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Effects of Extracorporeal Shock Wave Therapy on Motor Recovery, Arm Circumference, Subcutaneous Tissue Thickness and Skin Thickness in a Case with Breast Cancer Related Lymphedema Portrayed with Sonographic Technique

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Background: Breast Cancer Related Lymph edema (BCRL) is the progressive swelling of the affected upper extremity and adjacent trunk complication following breast cancer surgery. Extracorporeal shock wave therapy (ESWT) is a novel therapy, going beyond conventional rehabilitation modalities, that is effective in BCRL recovery. However, most of the current studies on the efficacy of ESWT assess skin thickness by skin fold caliper and subjective visual judgment, which makes it difficult to measure the true thickness of the tissue. The present report evaluates the clinical effect of ESWT treatment on the arm circumference via skin fold caliper, thickness of skin, subcutaneous tissue, and muscle by sonographic technique.

Case: We focus on a case of a 45-year-old woman with a progressive development of edema of the left upper extremity after the modified radical mastectomy, who showed dramatic improvement in range of motion, a decreasing difference in arm circumference, subcutaneous tissue thickness and skin thickness between the two sides after two months ESWT treatment.

We found that ESWT is effective in reducing arm circumference, skin thickness and lymph edema and facilitating ROM and ADL for patient with chronic Lymph edema (LE). (*Rehabil Pract Sci* 2023; 2023(1): 49 - 56)

Key Words: extracorporeal shock wave therapy, breast cancer related lymphedema, sonographic technique, subcutaneous tissue thickness, arm circumference

INTRODUCTION

Breast Cancer Related Lymph edema (BCRL) is one of the most common complications after breast cancer surgery, with a reported incidence ranging from 6% to

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30%.^[1] BCRL is a chronic, progressive swelling of the affected upper limb and adjacent trunk, as well as changes in the skin and underlying tissues that limit upper extremity function and cause impairment of daily living activities.^[2] The probable cause is mainly due to the chronic, progressive accumulation of protein-rich fluid within the interstitial and fibro-adipose tissue exceeds the capacity of the lymphatic system to transport the fluid resulting in edema.^[3] Until now, the most basic treatment for BCRL has been complex decongestant therapy, a combination of manual lymphatic drainage, external pressure and exercise to promote lymph flow, skin care, etc.^[4] However, the efficacy depends on each therapist's experience and the patient's ability to follow a normal lifestyle.^[5]

In fact, Extracorporeal shock wave therapy (ESWT) has been used as a physical therapy modality since the early 1990s^[6,7] and has also been reported in patients with BCRL. In past decades, ESWT promotes the modulations of shockwave treatment including neovascularization, differentiation of mesenchymal stem cells and local release of angiogenetic factors to produce regenerative and has been widely used in the tissue repair effect of musculoskeletal treatments.^[8]

A recent Korean study reported the efficacy of ESWT (Extracorporeal Shockwave Therapy) and CDT (Complete Decongestive Therapy) versus CDT alone in patients with stage 2 lymph edema the affected limb becomes firm and enlarged. The significant improvement was found in volume, circumference and skin thickness measurements in the ESWT group.^[9] However, most of the current study on the efficacy of ESWT, skin thickness was evaluated by measuring the skin fold caliper and subjective visual judgment which make it difficult to distinguish the thickness of the skin and subcutaneous tissue. Besides, the force applied during measurement might cause the thickness of the tissue to change, especially in the case of pitting edema and it was difficult to measure the true thickness of the tissue.

Therefore, to reduce errors and poor validity in assessing patient outcomes, we report a case that a patient with chronic lymph edema with irreversible fibrosis experienced a significant reduction in arm circumference after ESWT and the reduction in skin and subcutaneous tissue thickness was also confirmed by ultrasonographic measurements.

CASE REPORT

A 45-year-old female was diagnosed with invasive ductal carcinoma of left breast on 1999/05/21 and underwent Lt modified radical mastectomy and adjuvant chemotherapy with fluorouracil, epirubicin and cyclophosphamide followed by radiation therapy. Modified radical mastectomy removed a total of 21 lymph nodes covering Level I~III, 19 of which had metastasis. During the regular follow-up on 2015/04/09, she was referred to the Department of Rehabilitation Medicine due to the progressive development of edema of the left upper extremity and the inconvenience of performing activities of daily living (Figure 1). We measured the total arm circumference at 5cm above and below the elbow crease (referred as AE and BE circumference) and found left side (affected side) AE / BE circumference was 30.5 cm/29.5 cm and right side (unaffected side) AE / BE circumference was 29.0 cm/26.0 cm. The affected side circumference of the patient's upper limb is 1.5 cm and 3.5 cm larger than the same level of unaffected side AE / BE circumference respectively. Besides, muscle power (MP) of left upper limb was 3, range of motor (ROM) of left elbow joint was 0 to 130 degrees. The final diagnosis was BCRL over left upper limb, stage I Non-pitting edema secondary to pronounced fibrosis according to the International Society of Lymphology (ISL).^[10] Therefore, the traditional rehabilitation treatment include circulator, electric stimulation, low power LASER therapy, massage, strengthening, passive ROM exercise and previous stroke technique at a frequency of 2-3 times a week was arranged since April, 2015. Rehabilitation program continued for 6.5 years with a frequency of 3 times/week. On 2021/10/26, we measured arm circumference, MP and ROM at the same site. The results show that AE / BE circumference of the patient's left side upper limb was 33.5/30.0 cm and is also larger than the right side MP of left upper limb was 4, ROM of left elbow joint was 0 to 130 degrees. Results showed limited improvement in edema with conventional rehabilitation in this case.

Although it has been proven that symptoms of non-pitting edema can be improved with surgery such as lymphatic venous anastomosis surgery, a skilled microsurgeon with extensive skills and expertise in free flap

reconstruction does not guarantee super microsurgery for lymph edema.^[11,12] Success rates are multifactorial and reflect not only the skill, expertise, and experience of the surgeon. In this case, the patient was unwilling to undergo surgery, and instead sought a more conservative treatment as a relief of symptoms. Therefore, we decided to utilize Focused Extracorporeal Shock Wave Therapy (f-ESWT), which has recently been reported to be effective in treating lymph edema and other musculoskeletal disorders, while continuing to practice rehabilitation programs. During the ESWT period, the previous treatment was not affected, and the above physical therapy was still maintained at the original frequency and items. The patient received f-ESWT with 2500 shocks per session, 3 times/week for 12 weeks, totally 36 sessions with energy flux density of 0.15 mJ/mm² and frequency of 6Hz, using the Storz Medical Duolith SD1 Tower. During f-ESWT, the patient will be asked to raise the hand, and the treatment position will be from the axillary area to the anterior side of arm. Then ask the patient to straighten the hand, and the treatment position is from the posterior side of the arm to the posterior side of the forearm and then to the anterior side of the forearm. ESWT was performed of 500 shocks in each of the five area for a total 2500 shocks and the probe moves continuously at 4 cm/sec as evenly distributed over the treatment area as possible (Figure 2).

The measures of circumferences were collected from both upper limbs every five centimeters from wrist crease to axilla by using a tape measurement. The thickness of skin, subcutaneous tissue, and muscle were measured by sonographic [12-4 MHz broadband linear array ultrasound transducer (Sparq; Philips Healthcare, Bothell Everett Hwy, Bothell, WA, USA)] technique bilaterally at the 15 cm proximal to wrist crease, where largest difference in circumference of bilateral upper limbs (Table 1) (Figure 3). During the outpatient follow-up in October 2021, the greatest difference of arm circumference between affected and unaffected side (CDmax) located at 15cm proximal to wrist crease and the difference was 5.5cm. However, after the patient received ESWT for two months, this difference was reduced to 3.5cm, and the difference ratio was improved by 36% after treatment. Besides, initially, the skin thickness difference between the arms at CDmax was 0.08cm and also decreased to 0.06cm on 12/30, which is a 25% reduction from the previous difference. Moreover,

the difference in the thickness of the subcutaneous tissue on both sides before treatment was 0.43 cm and after treatment was 0.34 cm. The results showed that the difference in subcutaneous tissue thickness between the two sides improved by 21% after ESWT treatment. The patient has unlimited range of motion of both elbow joint and is able to perform most daily activities with both hands, with no treatment-related side effects reported.

DISCUSSION

Breast cancer is the most common female malignancy in Taiwan, and with advances in early detection, surgery and adjuvant therapy, treatment outcomes have greatly improved.^[13] In Taiwan, the 5-year survival rate of early breast cancer patients after proper treatment exceeds 90%, and the long-term survival rate even exceeds that of most parts of the world.^[14] However, breast cancer treatment is associated with side effects, one of which is lymph edema, a common and quite troubling complication for both medical staff and patients. Therefore, for breast cancer patients, in view of the high survival rate of breast cancer and the pursuit of quality of life after treatment, active treatment of daily life difficulties caused by upper extremity lymph edema after surgery is crucial to rehabilitation management.

In this case, ADL function and life quality was severely influenced due to the progression of BCRL with inflammation-induced skin and subcutaneous tissue fibrotic changes with limb size enlargement in the left upper extremity after treatment for breast cancer. However, after f-ESWT to the left upper arm, the patient's upper extremity measured circumference, skin and subcutaneous tissue thickness decreased, and ROM improved, as well as increased ability to perform daily activities.

In general, there are two different types of ESWT: f-ESWT and radial extracorporeal shockwave therapy (r-ESWT). The difference may lead to different therapeutic effects between f-ESWT and r-ESWT.^[15,16] We used f-ESWT as treatment instead of r-ESWT based on previous study.^[17] From a theoretical point of view, compared with r-ESWT, f-ESWT has a concentrated shape in which the pressure converges to an adjustable focus at a selected depth in body tissues and provides better penetration depth and sound pressure concentration to have an effect

on the fibrosis area located in the subcutaneous area.

Table 1. Left arm and upper arm (affected side) circumference (cm) over time

Date	Times	Wrist	5cm	10cm	15cm	20cm	25cm	30cm	35cm	40cm	Shoulder
2021/10/26	0	18.5	21.5	25	30	30	32	35	35	35	42
2021/11/2	3	18.5	22	25	30	30	32	34.5	35	36	39.5
2021/11/8	6	17.5	21	25	29	29	31	33.5	34.5	34	39.5
2021/11/15	9	18.5	21	25.5	29	29.5	30.5	34.5	35	34.5	41
2021/11/22	12	18	22	26	29	30	33	35	35	35	42
2021/11/29	15	18	22	24.5	29	30.5	31	34	35	36	42
2021/12/7	18	18	21	25	28.5	28.5	30.5	34	34.5	35	42
2021/12/14	21	18	20.5	24	28.5	29	30	34	35.5	35.5	41
2021/12/21	24	18	21	24.5	28	29	31	34.5	35	35.5	41
2021/12/30	27	18	21	24	28.5	28.5	31	33.5	33.5	34.5	40.5

Table 2. Right arm and upper arm (unaffected side) circumference (cm) over time

Date	Times	Wrist	5cm	10cm	15cm	20cm	25cm	30cm	35cm	40cm	Shoulder
2021/10/26	0	16	17.5	21	24.5	25.5	26	28	31	34	41
2021/11/2	3	16	17.5	20.5	24.5	24.5	25.5	28	30.5	35	41.5
2021/11/8	6	15.5	17.5	20	24	24.5	24.5	27.5	29.5	33	40
2021/11/15	9	16	17	20	24	25.5	26	28	29.5	34.5	40
2021/11/22	12	16	17	21	24	25	25.5	28	31	33	40
2021/11/29	15	16	17	20	24	25.5	26	29	30	33	41
2021/12/7	18	15.5	17.5	21	24.5	24.5	25	28	30.5	33.5	40
2021/12/14	21	16	16.5	19	23.5	24.5	24.5	26.5	29	33.5	38
2021/12/21	24	16	16.5	19.5	23.5	24.5	24.5	27	30	33	41
2021/12/30	27	16	17.5	22.5	25	25	26	28.5	31	34	41



Figure 1. Patient's left and right upper limbs

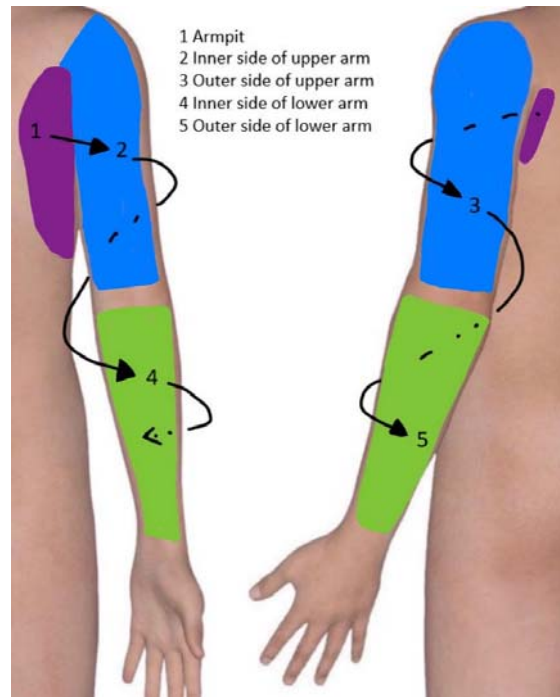


Figure 2. Position and sequence of patients receiving f-ESWT

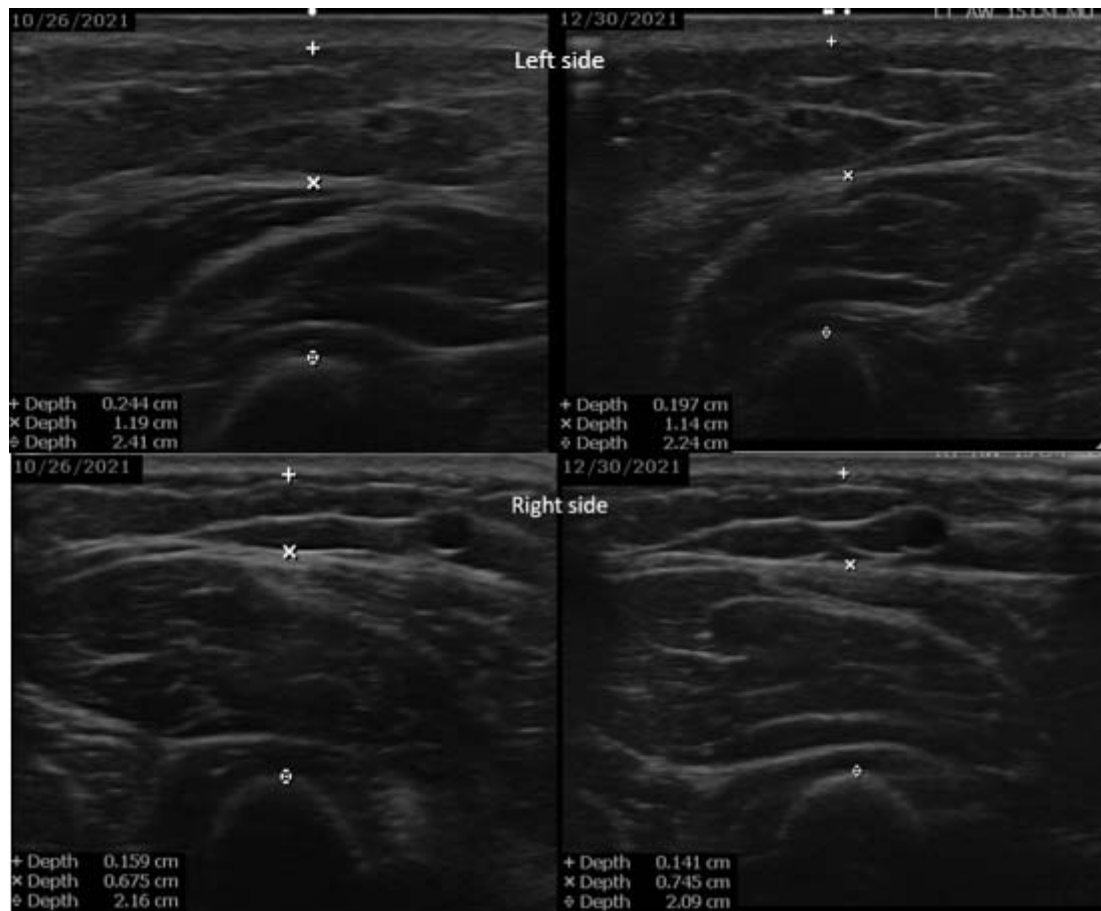


Figure 3. Comparison of the thickness (cm) of the patient's left and right wrist at 15 cm before and after ESWT

Table3. Comparison of thickness (cm) measured by ultrasound of right arm and upper arm before and after treatment

	Left			Right		
	skin	Subcutaneous	Muscle	skin	Subcutaneous	Muscle
2021/10/26	0.24	0.95	1.22	0.16	0.52	1.48
2021/12/30	0.20	0.94	1.1	0.14	0.6	1.35

This treatment result is consistent with recently published Egyptian study on BCRL.^[18] Mahran et al. compared 20 patients with ESWT plus conventional physical therapy and 20 without ESWT and found that arm volume and total circumference decreased significantly in the ESWT group. Although it is not a comparison on the same patient, the results show that the combination of ESWT could accelerate lymph edema reduction and improve the range of motion of the shoulder joint compared with traditional physical therapy alone. Additionally, and most significantly different from previous studies, our study is the first to measure skin, subcutaneous tissue, and muscle depth by ultrasonography. In our case, the skin thickness was reduced from 0.244 to 0.197 cm. Although the result which ESWT could reduce the thickness of the skin is the same as measured by skin fold caliper in the previous study, our approach has several strengths.^[19] First, this sonographic technique has previously been shown to have good validity in a variety of other conditions.^[20,21] A study recruiting 55 healthy young women also found that sonography quantitatively and precisely detected physical changes associated with physiological lower leg edema after daytime activity in healthy.^[22] Second, sonographic technique was more sensitive to treatment-induced skin changes than clinical skin scores.^[23] In addition, in the sonographic assessment of the skin, various influencing parameters are considered, such as: epidermal echo, thickness of dermis and subcutaneous tissue, surface area of specific layers, caliber of blood vessels, and presence or absence of blood flow.^[24] Consequently, further studies of larger cohorts are required to evaluate the characteristics of the patients with Lymph edema (LE) by using the gold standard technique

Taken together, in our case, we considered that ESWT is effective in reducing skin thickness and lymph edema and there are three possible reasons for the mechanism of symptom relief. First, ESWT might have a similar stretching effect which gives tension to the an-

choring filaments and effusion can flow back into the lymphatic lumen when the junctions open.^[25] In addition, it has also been reported that it relieves soft tissue adhesion around joints by increasing the production of nitric oxide in tissues and inhibiting the anti-inflammatory effect of inflammatory mediators.^[26] Finally, ESWT promotes the regeneration of normal tissue by inducing new lymph neogenesis and improving lymphatic circulation through VEGF-C, fundamentally improves the tissue structure altered by lymphedema, and maintains the long-term therapeutic effect.^[27] However, due to such effects of ESWT on cell regeneration, malignancy and metastases in the treated area are considered contraindications for ESWT.^[28] Although patients with BCRL have theoretically cleared malignant tumors after surgery, and no adverse reactions have been reported in previous review studies, considering the positive effects of ESWT on endothelial neovascularization and tissue growth, evaluation its safety on breast cancer survivors is crucial.

CONCLUSION

Based on this case, we found that ESWT could be effective in improving the volume of lymph edema, arm circumference, skin thickness, ROM and ADL for chronic LE.

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