Tools in Measurement of Treatment in Lipoedema

Subjects: Rehabilitation

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Due to insufficient knowledge of lipoedema, the treatment of Lipoedema is undoubtedly challenging. However, more and more researchers attempt to incorporate the most effective lipoedema treatment methods. When assessing a new therapeutic method, choosing correct, objective tools to measure the therapeutic outcome is very important. The tools used in evaluating the effectiveness of conservative treatment in women with lipoedema are: volume and circumference measurement, waist-to-hip ratio, body fat percentage, ultrasonography, VAS scale, quality of life scales (SF-36, RAND-36), symptom severity questionnaire (QuASiL), Lower Extremity Functional Scale and 6 min walk.

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1. Introduction

Lipoedema is a chronic disease of subcutaneous adipose tissue resulting in the pathological proliferation of adipose tissue, mainly around the lower extremities ^[1]. It mostly affects women, and the beginning is usually associated with puberty, pregnancy, or menopause ^[2]. Lipoedema is still not entirely understood ^[3]. Currently, the combination of genetic predisposition and hormonal changes is thought to be responsible for the occurrence of lipoedema, but the exact etiology is not yet established ^[2]. It is estimated that lipoedema prevalence among the general public is 1:72,000, but these data have also not been fully confirmed ^[4].

In recent studies, Michelini et al. discovered that mutation in the AKR1C1 gene can be related to the development of lipoedema ^[5]. Hormonal disturbances are also thought to be connected to lipoedema. Potentially, there is a disbalance between oestrogen receptors (ER alpha and ER beta) in adipose tissue of lipoedema affected certain areas, occurring as a result of faulty expression of oestrogen receptors. It can explain the abnormal proliferation of adipose tissue in the affected areas ^{[6][7]}.

A study by R. Crescenzi et al. has shown that there is an increase in the sodium content in the skin among lipoedema patients, which is a hallmark of inflammation thought to be responsible for pain in lipoedema ^[8].

The distribution of adipose tissue in lipoedema is always bilateral and symmetric, and feet remain unaffected ^{[1][2][9]}. Moreover, women with lipoedema experience painful ailments such as sensitivity on palpation, easy bruising, and heaviness in the legs ^{[6][11][12]}.

Insufficient knowledge of lipoedema and lack of specific diagnostic criteria often lead to incorrect diagnosis as obesity or lymphoedema ^[13]. It is usually a reason for delayed diagnosis and absence of the correct treatment which is associated with further disease progression and a worsening of the patient's condition ^[14].

At the moment, lipoedema is considered an incurable disease, and the proposed therapeutic options are mainly aimed at reducing symptoms and preventing their progression ^[15]. The current treatment of lipoedema is based on therapy methods normally used in the treatment of lymphedema ^[16]. Conservative treatment includes complex decongestive therapy (CDT) constituted of manual lymphatic drainage (MLD), compression therapy, skincare and physical exercises, and intermitted pneumatic compression (IPC) ^{[17][18]}. Other methods such as subcutaneous adipose tissue manual therapy and ketogenic diet are currently under examination ^{[19][20][21][22]}. Liposuction is the surgical treatment of lipoedema ^[23].

2. Volume Reduction

Seven studies reported volume measurement as a tool to assess the effectiveness of conservative lipoedema treatment methods [17][20][21][24][25][26][27]. Since in the majority of cases the lipoedema applies to the lower part of the body, only the lower extremity measurements were pursued. Various techniques were used to obtain the volume. The most frequently used method was the Kuhnke disc method [17][20][21][24][27]. In his technique, the volume of the lower limb is obtained by the collection of the circumference of the extremity in 4 cm intervals starting from the ankle and finishing at the highest point of the inner thigh [17][27]. Two of the studies, which used the abovementioned method, aimed to evaluate the effectiveness of subcutaneous adipose tissue manual therapy in lipoedema patients [20][21]. Subcutaneous adipose tissue (SAT) manual therapy is a deep tissue massage concentrated on fat, muscles and fascia to improve tissue quality ^{[20][21]}. The results showed significant volume reduction after a 4-week therapeutic program—on average, 2 L of reduction in the right leg and 1 L in the left in research conducted by Herbst, and 0.9 L volume reduction in a study by Ibarra ^{[20][21]}. A study of 38 women with lipoedema conducted by Szolnoky in 2008 showed a significant volume reduction (0.9 L) in women who participated in a 5-day complex decongestive physiotherapy (CDP) program in comparison to the control group not receiving any specific therapy ^[27]. In another study by Szolnoky, the application of complex decongestive physiotherapy with or without intermittent pneumatic compression (IPC) was assessed. Volume reduction was observed in both groups, but it was slightly higher in a group with added IPC, in comparison to the CDP group (1.1 L of reduction in left leg, 0.8 in right leg) ^[17]. The last research study which used the Kuhnke disc method as a tool to determine leg volume was conducted by Atan et al. $\frac{24}{2}$. The research aimed to determine whether the complex decongestive therapy (CDT) combined with exercises was more effective than the intermittent pneumatic compression combined with exercises in comparison to the application of exercises only. A decrease in the lower extremity volume could be observed among all participants. The biggest reduction was recognised in the CDT and exercise group. The difference in volume reduction was not substantially different in the IPC and exercise (0.5 L left and 0.7 L right limb) and exercise-only groups (0.6 L on both sides), but the result was still significant for the deneral outcome $\begin{bmatrix} 24 \end{bmatrix}$.

The research presented by Volkan-Yazıcı Melek et al. obtained the volume changes using Perometer 400NT ^[25]. The device is thought to provide a fast and reliable technique of limb volume measurement using infrared light. Perometer 400 is composed of a square frame in which the assessed extremity is placed. During the assessment, the diameter measurements were obtained using certain reference points in 4.7 mm intervals. These measurements are used to calculate the volume. The results of the study showed that after 24 days of the therapeutic program with manual lymphatic drainage, compression therapy and intermittent pneumatic compression, the mean volume reduction at 0.4 L and 0.7 L could be observed in the left and the right leg, respectively ^[25].

3. Waist-to-Hip Ratio, Body Mass Index and Weight

Weight measurement, body mass index (BMI) and waist-to-hip ratio are commonly used tools to evaluate outcomes of slimming. Studies presenting data on those tools in lipoedema treatment were identified to investigate whether they are beneficial in evaluating the effectiveness of conservative treatment in lipoedema.

The waist-to-hip ratio is a ratio of the circumference of the waist to the circumference of the hips. It can be used to determine a disproportion between the torso and lower limbs, which is a characteristic feature of lipoedema ^[20]. The researchers identified four studies reporting on WHR changes after conservative treatment in lipoedema patients ^{[19][20][21][24]}. All of the presented WHR values were less than 1 which could be expected of a gynoid-type of female body shape. Even though there were some changes in body weight in three studies, it ought to be noted that none of the presented studies showed a significant difference in WHR after the treatment independent from a therapy method employed ^{[19][20][21][24]}.

One study reported BMI changes after a conservative treatment program. There was a significant difference in BMI in a group with CDT and exercises and a group with exercises only. The group with the application of intermittent pneumatic compression did not show any significant changes in BMI ^[24].

4. Circumferences

In his study, Schneider compared the efficacy of manual lymphatic drainage with or without low-frequency vibrotherapy in a group of 30 women with lipoedema ^[28]. In both cases there was a decrease in circumference; however, the women after MLD with vibrotherapy presented a greater reduction. In the MDL group, the circumferences of the ankles, calves and thighs decreased by 0.2, 0.6 and 1.8 cm, respectively. On the other hand, the patients who attended MLD and vibrotherapy noted a reduction of 1.2, 1.8 and 2.6 cm in the ankles, calves and thighs, respectively. The circumference of the feet did not change significantly post-treatment ^[28].

Another study used circumference measurement in five reference points including the smallest circumference of the ankle, the largest circumference of the calf, the smallest below the knee, mid-patellar circumference and circumference in the middle of the thigh. The reduction of 4.5% and 1.9% was noted in the left and right thigh, respectively. The mid-patellar circumference decreased by 0.4% on the left and 1.2% on the right extremity and the

below-knee measurement showed a reduction of 1.6% on the left side and 0.23% on the right side. The calf circumference decreased by 2.2% on the left and 3.1% on the right leg. The ankle circumference did not change substantially ^[25].

In the case study of women with lipoedema, the circumferences of the upper extremity, the torso and the lower extremity were obtained pre- and post-treatment. All of the measurements decreased after the 22-month diet program, but the biggest reduction could be observed in the hips (27.98%), the thighs (27.03%), the arms (26.14% left and 24.42% right) and waist (23.85%) ^[19].

5. Bioimpedance and Dual X-ray Absorptiometry

Bioimpedance was used in three studies to measure therapeutic outcomes. Bioimpedance is a method of measuring body composition using electric current. R. Connataro et al. conducted body fat percentage (Bf%) analysis using bioimpedance in one lipoedema patient who had followed a ketogenic diet program. Initially, Bf% was about 47% and at the 22-month follow-up it was 27% ^[19].

Two remaining studies reported the usage of both bioimpedance and dual X-ray absorptiometry scan (DXA scan). DXA is originally used to measure bone density; nonetheless, it can be also used to indicate body composition and fat content ^{[20][21]}. A study by Ibarra aimed to use bioimpedance as a tool to evaluate body fluids in lipoedema patients. The results showed a significant decrease in total body water from 35.6 kg at baseline to 34.9 kg post-treatment. The same study used DXA to indicate total body mass and fat mass. Following the subcutaneous adipose tissue therapy, the leg fat mass decreased significantly from 17.8 to 17.4 kg. Other analysed features did not change significantly ^[21].

In comparison, Herbst et al. used bioimpedance to measure body weight, fat mass and muscle mass. The muscle mass increase could be observed post-treatment and the fat mass decreased from 19.7 to 17.8 kg. Mean body weight did not significantly change (90 at baseline, 90.7 at the end of the study). In the same study, DXA was used to measure the total body mass, the torso fat and the leg fat. None of the above features changed significantly post-treatment ^[20].

6. Ultrasonography

Ultrasonography was used to measure the effects of therapy in two studies ^{[20][21]}. Both studies were aiming to assess the effectiveness of SAT therapy in people with lipoedema. In studies conducted by Ibarra et al., ultrasonography was performed on the lower abdomen and lower extremities (anterior calf, lateral thigh, calf, posterior thigh and inner thigh) to assess the tissue consistency. In total, six out of seven patients presented at least one (min = 1, max = 8) hyperechoic mass in the calf or thigh region. The total number of hyperechoic mass instances in the patients before treatment was 22. After the SAT therapy, all issues of the previously found masses had been resolved, but seven (min = 1, max = 2) new masses in a total of five patients were identified at the end of the study. The mass accounted for was, on average, 0.7 cm under the skin, and the dimensions were 1.3 by 0.8

cm. Moreover, four of the assessed women had visual fluid accumulation prior to treatment which has been reduced after SAT therapy ^[21].

In a study by Herbst, ultrasonography was performed on the lower abdomen and the thighs. The ultrasound evaluation revealed that the tissue was more fibrotic in three patients at baseline in comparison to the status at the end of the study ^[20].

7. Visual Analogue Scale

The Visual Analogue Scale (VAS) is a commonly used tool in measuring the level of experienced pain. It is a 10point numerical scale, in which a patient is asked to indicate their level of pain by choosing a number (0—no pain at all; 10—maximum pain). Four studies provided information on the pain level before and after the treatment ^{[18][20]} [^{21][24]}. Significant pain decrease could be observed in two cases ^{[18][24]}. Szolnoky et al. presented a pain reduction of 2.55 points after conservative therapy [<u>18</u>]. Accordingly, Atan et al. reported a mean reduction of 3.4 points on the VAS scale regardless of the conservative treatment method ^[24].

8. Quality of Life

The level of quality of life and health was measured in three studies ^{[24][27][28]}. Schneider conducted a study involving 30 female lipoedema patients. The quality-of-life level was defined to evaluate the effectiveness of manual lymphatic drainage with or without low-frequency vibrotherapy. The questionnaire used in the assessment was "Quality of life with Chronic Disease", and it was focused on the following dimensions: physical performance, ability to relax, positive mood and negative mood. Each item included possible answers based on a 5-point-Likert scale—very bad, bad, moderate, good and very good. After both MLD and MLD with vibrotherapy treatment, an improvement in quality of life could be observed; however, patients undergoing manual lymphatic drainage with vibrotherapy experienced a greater (23%) improvement in quality of life, compared to an 8% improvement in patients undergoing MLD only ^[28].

In Cannataro's study, presenting the case of women with lipoedema undergoing a ketogenic diet plan, a RAND-36 questionnaire was used to investigate the quality of life. All of the aspects of the questionnaire improved significantly after the 22-month treatment: Physical Functioning from 60/100 to 85/100; Role Limitations Due to Physical Health from 25/100 to 100/100; Role Limitations Due to Emotional Problems from 35/100 to 100/100; Energy/Fatigue from 30 to 55/100; Emotional Well-Being from 35 to 65/100; Social Functioning from 75 to 100/100; Body Pain from 30 to 75/100; and General Health from 20 to 60/100 ^[19].

Atan et al. assessed the patients' health status employing the Short Form 36 Health Survey (SF-36), which is composed of dimensions similar to the abovementioned RAND-36. A total number of 31 patients were assigned to three different therapeutic groups: group 1 underwent complete decongestive therapy with an exercise program, group 2 had intermitted pneumatic compression therapy and an exercise program and group 3 participated only in the exercise program. Considerable improvement in all of the groups could be observed in the following aspects:

Physical Functioning (69% group 1, 36% group 2, 41% group 3), Social Functioning (51.5% group 1, 60% group 2, 34% group 3), Health Change (92% group 1, 62% group 2, 43% group 3) and Pain (89% group 1, 127% group 2, 57% group 3). The increase in Emotional Well-Being could be observed in group 1 and group 3 with the improvement of 46% and 24%, respectively. General Health, Role Limitations Due to Physical Health and Energy/Fatigue were enhanced only in the group 1 with 89%, 180% and 66% improvement, respectively. The Role Limitations Due to Emotional Problems did not change post-treatment in any of the groups ^[24].

9. Experiencing Symptoms

The severity of lipoedema symptoms was assessed in four case reports described by Amato, with the use of the Lipedema Symptom Assessment Questionnaire (QuASiL) created by Rapprich and adapted by Amato ^{[29][30]}. The questionnaire consists of 15 specific questions about lipoedema-related ailments, and the patients are asked to rate the severity of their symptoms on a 0–10 scale, where 0 means no ailment and 10 is maximum severity. In all of the cases, conservative treatment in the form of manual lymphatic drainage, aquatic exercises and an anti-inflammatory diet was introduced. The first patient scored 89/150 in QuASiL at baseline and after an 8-month therapeutic program the score reduced to 58/150. In the second case report, the therapy only lasted a 1 month, but the QuASiL decreased from 44 to 11/150. The next patient scored 103 on the QuASiL score at the beginning, and after 5 months of treatment, the score dropped to 22/150. The last patient scored 115 points at baseline, and after 11 months of therapy the score declined to 59/150. It should be noted that despite the length of the treatment, the Lipedema Symptom Assessment Questionnaire showed a significant reduction in ailments in all the cases ^[26].

10. Functional Scales

The Lower Extremity Functional Scale (LEFS) was used in two studies ^{[20][21]}. The LEFS scale consists of 20 questions aiming at the evaluation of the lower limbs function. In every question, the patient is rated from 0— extreme difficulty to 4—no difficulty. Herbst et al. reported a 17% improvement in LEFS after 4 weeks SAT therapy program ^[20]. However, in a more recent study, Ibarra et al. noted a 14.3% decrease in LEFS score after 4 weeks SAT therapy program ^[21].

Atan et al. in their study of 31 women with lipoedema used a 6 min walk test to evaluate the functional capacity and therapeutic response. During the test, the patient is asked to walk as long a distance as possible in 6 min. The therapeutic techniques in the study included MLD, IPC and exercises. Independent of the used method of treatment, the 6 min test improved from 318.22 m at baseline to 371 m at the end of the study ^[24].

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