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Comprehensive Decongestive Therapy as a Treatment for Secondary Lymphedema of the Lower Extremity and Quality of Life of Women After Gynecological Cancer Surgery

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Background: Lymphedema is a clinical manifestation of lymphatic system failure, caused by an imbalance between the transport capacity of the lymphatic system and the volume of the produced lymph. Lymphedema is complication and significantly worsens quality of life (QoL).

Material/Methods: There were 50 patients diagnosed with secondary lymphedema of the lower extremities after gynecological cancer followed by radiotherapy included in this study. The average age was 57.76 years (standard deviation±10.08). Patients were treated at the Department of Physiotherapy, Balneology and Medical Rehabilitation, in hospital NsP in Bardejov. During therapy, we applied manual lymphatic drainage, instrumental lymphatic drainage, multilayer bandage, vascular gymnastics (with loaded external compression), hydrotherapy, and patient education on the adjustment necessary for a life-long regimen. The circumference of the limb was measured using the Kuhnkes disk method, QoL was assessed using the LYMQOL LEG questionnaire, and for assessment of pain the Visual Analogue Scale (VAS) was used.

Results: After treatment, we found a reduction in lymphedema ($P<0.001$), an increase in QoL ($P<0.001$), and a reduction in pain ($P<0.001$). We found a significant relationship between QoL change and pain in the domains of symptoms, function, and overall QoL ($P<0.005$). The results showed that reduction of lymphedema was not a significant predictor of QoL ($P>0.001$).

Conclusions: We found a positive effect in the treatment of secondary lymphedema of the lower extremity on the QoL of women after uterine cancer surgery, and also found that reduction of lymphedema and age were not predictors of improvement in QoL.

MeSH Keywords: Gynecologic Surgical Procedures • Lymphedema • Quality of Life

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Background

Oncological diseases are one of the main causes of mortality worldwide and are on an upward trend [1]. An increase in oncological diseases leads to an increase in possible complications after oncological treatment [1,2]. The fourth most common female cancer is endometrial cancer [3,4] and it is the most prevalent pelvic malignancy among gynecological cancers [3,5]. Lower limb lymphedema (LLL) is a chronic, progressive, and frequently incurable condition leading to disability that can affect women cured of gynecological cancer [3,6–9]. A study by Mirandola et al. [3] indicated that secondary LLL is the result of lymphatic system insufficiency and impaired lymph transport with increased limb volume related to cancer treatments, such as the surgical removal of pelvic and para-aortic lymph nodes and radiation therapy [3,10,11]. A late-diagnosed and inadequately treated lymphedema can have a significant negative impact on a patient's somatic, social, and psychological state, which can lead to permanent disability [1,12]. For secondary lymphedema of the lower extremities in patients who have undergone lymph node surgery, radiation, or chemotherapy in the treatment of cancer, the prevalence is 20–27.2% of patients [3,7,13–16].

The high increase in oncological diseases leads to increased complications following oncological treatment [1,2]. The fourth most common type of cancer in women is endometrial cancer [3,4] and it is the most common pelvic malignancy among gynecological cancers [3,5]. Lower limb lymphedema (LLL) is a chronic, progressive, and incurable disability, particularly affecting women treated for gynecological cancer [3,6–9]. Mirandola et al. [3] report that secondary LLL is the result of lymphatic system deficiency resulting in disruption of lymph transport, resulting in increased limb volume associated with cancer treatment, such as surgical removal of pelvic and periaortic lymph nodes as well as radiation therapy [3,10,11]. A late-diagnosed and inadequately treated lymphedema has a negative impact on a patient's somatic, social, and psychological state, which may lead to permanent disability [1,12]. In the case of secondary lower limb lymphedema, the incidence of lymphedema in patients who have undergone lymph node surgery followed by radiation or chemotherapy is 20–27.2% [3,7,13–16].

LLL has a negative impact on domestic work, physical activity, mobility, social activities, and psychological well-being [7,17,18]. If patients with LLL are not treated properly, LLL will gradually worsen, causing disability in daily life activities (ADL) and reducing QoL [7,17–21]. The key to LLL treatment is prevention, early diagnosis, and early treatment [7,14].

There is no standard approach that is applicable to all patients, despite the numerous therapies available in the treatment of LLL [22,23]. Initially conservative measures were recommended for the treatment of lymphedema, while surgical management was generally considered palliative [25].

The International Society of Lympho Logs (ILS) Consensus Document suggests both operative treatment and non-operative treatment for lymphedema management. Various non-operative treatments such as complete decongestive therapy (CDT), compression garment, massage, intermittent pneumatic compression, aquatic therapy, drug therapy, and psychosocial rehabilitation are suggested [1,25]. However, there is still a lack of research on which of these methods are most effective and appropriate, and more research and a systematic review of studies is needed [25,26]. Today, the basis of successful treatment of lymphedema is CDT, which has 2 phases. Phase 1 is swelling reduction to maximize lymphedema volume loss and phase 2 is stabilization to sustain lymphedema loss in the long term [1]. The aim of our study was to determine whether reduction of lymphedema is a predictor of improvement in QoL and what effect CDT as treatment of secondary lymphedema of the lower extremity has on the QoL of women after gynecological cancer surgery.

Material and Methods

The study group consisted of 50 patients diagnosed with secondary lymphedema of the lower extremities after gynecological cancer followed by radiotherapy. Patients were 39 to 79 years old. The mean age was 57.76 years (standard deviation±10.08). Patients were treated at the Department of Physiotherapy, Balneology and Medical Rehabilitation, in hospital NsP in Bardejov for 14 to 15 days. During therapy, we applied the following: manual lymphatic drainage of the lymphedema, instrumental lymphatic drainage of the lymphedema, multilayered lymphedema bandage (with Idealflex short-bandage and Mobiderm or mobilizing clothing, vascular gymnastics of the lymphedema (according to the instruction with loaded external compression with multilayer bandage, sleeve or Mobiderm autofit), hydrotherapy and patient education on the adjustment needed for a life-long regimen. Exclusion criteria were the following: cellulite, lymph fluid leakage, deep vein thrombosis, severe heart disease, or pulmonary embolism, as well as patient non-cooperation or non-consent to participate. The research conformed to the Helsinki Declaration and was approved by the ethics committee of the treatment facility. Informed consent was signed all patients.

Measurements

The effect of physiotherapy on the reduction of lymphedema was monitored by measuring the circumference of both lower extremities using a centimeter marked type. We used the

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Table 1. Reduction of lower limb volume.

Reduction of lymphedema	Treatment	n	Average (SD)	Mean reduction (cm)	Decrease (%)	*P* value
LLL reduction (cm)	Before	50	724.68±143.59	30.32	4.19	**0.000**
	After	50	694.36±127.60			
PLL reduction (cm)	Before	50	708.82±106.23	30.24	4.27	**0.000**
	After	50	678.58±98.53			

SD – standard deviation; LLL – lower limb lymphedema.

Kuhnkes disk method, such that the circumference of the extremity was measured from distal to proximal in 4-cm intervals [6]. A measuring board was used. We measured 16 identical sites on the lower extremities at the beginning and at the end of treatment [6,13,27].

The QoL of patients with LLL we evaluated using the standardized questionnaire LYMQOL LEG. The LYMQOL was developed by experienced healthcare professionals who worked with patients suffering from lymphedema. It was developed separately for lymphedema of the upper limb and lower limb [6,14,28]. The questions concern 4 domains (regions) [28]: symptoms (questions 1a–1f, 2, and 3), body image appearance (questions 4–10), function (questions 11–15), and mood (questions 16–21). Keeley et al. [28] and Wedin et al. [29] reported that each item in each domain is scored by a probability scale from 1 to 4: where 1=not at all, 2=a little; 3=quite a bit; and 4=a lot. Domain totals are calculated by adding individual scores and dividing the total by the number of questions answered for symptoms, body image/appearance, function, and mood. Overall QoL (Q22) is scored by a patient-scored score of 0 to 10, where 0 is the worst-rated QoL and 10 is the best-rated QoL [28,29].

Pain was scored according to the Visual Analogue Scale (VAS) ranging from 0 to 10, with 0 meaning no pain and 10 meaning maximum, unbearable pain. Woodforde and Merskey [30] first reported the use of VAS pain scale with descriptor extremes "no pain at all" and "my pain is bad as it could possibly be" in patients with a variety of pains [30].

Statistical analysis

The evaluation was performed by comparing before and after treatment (treatment lasted±16 days). Descriptive statistics, lymphedema reduction, pain, and QoL were evaluated using a paired *t*-test. With Pearson's correlation analysis, we found a relationship between improvement in QoL domains after CDT in patients with lymphedema and baseline values of LLL, PLL, pain, age, and lymphedema reduction. We used linear regression and logistic regression to determine predictors. Age and lymphedema reduction of lower limbs were identified as predictors of improvement in QoL. The statistical analysis was performed using the IBM SPSS 19 software. Data are presented as mean±1 SD or as% percentages. The level of statistical significance was set at $P<0.05$.

Results

The average age of patients was 57.76±10.08 years. After gynecological cancer patients received CDT. After treatment, we noted a reduction in LLL of 30.32 cm (4.19%) and PLL of 30.24 cm (4.27%) (Table 1).

We evaluated the QoL using the LYMQOL questionnaire before and after treatment. Using a paired *t*-test, we found statistical significance ($P<0.005$) for all domains. Overall evaluation of QoL (Q22) was evaluated before and after treatment separately on a scale of 0 to 10 (where 0 is the worst QoL assessed) and we found a statistical significance ($P<0.005$) through paired *t*-test. Pain (VAS) decreased by 1.84 points (Table 2).

Using a Pearson correlation analysis between improvement in QoL domains after CDT in patients with lymphedema and baseline values of LLL and PLL reduction, no significant relationship was found ($P>0.005$). The change in QoL was not affected by age ($P>0.005$). We found a significant relationship between change in QoL and pain in the domains of symptoms, function, and overall QoL ($P<0.005$) (Table 3).

The predicted predictors of improvement in QoL were the reduction of LLL and age. The results show that predictors are not significant for improving QoL ($P>0.005$) (Tables 4, 5). Age and PLL reduction were not predictors of improvement in QoL ($P>0.005$).

Discussion

Lymphedema is a progressive chronic disease due to insufficient lymphatic system activity and impaired lymph transport [1].

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Table 2. Assessment of QoL with LYMQOL.

Parameters	Treatment	n	Average (SD)	t	*P* value
LYMQOL symptoms	Before	50	2.56±0.68	5.50	**0.000**
	After	50	2.22±0.57		
LYMQOL Body image/appearance	Before	50	2.77±0.71	4.80	**0.000**
	After	50	2.52±0.65		
LYMQOL function	Before	50	2.74±0.68	5.80	**0.000**
	After	50	2.37±0.76		
LYMQOL mood	Before	50	1.80±0.61	4.99	**0.000**
	After	50	1.56±0.55		
LYMQOL overall QoL	Before	50	5.62±1.64	11.87	**0.000**
	After	50	6.96±1.68		
VAS	Before	50	5.40±1.98	13.62	**0.000**
	After	50	3.56±1.97		

QoL – quality of life; LYMQOL – Lymphoedema Quality of Life; VAS – Visual Analogue Scale; SD – standard deviation.

Table 3. Pearson correlation analysis between improvement in QoL domains after CDT and baseline values of reduction LLL, PLL, pain, and age.

Δ LYMQOL	Age		Pain (VAS)		Reduction of LLL		Reduction of PLL	
	r	*P*	r	*P*	r	*P*	r	*P*
Δ Symptoms	–0.082	0.570	0.291	**0.041**	0.159	0.271	0.081	0.576
Δ Body age/appearance	0.087	0.546	0.167	0.247	0.114	0.433	0.125	0.387
Δ Function	0.132	0.359	0.362	0.010	0.024	0.868	–0.038	0.791
Δ Mood	–0.131	0.364	0.204	0.155	0.010	0.945	0.037	0.801
Δ Overall QoL	–0.254	0.076	–0.501	**0.000**	–0.125	0.386	–0.048	0.741

QoL – quality of life; CDT – complete decongestive therapy; LLL – lower limb lymphedema; VAS – Visual Analogue Scale; LYMQOL – Lymphoedema Quality of Life.

Despite the numerous therapies available for the treatment of LLL, there is no standard approach for all patients [22]. Bakar and Tuğral. [6] indicated in their study that after pelvic lymph node dissection the incidence of lower limb lymphedema in patients with gynecologic malignancies ranges between 2.4% to 41%. Thus, the management of lower extremity lymphedema in patients after gynecologic cancer surgery is an important issue [6,15,31,32]. CDT is still the gold standard of lymphedema management [6,15,31,32]. Baumann et al. [33] conducted a systematic review examining the effects of physical exercise as part of rehabilitation. In 13 studies, they found that the studies involved conclude the positive effect of physiotherapy. Only a few studies have been conducted to determine the effects of manual lymphatic drainage (MLD) and compression therapy in the treatment of lymphedema [6,15,34–36]. Two controlled studies have shown that compression therapy with or without manual lymphatic drainage was equally effective for patients with lymphedema after cancer [36–39]. Andersen et al. [40] conducted a randomized, controlled study comparing manual lymphatic drainage and compression (n=20) with a control group that was only treated with compression therapy (n=20). Indeed, after 2 weeks, the control group had a greater percentage reduction in absolute swelling (60%) compared to the MLD group (48%). In both groups the symptoms of difficulty and swelling were reduced equally, but the QoL was also improved in the control group [15]. Singh et al. [41] in his study describes that patients with secondary lymphedema can safely participate in progressive, regular exercise without experiencing a worsening of lymphedema or related symptoms. There is insufficient evidence to support or refute the current clinical recommendation to wear compression garments during regular exercise [6,15,19].

Lymphedema can have adverse effects on psychological and social wellbeing and limit mobility and ability to perform daily

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Table 4. Predictors of achieving a significant improvement in QoL (reduction of LLL).

Δ LYMQOL	R^2	F	P	Age			Reduction of LLL		
				b	β	*P*	b	β	*P*
Δ Symptoms	0.031	0.753	0.477	–0.003	–0.077	0.096	0.018	0.156	0.283
Δ Body image/appearance	0.021	0.510	0.604	0.003	0.092	0.529	0.011	0.013	0.423
Δ Function	0.136	0.440	0.647	0.006	0.133	0.361	0.003	0.029	0.843
Δ Mood	0.131	0.412	0.664	–0.004	–0.131	0.370	0.000	0.005	0.970
Δ Overall QoL	0.287	2.106	0.133	–0.020	–0.258	0.071	–0.028	–0.134	0.342
Δ Pain	0.094	0.210	0.811	0.009	0.090	0.538	–0.006	–0.024	0.867

QoL – quality of life; LLL – lower limb lymphedema; LYMQOL – Lymphoedema Quality of Life.

Table 5. Predictors of significant improvement in QoL (reduction of PLL).

Δ LYMQOL	R^2	F	P	Age			Reduction of PLL		
				b	β	*P*	b	β	*P*
Δ Symptoms	0.011	0.264	0.769	–0.003	–0.069	0.644	0.008	0.067	0.652
Δ Body image/appearance	0.029	0.697	0.503	0.004	0.117	0.429	0.014	0.148	0.317
Δ Function	0.018	0.426	0.657	0.006	0.130	0.383	–0.001	–0.013	0.933
Δ Mood	0.017	0.414	0.663	–0.004	–0.129	0.386	0.001	0.013	0.942
Δ Overall QoL	0.074	1.888	0.163	–0.022	–0.274	0.062	–0.021	0.030	0.478
Δ Pain	0.019	0.445	0.644	0.007	0.070	0.635	–0.026	–0.104	0.486

QoL – quality of life; LYMQOL – Lymphoedema Quality of Life.

activities [6,15,19,43]. To change in the clinical measured of lymphedema more emphasis in evaluating the effect of treatment as the results themselves QoL [6,15,19,43]. Considering that treatment for lymphedema involves a significant and ongoing commitment from patients, it is essential to determine whether the benefits to patients outweigh the burden associated with treatment [6,19]. We evaluated the QoL of patients with lymphedema of the lower extremities using the standardized questionnaire LYMQOL LEG. LYMQOL has good reliability and validity and builds on international research [44,45].

New interdisciplinary guidelines from the Netherlands appear to help improve the quality of day-to-day care for patients with lymphedema, as reported by Van de Pas [45]. In particular, this refers to a new approach to chronic diseases in which patients play a central role by actively participating in their treatment. Van de Pas [45] also points to the important role of the ICF (International Classification of Functioning, Disability and Health), which aims to use proper assessment, therapy, education and assistance for patients with specific diseases with respect to specific aspects of human body function [45–47].

The pain VAS originated from continuous visual analog scales developed in the field of psychology to measure well-being [47,48]. Smoot et al. [49] included 3 studies reporting VAS scores in their meta-analysis. The reported results were statistically homogeneous, Q=1.4 (*P*=0.49). The meta-analysis using the fixed-effect model revealed a statistically significant, moderate magnitude of the effect of MLD on pain reduction (d=–0.62; CI=–1.06, –0.19). Positive association of depressive symptoms, pain intensity, and beliefs about body integrity were reported by Teo et al. [50]. The relationship between pain and depressive symptoms was mediated by dissatisfaction with body image, further suggesting that a higher level of pain led to a higher level of dissatisfaction with self-perception, resulting in greater symptoms of depression. Also, the relationship between the conviction of physical integrity and the symptoms of depression was mediated by dissatisfaction with self-perception. This suggests that a negative belief in physical integrity led to greater body dissatisfaction and consequently to more pronounced symptoms of depression [50].

Similarly, the study by Micha et al. [24] suggests that conservative CDT lymphedema is effective and has a beneficial effect on limb volume reduction, which is strongly related to improving

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the QoL (pain and depression relief) of lymphedema patients. Despite this, we also encountered patients whose lymphatic drainage disorder worsened despite well-managed conservative therapy. Surgical therapy for lymphedema may be considered in these patients.

The study by Klernäs et al. [42] reported that lymphedema had an effect on the QoL in 20% of patients. QoL assessment tended to decrease with age, with a significant correlation in the psychosocial area (rs=0.194, *P*=0.028). Compared to the general Swedish population, patients with lymphedema evaluated their overall health, vitality,and social functioning by SF36 as significantly lower [42]. In our study, we assumed that lymphedema reduction and age would be predictors of improved QoL assessment in patients. However, the results showed that the predictors were not significant. Despite the reduction, predictors of QoL improvement were not demonstrated.

Regular exercise reduces the symptoms of lymphedema by reducing local swelling [51,52]. Exercise and physical activity are essential for treatment as they increase physical and emotional fitness, vitality, and quality of life [52–56]. What is important is the level and intensity that must be considered [3,51]. Studies have shown that strength training must be adaptable to patients [52,54]. The recommended exercises for post mastectomy women are walking, dancing, gymnastics, cycling, swimming, and Nordic walking [51]. Puszczalowska-Lizis et al. [51] investigated the quality of life (WHOQOL-BREF) of active and inactive women after postmastectomy. Women who performed physical activity rated their quality of life better in each domain than women who did not exercise [51].

There is scant research that has determined the level of physical activity in LLL patients during the treatment of cancer [15,57].

The need to learn all the rules to facilitate disease management related to the lifestyle of patients with chronic lymphedema has been described by Biglia et al. [31] and Gloviczki et al. [36]. These authors reported that after treatment of gynecological carcinoma, this chronic condition responds poorly to treatment interventions and thus has a significant impact on the QoL. They further state that the difference in secondary lymphedema incidence values is due to inconsistencies in the diagnostic evaluation system. The correct management after diagnosis and the real state of occurrence is unknown. The primary cause of LLL is lymphadenectomy whose side effects may become worse due to other most common risk factors [31,36].

Lymphedema affects millions of people. Its prevalence and morbidity have been underestimated, often shifted from the disease category to the "cosmetic error" category. Lymphedema is a progressive disease and requires lifelong treatment. Lymphedema can be significantly improved using contemporary traditional (conservative) and surgical treatment methods [36]. Conservative treatment always involves CDT, compression pumps and clothing. Pharmacotherapy and surgical treatment are optional. Surgery may be reconstructive or excision. Although non-surgical intervention has been effective in reducing lower extremity edema, other effects, such as pain and heaviness. have been measured differently for each study, and with a limited expectation of a definite effect. However, non-invasive therapies have shown positive effects, including improving the QoL and lowering extremity edema in cancer patients.

Conclusions

We found a positive effect in the treatment of secondary lymphedema of the lower extremity on the QoL of women after uterine cancer surgery. We also found a reduction in the volume of the lower limbs in these patients. However, despite positive changes in these parameters, our research did not find that reduction of lymphedema and age were predictors of improvement in QoL.

Conflicts of interest

None.

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