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ORIGINAL ARTICLE

Efficacy of manual lymphatic drainage and intermittent pneumatic compression pump use in the treatment of lymphedema after mastectomy: a randomized controlled trial

Hulya Uzkeser · Saliha Karatay · Burak Erdemci · Mehmet Koc · Kazım Senel

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Abstract
Background This study has two aims. The first was to investigate the efficacy and contribution of an intermittent pneumatic compression pump in the management of lymphedema, and the second was to evaluate the correlation of our measurement methods.
Methods This study was designed as a controlled clinical trial at the Physical Medicine and Rehabilitation Department of Ataturk University Faculty of Medicine. Thirty-one patients with upper extremity lymphedema following mastectomy participated in the study. The patients were divided into two groups. The complex decongestive physical therapy (CDT) group (group 1, $n = 15$) received allocated treatment, including skin care, manual lymphatic drainage, compression bandages, compression garments, and exercises. The other group had CDT combined with an intermittent pneumatic compression pump (group 2, $n = 16$). Both groups were treated five times a week for 3 weeks (for a total of 15 sessions). Patients were assessed according to circumference measurements of landmarks, limb volume difference, dermal thickness with ultrasonography (USG), and pain.
Results We observed significant differencse in both groups when comparing them before and after therapy. The baseline median volume difference of group 1 was 630 (180–1,820), and after therapy it was 480 (0–1,410). In group 2, the beginning median volume difference was 840 (220–3,460), and after therapy it was 500 (60–2,160). However, no significant differences were observed between the two groups in terms of the above-mentioned parameters.
Conclusion We concluded that the pneumatic compression pump did not contribute to the reduction of lymphedema. In addition, gauging dermal thickness using USG may prove to be a useful measurement method in the evaluation of lymphedema.

Keywords Lymphedema · Intermittent pneumatic compression · Manual lymphatic drainage · Measurement methods

Introduction

Lymphedema can be defined as the abnormal accumulation of interstitial fluid occurring primarily as a consequence of malformation or acquired disruption of the lymphatic circulation [1]. Typically, 80 % of the lymphatic circulation of the upper extremity drains to axilla in which there are approximately 20–30 lymph nodes [2, 3]. Removing the axillary lymph nodes for any reason leads to lymphedema in the arm of the same side. For this reason, patients with breast cancer frequently develop lymphedema because of both the nature of the cancer itself and that of the treatment for this cancer [4, 5]. The probability of lymphedema progression increases according to the type of surgery applied and the number of lymph nodes removed [6, 7].

H. Uzkeser (✉) · S. Karatay · K. Senel
Department of Physical Medicine and Rehabilitation, Medical Faculty, Ataturk University, 25240 Erzurum, Turkey
e-mail: drhulyauzkeser@hotmail.com

B. Erdemci
Department of Radiation Oncology, Medical Faculty, Ataturk University, Erzurum, Turkey

M. Koc
Department of Radiation Oncology, Meram Faculty of Medicine, Selcuk University, Konya, Turkey

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Moreover, it is also known that performing chemotherapy and radiotherapy after surgery increases the risk of lymphedema [8]. The incidence of lymphedema, one of the severe complications that can present after a mastectomy, is 42 % [9].

Currently, complex decongestive physical therapy (CDT) is accepted as the international standard treatment for the treatment of lymphedema [10, 11]. CDT includes skin care, manual lymphatic drainage, compression bandages, compression garments, and exercise [10]. Manual lymphatic drainage is a massage technique that is done from distal to proximal, and the duration of the massage should be 45 min [12]. This decreases edema, providing for the elimination of lymph liquid by the lymph nodule. In addition, it prevents tissue fibrosis, thus rendering the tensed tissue flaccid [13]. An intermittent pneumatic compression pump, which is comprised of gradual pressure gradients on lymph vessels, facilitates the lymph flow [14]. Although the devices can apply different pressures (between 0 and 300 mmHg pressure), pressures between 30 and 60 mmHg are generally preferred in the treatment. It is believed that intermittent pneumatic compression devices can reduce lymphedema more successfully in the early phase and can be more beneficial if they are used with compression garments [12]. Contradictory results have been reported in studies investigating the contribution of the intermittent pneumatic compression pump in the treatment of lymphedema [15, 16]. According to the 2009 Consensus Document of the International Society of Lymphology, the act of combining an intermittent pneumatic compression pump with manual lymphatic drainage has not been sufficiently evaluated [17].

This study was carried out to investigate the efficacy and contribution of the intermittent pneumatic compression pump in the management of lymphedema.

Methods

The study was performed at the Physical Medicine and Rehabilitation Department of Atatürk University Faculty of Medicine. It was a controlled clinical trial. Thirty-one patients with unilateral upper extremity lymphedema following their mastectomy were enrolled in the study. All patients signed an informed consent form, and the local ethics committee of Atatürk University approved the study protocol.

The trial's eligibility criteria were patients with unilateral lymphedema following their mastectomy, no history of physical therapy before the trial, and a more than 2 cm difference at the circumference of the measurements or a more than 10 % difference in volume between the two arms. Patients who had bilateral lymphedema, current metastases, continuing radiotherapy, cellulites, venous thrombosis, elephantiasis, infection, lymphangiosis carcinomatosa, and congestive heart failure and those using any medications that affect the body fluid and electrolyte balance were excluded from the study.

The affected and unaffected upper limbs of the patients were measured with tape at four anatomic sites, including the metacarpophalangeal (MCP) joint, wrists, and 10 cm below and above the lateral epicondyles [18]. However, the water immersion method is still the gold standard described in the literature for the calculation of lymphedema [4, 19]. Lymphedema was defined as a more than 2 cm difference at the circumference of the measurements or a more than 10 % difference in volume between the two arms. Dermal thickness was measured with ultrasonography (USG) (Toshiba Xario Prime, 7.5-MHz probe) at the affected and unaffected limbs. Circumferences, dermal thickness, and the volume of the affected and unaffected limbs were calculated, and the difference between affected and unaffected limbs values was recorded as delta (Δ). In addition, patients were questioned about pain complaints. Pain was measured by the visual analog scale (VAS) as 0–10, ranging from no pain to very severe pain.

Initially, 45 patients were planned to be included in the study. Ten of the 45 patients who were voluneers had differences of less than 2 cm between two arms at measurements made before the trial, so they were not included in the study. We detected congestive heart failure in two previously undiagnosed patients. Two patients wanted to leave the study before starting the trial. Finally, the study was organized with 31 patients (Fig. 1).

Patients were randomly divided into two groups by consecutive alternate allocation according to the time of admittance. The physician who randomized the patients was blind to the groups. The CDT group (group 1, $n = 15$) received allocated treatment, including skin care, manual lymphatic drainage, compression bandage, compression garments, and exercises. The other group had CDT in combination with the intermittent pneumatic compression pump (group 2, $n = 16$). We applied the intermittent pneumatic compression pump after manual lymphatic drainage with a pressure of 40 mmHg for 45 min (MARK III Plus, model MK400). All groups were treated five times a week for 3 weeks (for a total of 15 sessions).

The demographic features of the patients, including the age, number of chemotherapy and radiotherapy sessions, duration of the lymphedema period, stage of lymphedema, and number of lymph node dissections, were recorded. In addition, the difference between circumference measurements of the MCP joints, wrists, 10 cm below and above the lateral epicondyles, the limb volume difference, dermal thickness, and pain were assessed initially, after therapy (week 3), and 1 month after completing therapy (week 7)

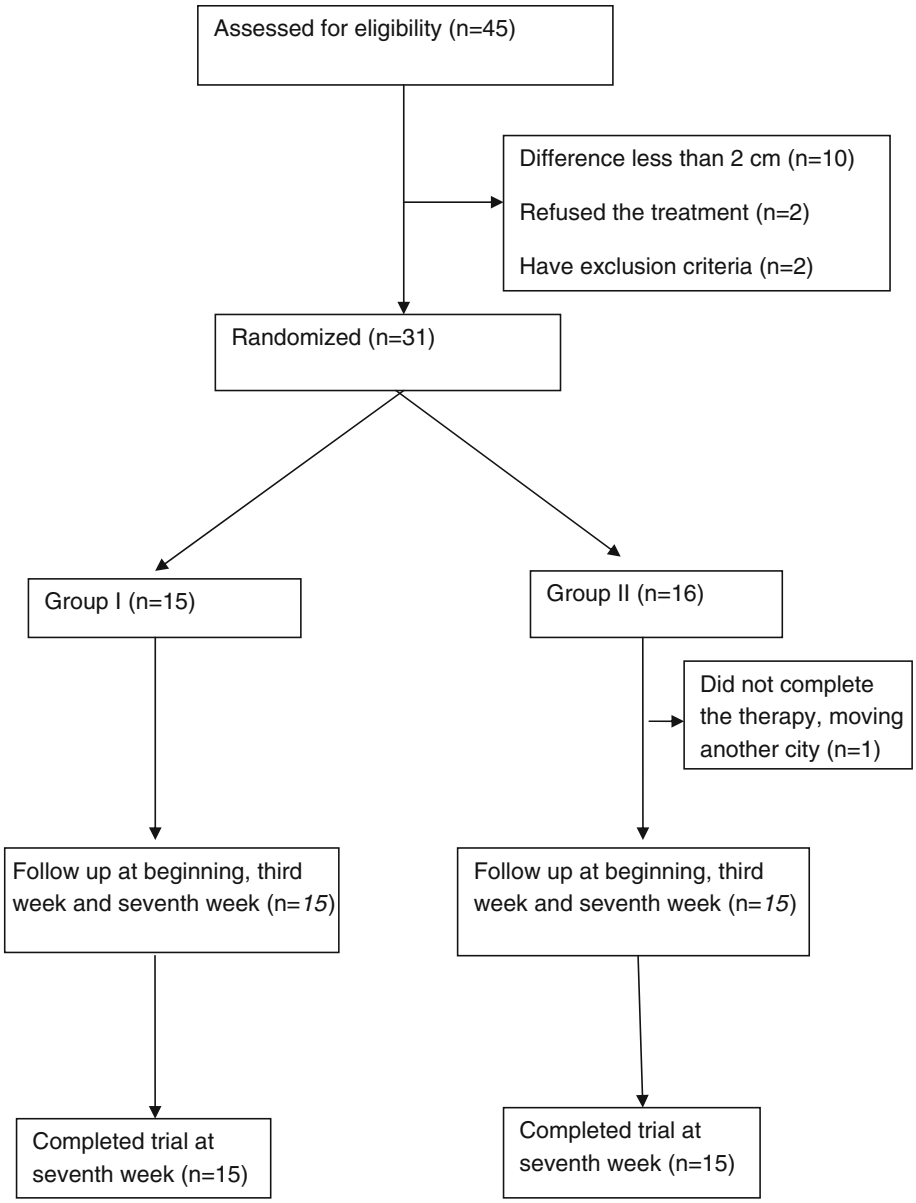

Fig. 1 Flow of participants through the study trial

by the same physician. The physician who assessed the patients was blind to the treatment groups.

Statistical analysis

Statistical analysis was performed using SPSS version 11.0 for Windows (SPSS Inc., Chicago, IL, USA). The Mann-Whitney *U* test and the chi-square test were used to compare the variables between the two groups. The Wilcoxon test was used to evaluate pre- and post-treatment values within the groups. Correlation analysis between the measurement methods was performed with Pearson's correlation test. The level of statistical significance was set at $p < 0.05$.

Results

One patient left the city so not continue the therapy. Thirty patients completed the study. The demographic variables, such as age, body mass index (BMI), duration of lymphedema, number of lymph node dissections, and type of surgery, were similar between the two groups ($p > 0.05$) (Table 1). There was no significant difference in the evaluation of lymphedema between the two groups before the treatment ($p > 0.05$). High BMI may increase the risk of lymphedema, and changes in BMI may affect the measurements, so we evaluated BMI after the treatment and at week 7. We did not observe any differences.

Table 1 Demographic characteristics of patients in both groups [median (minimum–maximum)]

	Group 1	Group 2	*p*
Age (years)	56 (37–75)	55 (42–75)	0.73
Weight (kg)	79 (61–93)	79 (60–102)	0.74
Height (cm)	157 (140–165)	158 (140–165)	0.98
BMI (kg/m^2)	32.79 (26.62–41.07)	32.44 (23.80–43.01)	0.48
Duration of lymphedema (months)	8 (2–108)	14 (1–72)	0.10
Lymphedema stage	2 (1–2)	2 (1–2)	0.65
Number of received cycles of chemotherapy	6 (2–10)	6 (4–12)	0.73
Number of fractions of radiotherapy	25 (20–30)	25 (20–32)	0.70
Number of lymph node dissections	10 (7–23)	10 (3–22)	0.78

BMI body mass index

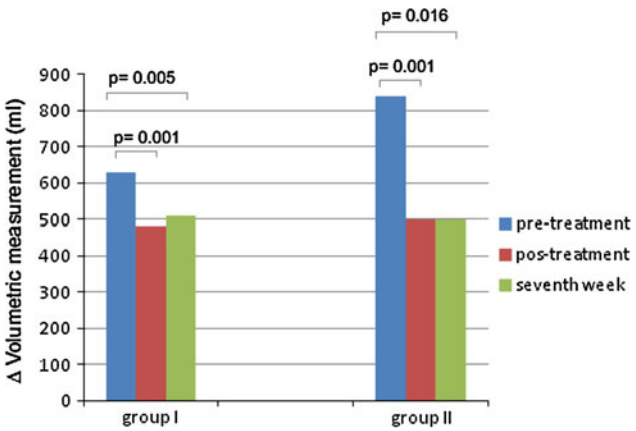

Fig. 2 Alterations in the limb volume in both groups

We observed significant differences in both groups when we compared them before and after therapy utilizing the volumetric measurement method, which is the gold standard for lymphedema. At baseline, the median volume difference of group 1 was 630 (180–1,820) ml, and this volume difference reduced significantly with therapy to 480 (0–1,410) ml ($p = 0.001$). Although at 7 weeks mild increases in volume up to 510 (50–1,430) ml were detected, volume reduction still continued when we compared baseline and week 7 ($p = 0.005$) (Fig. 2). In group 2, the baseline median volume difference was 840 (220–3,460) ml, and after therapy, it also reduced significantly to 500 (60–2,160) ml ($p = 0.001$). The volume difference in group 2 at week 7 was 500 (180–2,080) ml. When we compared baseline and week 7, we observed a significant reduction in group 2 ($p = 0.016$).

When we compared circumference measurements at baseline and immediately after therapy, there were significant differences (except for in the MCP joints) in group 1, and there were significant differences (except in the arm region) in group 2 at week 7 (Tables 2, 3). Comparing initial measurements and those taken at week 7, there were significant differences in circumference measurements in group 1. However, there was only a significant difference in the wrist region in group 2 (Tables 2, 3).

Δ Forearm dermal thickness and Δ arm dermal thickness with USG had decreased significantly in group 1 when we compared them before and after therapy ($p = 0.001$). In group 2, both Δ forearm dermal thickness and Δ arm dermal thickness with ultrasound had decreased significantly: $p = 0.006$ and $p = 0.002$, respectively (Tables 2, 3). At the 7-week evaluation, there were significant differences in dermal thickness in group 1 ($p = 0.001$). Despite this, we could not find any significant difference between the pre-therapy and 7-week measurements in group 2 (Tables 2, 3).

There was no significant difference in VAS pain assessment between the groups before and after treatment. However, significant differences were observed within groups when we compared them before and after therapy ($p = 0.001$, group 1; $p = 0.003$, group 2). At the 7-week evaluation, there were significant differences in VAS pain assessment in both groups 1 and 2 ($p = 0.002$ and $p = 0.003$, respectively) (Tables 2, 3).

We found a significant correlation between dermal thickness using USG and the water immersion method on the forearm region ($r = 0.648$; $p < 0.001$) (Fig. 3). We also found a significant correlation between dermal thickness using USG and the circumference of measurements on the forearm region ($r = 0.620$; $p < 0.001$) (Fig. 4).

In addition, there was no significant difference between groups in any parameters after therapy and 1 month after completing therapy; however, there were significant decreases immediately after therapy and 1 month after completing therapy in both groups. In fact, the volume reduction in group 2 (340 ml) was greater than in group 1 (150 ml) after treatment. However, we did not find a significant statistical difference between the two groups.

Discussion

Breast cancer is the most common tumor type in women [20]. Lymphedema is one of the complications of breast

Table 2 Comparison of measurements at pre- and post-treatment and week 7 in group 1 [median (minimum–maximum)]

	Pre-treatment	Post-treatment	Week 7	p^a	p^b
Δ MCP circumference (cm)	1 (−0.5 to 5.5)	0.5 (−0.50 to 4)	0.5 (−0.5 to 3.5)	0.19	0.049
Δ Wrist circumference (cm)	2 (−0.02 to 3.5)	1 (0 to 2)	1 (0 to 2)	0.004	0.024
Δ Forearm circumference (cm)	4.2 (1.5 to 9.3)	2.5 (0 to 5.5)	2.5 (0.5 to 7)	0.001	0.007
Δ Arm circumference (cm)	3.5 (0.50 to 7.5)	2 (0 to 4.5)	2.5 (0 to 5.5)	0.001	0.038
Δ Dermal thickness of forearm with USG (mm)	8.4 (0 to 19.4)	1.9 (−1.3 to 12.7)	2 (−1.6 to 8.6)	0.001	0.001
Δ Dermal thickness of arm with USG (mm)	4.6 (−0.10 to 24)	0.8 (−2 to 6.2)	2.1 (−1.1 to 6.7)	0.001	0.001
VAS	4 (0 to 7)	2 (0 to 5)	1 (0 to 5)	0.001	0.002

Δ, affected extremity-unaffected extremity

MCP metacarpophalangeal joint, *VAS* visual analog scale, *USG* ultrasonograph

[a] *p* value of pre- and post-treatment

[b] *p* value of pre-treatment and week 7

Table 3 Comparison of measurements at pre- and post- treatment and week 7 in group 2 [median (minimum–maximum)]

	Pre-treatment	Post-treatment	Week 7	p^a	p^b
Δ MCP circumference (cm)	1 (0 to 5.5)	0.5 (0 to 4.5)	0.5 (0 to 4.5)	0.040	0.090
Δ Wrist circumference (cm)	2.5 (0 to 8)	1.5 (0 to 4.5)	1 (0 to 3.5)	0.005	0.010
Δ Forearm circumference (cm)	5 (0 to 16)	4 (0 to 12.5)	4 (0 to 11.5)	0.001	0.107
Δ Arm circumference (cm)	3 (0.50 to 11)	2.5 (0 to 7.5)	2.5 (0.5 to 13)	0.06	0.196
Δ Dermal thickness of forearm with USG (mm)	5.2 (0 to 37.7)	4.2 (−0.2 to 12.5)	5.8 (0 to 14.2)	0.006	0.396
Δ Dermal thickness of arm with USG (mm)	5.1 (0.4 to 12.3)	2 (0 to 9)	2 (0 to 16.2)	0.002	0.064
VAS	4 (0 to 10)	1 (0 to 8)	1 (0 to 8)	0.003	0.003

Δ, affected extremity–unaffected extremity

MCP metacarpophalangeal joint, *VAS* visual analog scale, *USG* ultrasonography

[a] *p* value of pre- and post-treatment

[b] *p* value of pre-treatment and week 7

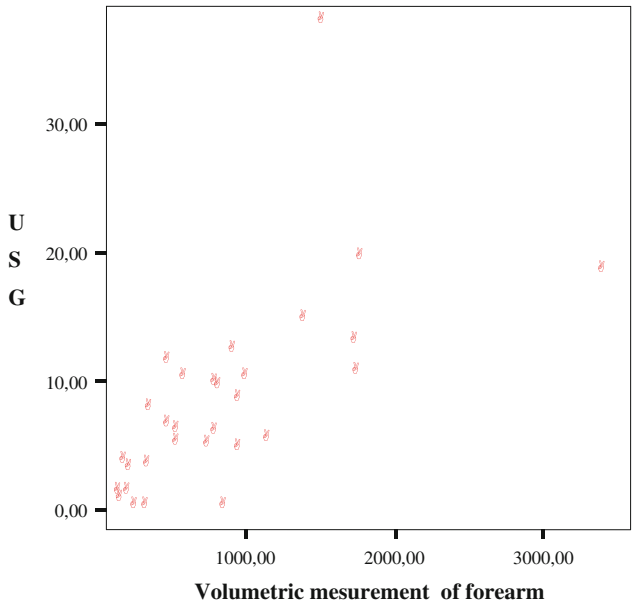

Fig. 3 Correlation between USG and the water immersion method on the forearm region

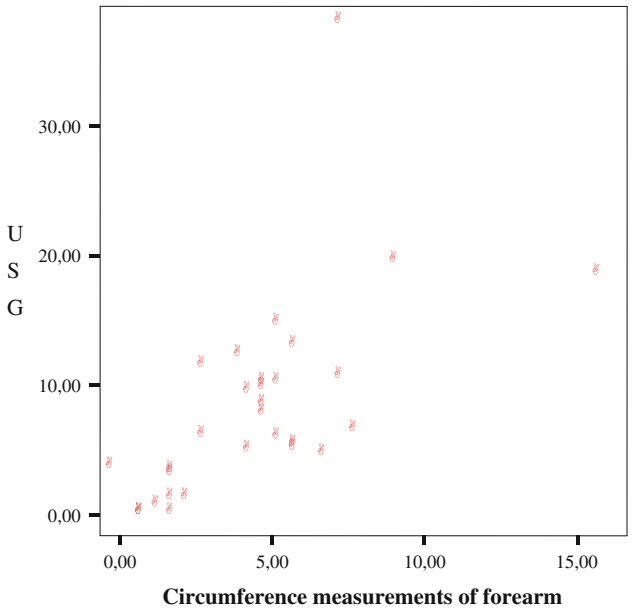

Fig. 4 Correlation of USG measurement with the circumference of the forearm region

cancer, especially post-mastectomy. Lymphedema is the abnormal accumulation of interstitial fluid that occurs as a consequence of malformation or the acquired disruption of lymphatic circulation. Patients with breast cancer frequently develop lymphedema because of both the nature of the cancer itself and that of the treatment. It can also lead to some serious conditions, such as cellulitis, lymphangitis, decreased range of motion of the affected limbs, and pain, while psychological problems including anxiety, depression and emotional distress adversely affect the quality of life for these patients [21, 22]. Currently, CDT is accepted as the international standard treatment approach for the treatment of lymphedema. CDT includes skin care, manual lymphatic drainage, multilayered compression bandages, compression garments, and exercise. Sometimes, the use of an intermittent pneumatic compression pump is combined with CDT.

In this study, we applied CDT to both groups, including skin care, manual lymphatic drainage, multilayered compression bandages, compression garments, and exercise. We also added the intermittent pneumatic compression pump to group 2. Significant improvements were observed in both groups after treatment. These improvements may have been caused by the effective components of CDT. The drainage of lymphatics by manual lymphatic drainage and applying compression may provide a significant reduction in lymphedema. Manual lymphatic drainage stimulates the contraction of lymph collectors while the lymph liquid is eliminated by the lymph nodule [13]. When we applied the bandage, an antagonistic force between the muscle and the bandage led to a pump effect, and this facilitated lymph transportation [23]. Exercise increased the sympathetic tonus, and because of this, contraction occurred in the lymph vessels. The effectiveness of CDT on lymphedema reduction has been shown in various trials. Some of trials were with patient numbers ranging from 62 to 135 and reported volume reductions of 13–58.9 %, varying from 6 to 26 treatment sessions [24–27].

The intermittent pneumatic compression pump, which is comprised of gradual pressure gradients that help the lymph flow through the lymph vessels, provides a way to organize the lymph flow. In our study, significant improvements in the dermal thickness and circumferential measurements were realized with a decrease at week 7 compared with after therapy in group 2, which added the pump. This result leads to the question of whether the pump can have a negative effect on the lymph vessels. Appropriate pump pressure and execution time in the treatment of lymphedema are still debated issues. Although the devices can apply different pressures (between 0 and 300 mmHg pressure), pressures between 30 and 60 mmHg are generally preferred for this treatment [12]. Leduc et al. [13] reported that lymphatics could be collapsed over a pressure of 40 mmHg. Therefore, we applied a preferred pressure of 40 mmHg in the present study. However, this study did not research the effect of the pump on lymph vessels. To shed light on this issue, randomized controlled studies are needed to investigate the effect of the pneumatic pump on lymphatic vessels while applying different pressures and different sessions.

Although various methods have been used to treat lymphedema, the number of prospective randomized trials comparing these modalities is not sufficient, and their results are contradictory [28, 29].

Szuba et al. [30] reported that the intermittent pneumatic compression pump has a significant effect on lymphedema. They performed a study with 23 patients who were randomly divided into two groups. The first group had therapy, including manual lymphatic drainage combined with the use of an intermittent pneumatic compression pump. The second group had therapy with only manual lymphatic drainage. At both the end of 2 weeks and 40 days, volume reductions were 45.3 and 30.3 %, respectively, in group 1. In group 2, at the end of 2 weeks and 40 days, volume reductions were 26 and 27.1 %, respectively. They reported that the addition of the intermittent pneumatic compression pump to standard CDT yielded an additional mean volume reduction. Treatment regimens in this study were similar to those used in our study. The treatment period was 10 days in Szubas' trial. Unlike in this study, however, we performed therapy for 15 days. In addition, Szuba et al. used the water displacement method for assessment, as we did. However, we also used dermal thickness with USG and circumference measurement methods in the assessment of lymphedema. We found this treatment to be effective in both groups. Contrary to Szuba et al., we did not find any superiority in the treatment that included the intermittent pneumatic compression pump.

In our study, we used other methods for assessing lymphedema, such as dermal thickness with USG and circumferential measurements, in addition to the gold standard water immersion method. We found a positive correlation between dermal thickness measurement with USG and the water immersion method in the forearm region. We also found a correlation between dermal thickness using USG and circumference measurements in the forearm region. Mellor et al. [31] reported that dermal thickness measurement using USG may constitute a useful measurement method in the diagnosis of lymphedema. However, Mellor did not assess dermal thickness during the CDT for evaluating lymphedema. Changes in dermal thickness and their correlation with other measurement methods during the course of CDT were observed in this study.

The present study has several strengths. Only one patient dropped out after starting therapy, so we were confident

that the manual lymph drainage was effective. We evaluated BMI at baseline, after treatment, and 1 month later at the follow-up, so we ruled out weight gain or loss. However, our study has some limitations, such as lack of long-term follow-up and the small sample size. We initially planned to include 45 patients in the study. However, as mentioned in the Methods section, we performed the study with 31 patients for a variety of reasons.

We suggest that manual lymphatic drainage is an effective and safe treatment for reducing lymphedema. Improvements may have been observed because of the effect of manual lymphatic drainage in both groups. Our results showed that pneumatic compression pumps do not have the additional effect of reducing lymphedema. Moreover, pneumatic compression pumps may increase the time period and total cost of treatment. Although we did not find any statistically significant difference in the reduction of lymphedema between the two groups, numerically larger reductions were observed in group 2. The sampling interval may have affected the statistical significance. Therefore, further controlled studies involving a greater number of patients over a longer period are needed to facilitate a more in-depth investigation of lymphedema treatment. In addition to manual lymphatic drainage, the patients were given instructions to perform daily exercises and skin care and use compression garments for the rest of their lives.

Conflict of interest The authors have no conflict of interest.

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