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ORIGINAL RESEARCH

Extracorporeal Shock Wave Therapy for Breast Cancer—Related Lymphedema: A Pilot Study

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Abstract

Objective: To investigate the clinical effect of extracorporeal shock wave therapy (ESWT) in patients with secondary lymphedema after breast cancer treatment.

Design: Prospective clinical pilot study.

Setting: Education and research hospital.

Participants: Women with a diagnosis of lymphedema secondary to breast cancer (N = 11).

Interventions: Patients were treated for 12 sessions of ESWT with 2500 impulses each. The treatment frequency was 4Hz in multiple shock mode. The energy flow density during treatment was equal to a working pressure of 2 bar.

Main Outcome Measures: The primary outcome measure was volumetric measurements. The secondary outcome measures were the short version of the Disabilities of the Arm, Shoulder and Hand Questionnaire (QuickDASH) and the brief version of the World Health Organization Quality of Life (WHOQOL-BREF). Assessments were conducted by the same investigator at baseline, posttreatment, and at 1, 3, and 6 months after treatment for all patients.

Results: Significant reduction was found in the amount of lymphedema with ESWT treatment in all patients, and this reduction was maintained for 6 months. A statistically significant reduction was observed in volumetric measurements for the follow-up period ($P = .001$). The mean volume displacement of the affected upper extremity before treatment was 870.45±384.19mL at 6 months, and after the treatment it was 604.54±381.74mL. In addition, improvements were observed in the QuickDASH functional assessment tool and in the physical health domain of the WHOQOL-BREF questionnaire ($P = .002$ and $P = .007$, respectively).

Conclusions: ESWT was shown to provide a reduction in the amount of lymphedema in patients with lymphedema secondary to breast cancer. Also, a marked improvement was observed in the functional status and quality of life of study patients. Treatment efficacy was maintained in the long term. As a noninvasive, novel, and effective method, ESWT is a promising treatment modality for the treatment of lymphedema, which is a chronic, progressive, and refractory condition.

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Lymphedema is the accumulation of protein-rich interstitial fluid in tissues caused by insufficiency of the lymphatic system.[1-3] Primary lymphedema occurs as a result of a congenital anomaly of lymphatic vessels. Secondary lymphedema develops after resection or obstruction of lymphatic vessels or lymph nodes.[2,3] Secondary lymphedema may also develop as a major complication of cancer surgery or radiotherapy.[1-3]

One of the most important complications of breast cancer treatment is the development of lymphedema in an upper extremity.[2,3] Patients with breast cancer are at increased risk for lymphedema after axillary lymph node dissection and radiotherapy.[1,2] The incidence of breast cancer—related lymphedema is reported at 6% to 30%.[3,4]

Lymphedema is a chronic and progressive condition that is refractory to treatment.[3,5] It causes swelling, pain, limitation of movement, susceptibility to infection in the extremities, and sensitivity of the skin.[1,4,5] Because there is no cure for lymphedema, the aim of treatment is to reduce the swelling, increase joint mobility, and

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decrease discomfort.[2] One of the most common forms of lymphedema treatment is complex decongestive therapy (CDT). CDT includes the application of low-stretch bandaging, manual lymph drainage, compression therapy, exercise, and skin care.[5-8] Reviews consistently concluded that CDT is an effective therapy for lymphedema.[7,9] Although CDT benefits most patients with lymphedema, the interventions are labor-intensive, time-consuming, and expensive. The potentially uncomfortable and visible garments may adversely affect the patient's quality of life (QOL).[10]

There are some studies investigating the use of alternative treatment methods (eg, laser therapy, acupuncture, kinesio taping) for the treatment of lymphedema.[11-14] These treatments have yielded mixed results. In some studies, low-level laser therapy was found to help reduce the swelling in the arm, break down scar tissue, and increase range of motion.[11,12] Early clinical trials have shown that acupuncture can decrease limb swelling and improve the symptoms of lymphedema in both the lower and upper extremities.[13] In a pilot study, kinesio taping appeared to be ineffective at breast cancer–related lymphedema.[14]

For many years, extracorporeal shock wave therapy (ESWT) has been used for various musculoskeletal system disorders, including plantar fasciitis, lateral epicondylitis, and shoulder tendinitis.[15,16] ESWT induces neovascularization by stimulating the release of angiogenic growth factors from cells (eg, nitric oxide, vascular endothelial growth factor [VEGF], bone morphogenetic protein). Because of this mechanism of action, several new areas have emerged for ESWT use, including treatment of spasticity, chronic skin ulcers, burn scars, avascular necrosis, and myocardial ischemia.[17,18]

Animal studies have found that ESWT stimulates lymphangiogenesis and reduces lymphedema by inducing increased release of the VEGF.[1,15] In 1 study, low-energy shock wave therapy induced therapeutic lymphangiogenesis by upregulating VEGF-C (a protein that is a member of the VEGF family) and basic fibroblast growth factor and improved lymphedema in a rat tail model.[1] In another study, low-energy ESWT was used for the treatment of lymphedema in a rabbit ear model; compared with the nontreated group, the treated group showed a marked reduction of lymphedema and a significant upregulation of VEGF receptor 3 in the lymphatic vessels.[15]

Only 1 study was available in the literature that examined the effectiveness of ESWT for the treatment of breast cancer–related lymphedema. In that study, although ESWT was found to be effective in reducing lymphedema, its long-term effectiveness was not investigated.[16]

Breast cancer–related lymphedema significantly compromise QOL. Physical arm morbidities caused by lymphedema can lead to negative feelings, particularly regarding one's body image. Patients with lymphedema have been shown to experience stress, anxiety, sadness, anger, and guilt because of their condition. QOL and improved function are 2 important results of treatment, but they were examined in only a few studies.[19,20]

List of abbreviations:

CDT	**complex decongestive therapy**
ESWT	**extracorporeal shock wave therapy**
QOL	**quality of life**
QuickDASH	**short version of the Disabilities of the Arm, Shoulder and Hand Questionnaire**
VEGF	**vascular endothelial growth factor**
WHOQOL-BREF	**brief version of the World Health Organization Quality of Life**

In this study, we aimed to examine the long-term effectiveness of ESWT in breast cancer–related lymphedema. Additionally, we evaluated the QOL and functional status of the patients.

Methods

Participants

This prospective clinical pilot study was conducted in women in the medical oncology department with a confirmed diagnosis of breast cancer and clinical manifestations of lymphedema. Ethical approval for the conduct of the study (no. 2014/44) was granted by the Erciyes University Ethical Committee for Clinical Trials, and informed consent was obtained from each subject.

The patients were included if they had completed their chemotherapy or radiotherapy treatments within no more than 6 months and had a volume difference >200mL and a circumference difference >2cm between their 2 arms. Patients with the following characteristics were excluded from the study: those with bilateral breast cancer, those with bilateral lymphedema, those with metastasis, those with acute deep vein thrombosis, those suffering from acute or untreated infections on the affected arm, and those who had undergone any lymphedema treatment within a 6-month period.

Interventions

Patients received a total of 12 sessions of ESWT 3 times per week. A Vibrolith Ortho[a] ESWT device was used. ESWT was applied using the same parameters for all patients: 2500 shocks per session with a frequency of 4Hz at 2 bars of pressure.[18] Patients were placed in a supine position on the examination table. During treatment, a 15-mm head was used without local anesthesia. Then 750 shocks were applied to the axillary lymph nodes and 250 shocks were applied to the cubital lymph nodes. The remaining 1500 shocks were applied to the arm, forearm, and hand. All patients were treated by the same physical therapist at each session.

Primary outcome measurements

Volumetric measurements

For lymphedema follow-up, the volumetric measurement method is accepted as the criterion standard.[5,21,22] In this method, the patient's arm is immersed into a cylindrical container filled with water, and the volume of the overflowed water is measured in milliliters. The difference of the overflowing water volume of the 2 extremities determines the amount of lymphedema.[5,6,16]

In this study, the patient's extremity was immersed in a cylindrical container filled with water up to the axilla level, with the arm and forearm in the extension position and the fingers in the abduction position before the volume of the displaced water was measured. The volume displacement between the unaffected arm and the arm with lymphedema was determined.

For all patients, the intensity of lymphedema was assessed using Tracey volume category.[23] As such, a volume difference of 150 to 400mL between the 2 upper extremities was considered mild, 400 to 700mL was considered moderate, and ≥700mL was considered to be severe lymphedema.