immersion tank (17).

Anderson et al. (18) compared standard therapy (compression garment + education + exercise) with complex physical therapy (manual lymphatic drainage + self massage + standard therapy) in women with LE following breast cancer treatment. There was a reduction in edema in both groups over a 3-month period but no significant difference between treatments. There were no significant differences in symptom improvement between the groups.

There is insufficient evidence to support an evidence-based recommendation on which to base a practice guideline for the treatment of LE. Although many researchers have developed different treatment methods for LE, there is no current evidence to support the use of different treatments. The limited amount of controlled research in this field contributes to the controversy about the efficacy of individual treatment approaches and how treatments should be combined in specific situations. The aim of this study was to assess the effectiveness of exercise and the use of compression garment in the treatment of breast cancer related LE.

Materials and Methods

This randomized controlled, prospective, and single-blind study was carried out in breast cancer related LE patients who had admitted to the Uludağ University Physical Medicine and Rehabilitation Outpatient Clinic. Ethical approval was granted by Uludağ University Faculty of Medicine Local Research Ethics Committee. Prior to testing, informed consent was obtained from each subject.

Patients with the following characteristics were excluded from the study: Those who had been operated less than 4 months ago, those who had recurrence, those with bilateral breast cancer, elephantiasis, congestive heart failure, acute deep vein thrombosis, those suffering from acute or untreated infections on the affected arm by cancer, those with active breast cancer, and those with stage 4 breast cancer.

Demographic characteristics and risk factors related to LE had been assessed prospectively. For each patient; the type and side of operation, the stage of the tumor, the results of the biopsy, the number of lymph nodes removed from the axilla, and the duration of the LE were recorded.

Same researcher assessed the patients' shoulder range of motion (ROM), shoulder tenderness, and the circumference arm measurements before the treatment, 2nd week, 1st month, 3rd month, and 6th month of the study period. Prior to the treatment, the patients were randomized into two groups by another researcher. The first group was only treated with exercise treatment. Second group was treated with the compression garment and the exercise treatment program similar to the program given to the first group.

Each patient was informed about skin care and LE education (the formation/progression of LE and the effects of the exercises on the drainage of lymphatic flow). Prevention efforts and the importing of information about LE were explained. Simple suggestions were made to patients not to lift heavy objects, not to get blood drawn, and not to have blood pressure measurement from the limb at risk. They were also given booklets containing information about skin care and LE education.

The exercise program consisted of upper extremity ROM exercises and light resistive exercises including bilateral and unilateral cane stretches, external rotation/horizontal abduction, "praying child", wall walking, and pulleys. Both groups were given the same exercise program in printed form and the exercises were also practiced with them. They were asked to carry out these exercises 3 times a day, with 10 repetitions each time. At every visit, the patients were questioned about whether they were doing their exercises regularly or not. If not, they were asked to do them regularly as well as to pay attention to the precautions.

The patients in the second group were prescribed compression garments that deliver 40 mmHg of pressure. They were asked to wear the garments on at all times expect when they go to sleep for the duration of 6 months.

Blinding was maintained for the researcher responsible for assessing the patients. Another researcher did the randomization.

Assessment Parameters:

1-Visual Analog Scale (VAS): VAS was used to measure the intensity of pain.

2-Shoulder tenderness: The severity of tenderness on the shoulder was assessed according to the scale of 0-3.

3-Shoulder ROM: Measured with goniometry in all directions.

4-Circumferential measurements: Arm circumferences were determined at 4 sites - The carpometacarpal region, the wrist, 15 cm proximal and 10 cm distal to the lateral epicondyle (19). Measurements were taken keeping both the limbs in a similar position with arms relaxed by their sides and elbows straight. The differences of both of upper extremity measurements were recorded.

All of the measurements were carried out between 11:00 and 14:00 to have the standardization.

Statistical Analysis:

The statistical analysis was performed by Statistical Package for the SPSS for Windows (SPSS, Inc Chicago, IL) and an alpha level of 0.05 was considered significant. Demographic characteristics are reported with descriptive statistics. Continuous measures are reported as means and standard deviations (±SD), while categorical variables are reported as proportions. We used the Wilcoxon test to determine whether changes in pain, tenderness, ROM and circumference measurement scores from baseline to 2nd week, 1st month, 3rd month, 6th month evaluations for each group were significant at a value of $p<0.05$. Mann-Whitney U test was used to define the differences between groups at every visit.

Results

Twenty-one patients who had all received surgery and radiotherapy were included in the study. Because one of the 10 patients in the first group occurred deep venous thrombosis, and one of the 11 patients in the second group developed lymphangitis, this study was completed with 19 subjects: 9 patients in the Group 1 (exercise treatment alone) and 10 patients in the Group 2 (exercise treatment + the use of compression garments).

Mean age was 51.1±8.1 (33-64) years. Demographic and disease related characteristics were shown in Table 1.

There were no significant differences in the type of surgery, affected side, tumor stage and pathological diagnosis between the groups.

All women received radiation therapy.

The distribution of number of lymph node and the subjects' LE duration according to groups is shown in Table 2. Due to the fact that the number of samples was quite low, we could not carry out a statistical analysis comparing the groups.

At the baseline evaluation, only one patient had pain and tenderness; therefore, we did not detect any statistically significant level of recovery in intra-group comparisons (Wilcoxon test, $p>0.05$).

The ROM analysis also showed that only one patient had restricted shoulder flexion and abduction. Therefore, we did not find out any statistically difference of recovery for the whole sample (Wilcoxon test, $p>0.05$).

Table 3 shows the baseline and the follow-up differences of circumference measurements. We found statistically no significant differences between the groups concerning the comparison of the baseline and follow-up circumference measurements of all measurement sites (Mann-Whitney U test, $p>0.05$).

At the circumference measurements of carpometacarpal joint site, for both groups, the follow-up measurements did not statistically difference from the baseline measurements (Wilcoxon test, $p>0.05$). Intra-group analysis showed that the 2nd week, 1st month, 3rd month, and 6th month circumference measurements of the wrist were statistically significant difference from the baseline value (Wilcoxon test, respectively $p=0.032$, $p=0.046$, $p=0,009$, $p=0.008$) for the group 2 (Figure 1).

For the group 2, we have determined statistically significant improvements in the distal circumferential measurements taken in the 2nd week, 3rd month, and 6th month (Wilcoxon test, respectively $p=0.05$, $p=0.005$, $p=0.05$) (Figure 2).

For the group 1, the circumference measurements of proximal showed statistically significant improvement in the only 1st month measurements (Wilcoxon test, $p=0.043$).

Table 1. Demographic and disease-related characteristics.

Age (Years) mean±SD (min-max)	51.6±8.8 (33-64)	No. of patients	%
Menopause	Premenopause	9	47.4
	Postmenopause	10	52.6
Comorbidity	No medical problems	10	52.6
	One or more medical problems	9	47.4
Breast Cancer in the history	No	18	94.7
	Yes	1	5.3
Type of surgery	Lumpectomy+axillary dissection	7	36.8
	Modified radical mastectomy	12	63.2
Affected side	Right	10	52.6
	Left	9	47.4
Tumour stage	Tis	1	5.3
	T1	1	5.3
	T2	10	52.6
	T3	7	36.8
Pathological diagnosis	Infiltrative ductal carcinoma	17	89.4
	Infiltrative lobular carcinoma	1	5.3
	Mixed type carcinoma	1	5.3

Discussion

Upper extremity LE is the most significant long-term complication of breast cancer treatment. It causes upper extremity function loss, therefore decreases quality of life (20).

Every female whose lymph canals have been surgically removed carries the risk of LE. Pezner et al. (21) claim the rate of LE is 25% for females above 60, whereas it is 7% for females less than 60. Kiel and Rademacker (22) claim the age of the patient at the time of diagnosis is the most significant factor for arm edema. In their study, the rate of arm edema formation was shown to be 56% for females above 55 and 23% for below. Marcks (23) suggests that this fact is related to the formation of lymphovenous anastomosis in younger patients. Autopsy results show that lymphovenous anastomosis is less common in older women. The average age of the study group was 51.5±8.2; only 35% of our subjects were over 55. Therefore, the patient group was a relatively young one.

As there is no cure for LE, the aim of the treatment is to reduce the swelling, increase joint mobility and to decrease discomfort. One of the most important aspects of treatment is the education of patients about the structure and function of the lymphatic system, as well as helping them cultivate an awareness regarding what factors and activities exacerbate their condition and what strategies best control it. The patients must be informed about the risk factors, symptoms, and findings of the LE. If the patients themselves learn to identify the LE symptoms for early diagnosis, it may prevent the progression of LE and decrease the possibility of delay of treatment (24-26). In our study, all of the patients were also informed about skin care and LE education.

Pain can be felt in both the shoulder joint due to restricted movement and in the arm due to the formation of LE after breast cancer treatment. In Bendz and Olsen's study (27) only a few patients were suffering from such pain. Pain is an isolated symptom related with movement restriction and/or LE. At our study we detected that 5.2% of our subjects (only one patient) suffered from mild pain and mild tenderness on the ipsilateral shoulder. In addition, all of the patients included in our study except one had full shoulder ROM. The restriction of ROM and shoulder pain may develop in the early stages of the breast cancer treatment. The most of the subjects included in our study were in the late stages of the post-operative period. This may be also related to the education and exercise program given in early postoperative stage. We determined LE related arm pain in none of our patients. It is being argued that the tightening of the soft tissues causes arm pain related LE and that it is a more significant finding for acute and/or progressive LE. The fact that none of our patients suffered from arm pain might be related to the fact that most of them had chronic LE and also tissue fibrosis.

Various strategies for management of LE are available. Conservative treatment of LE includes procedures such as elevation, exercise, massage, manual lymphatic drainage, compression garments and intermittent pneumatic compression pumps. Studies have shown that use of physical treatments is effective in reducing the amount of swelling in affected limbs. The specific type, amount, and combination of these treatments

Table 2. Group distribution of number of lymph node and LE duration.

	Total	Group 1	Group 2
Number of lymph node			
mean±SD (min-max)	16.2±6.8 (0-25)	16.7±7.8 (0-25)	15.7±6.1 (8-24)
Lymphedema duration (months)			
mean±SD (min-max)	23.5±16.8 (3-60)	26.6±17.4 (5-60)	20.8±16.6 (3-60)
	n (%)	**n (%)**	**n (%)**
1-6 months	2 (10.5)	1 (%)	1 (%)
7-12 months	5 (26.3%)	2 (%)	3 (%)
>12 months	12 (63.2%)	6 (%)	6 (%)

Table 3. The baseline and the follow-up differences of circumference measurements.

	CMC* mean±SD min-max		**Wrist mean±SD min-max**		**DİST** mean±SD min-max**		**PROX*** mean±SD min-max**	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
Baseline	0.6±0.6 (0.1-2)	0.6±0.4 (0.3-1.5)	0.7±0.71 (0-1.8)	1.4±0.77 (0-3)	2.3±1.90 (0.2-6)	3.3±1.75 (1-7.3)	3.4±1.38 (0.2-5)	2.5±1.48 (0-4.7)
2nd week	0.5±0.37 (0-1)	0.4±0.27 (0.1-0.9)	0.8±0.55 (0.2-1.8)	0.9±0.31 (0.5-1.3)	2.0±2.32 (0.1-7)	2.7±1.27 (0.7-4.8	3.2±1.23 (1-5.4)	2.7±1.19 (0.6-4.4)
1st month	0.4±0.27 (0.1-0.8)	0.5±0.29 (0.2-1)	0.9±0.64 (0-2)	0.9±0.34 (0.3-1.3)	2.1±1.87 (0.1-6.5)	2.7±1.34 (0-4.6)	2.7±1.62 (0-4.5)	3.1±1.35 (0.3-5)
3rd month	0.3±0.26 (0-0.8)	0.4±0.18 (0.1-0.7)	0.9±0.71 (0.1-2)	0.7±0.43 (0.2-1.3)	2.3±1.67 (0.3-5)	2.3±1.01 (0.9-4.1)	3±1.3 (0.8-5.7)	2.7±2 (0.-6.6)
6th month	0.3±0.33 (0-1)	0.5±0.21 (0.2-0.9)	0.8±0.52 (0.1-1.6)	0.6±0.39 (0.-1.3)	1.9±1.58 (0-4)	2.5±0.73 (1-3.5)	3.4±1.86 (0.6-7)	3.0±2.15 (0.4-7.7)

* : The carpometacarpal region. ** : 15 cm proximal of the lateral epicondyle *** : 10 cm distal of the lateral epicondyle

continue to be debated. There is limited number of randomized controlled studies showing the effectiveness of these methods, either separately or combined (3,28).

Exercises are an essential part of the LE treatment both during treatment and in the maintenance phase. Although the role of exercise in the management of breast cancer related LE is not well defined, the rationale behind the use of exercise in the LE patient is predicated on the observation that muscle contraction promotes lymph flow and increases protein absorption (29,30). This "muscle pump" effect results from changes in tissue pressure that stimulate the initial lymphatic vessels to open and close and thus encourage movement of interstitial fluid into the lymphatic system. The use of nonfatiquing exercises and activity represents the ideal method because these will not trigger additional interstitial fluid production (30). They must be specially designed for patients with LE to be maximally effective. Exercises should be taught to the patients when they first start a treatment course and the patients should be followed-up carefully.

Box et al. has reported that an early exercise program decreases the incidence of secondary LE. The rationale for starting the exercise program early is the attainment of a wide ROM and facilitating the formation of lymphatic compensatory mechanisms (28). Our study failed to get positive responses from the patients enrolled in the exercise program. But the fact that 89.5% of our patients were in the chronic stages of the disease might have played a role in this.

In some studies, it was widely accepted that aerobic exercise and upper extremity training should be contraindicated for women with breast cancer (31,32). But recent studies have provided preliminary evidence to suggest that exercise may be safe (33,34). In our study, we didn't recommend vigorous exercise and strenuous exertion. So we don't think that our exercise program might have a negative effect on LE. There is the possibility that exercise may be useful in the prevention and treatment of LE. But further investigation is required to see what physiological changes may be taking place at the tissue level in the affected arm in response to short- and long-term exercise.

Compression garments are frequently used in the treatment of LE. If lymph edema is discovered early, and in acute state, treatment will more likely to be successful then if it were attempted in a later brawny, nonpitting stage. The compression garments increase the lymph circulation in the arm thereby preventing the formation of edemas. The limited number of studies on this subject has shown that compression garments are useful for resolving peripheral LE (25,35-38). Anderson et al. (18) has reported that the patients received the best response to early treatment. They have argued the response to treatment is also related with the characteristics of the patient as well as her cooperation. A prospective study by Collins et al. (36) has demonstrated significant decreases in LE in 27 women using the garments. The CT scans exam was used to compare unaffected arms with LE arms using compression for 1st, 3rd, and 12th weeks of treatment. A study has compared the use of a compression garment/elastic sleeve with no treatment. No significant difference was observed in the rate of edema between the two groups (55% with compression garments versus 45% for no treatment) (16).

It has been also reported that the use of combination therapies have produced significant benefits in women with LE (37). In addition, such a program also enhances the overall level of function of the extremity and the patient (38). However it has been suggested that the reduction obtained is very largely dependent on the degree of patient compliance with continuing compression garments, skin care, exercises, and avoidance of trauma to the affected extremity. Patients should be informed that LE is a lifelong condition and that compression garments must be worn on a daily basis. In our study, our patients wore it from morning to night and removed it at bedtime. Our findings showed that circumference measurements of the wrist and distal part were statistically different from the initial value in the group 2 (Figure 1 and 2). But there was only statistically significant improvement for the differences of proximal circumferential measurements in the 1st month (Wilcoxon test, p=0.043) for group 1. In addition there was statistically no significant difference for the circumference measurements of metacarpophalangeal site of both groups. These results showed that the combination of compression garment and exercise therapy is partially effective but this therapy is more effective than the exercise therapy. This might be because the patients might have paid more attention to the precautions as they were wearing the compression garment. The efficiency of the compression garment is may be related with the fact that it can be utilized easily at home and that it can be utilized for long durations.

In our study, 10.5% of our patients had been suffering from LE for 1-6 months, while 26.3% had had the symptom for 7-12 months, and 63.2% had been suffering from it for more than a year (Table 2). It is important for the efficiency of the treatment procedures that LE is diagnosed early and that treatment starts immediately. As LE lasts longer, the fat tissue under the skin becomes hypertrophic and fibrosis occurs which reduces treatment efficiency (39).

It is argued that early diagnosis and treatment makes the overall treatment process more effective and that this is so most probably because the venous system loses a large amount of fluid. There exists a consensus that the treatment is more

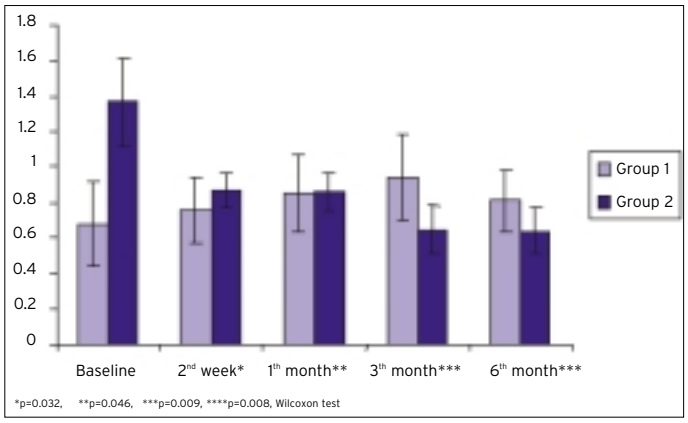

Figure 1. Wrist circumference differences between the baseline and follow up measurements.

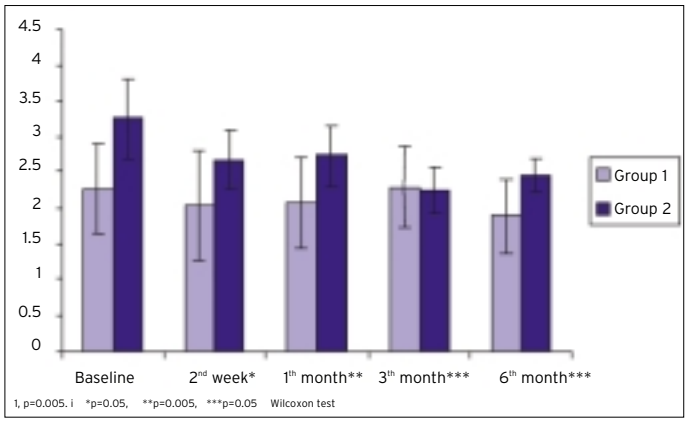

Figure 2. Distal circumference differences between the baseline and follow up measurements.

successful during the acute stage (28,40,41). Since 89.5% of our patients had been suffering from it for more than 6 months, they were accepted to be in the chronic phase and this might be effective for the formation of fibrosis, the loss of elasticity, and the response to the treatment. Since we had few acute patients, we were unable to assess the correlation between the efficiency of the compression garment and the duration of the disease. Our results showed that LE has never totally disappeared. It is exceptional to reduce the edema entirely and to return the treated limb to its healthy state aspect. Therefore, it is concluded that the success of the therapy depends on the duration of the disease.

It is suggested that the combination of exercise therapy and compression garment is more effective than exercise alone program in the treatment of breast cancer related LE. Since our sample size was small, this need to be further examined in a larger patient group. Exercise alone is not sufficient , especially when the disease becomes chronic, and that the compression garment, which can easily be utilized at home for long periods of time, is useful in the treatment of breast cancer related LE. As a conclusion, it can be suggested that the combination of compression garment and exercise therapy is an effective and simple way of treating LE. Since none of the treatment methods offer full recovery, educating the patients about the formation and characteristics of LE and preventive measures are very important.

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