Quality of Life in Patients With Venous Leg Ulcers Treated by Means of Local Hyperbaric Oxygen Therapy or Local Ozone Therapy – A Single Center Study

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Article

Quality of Life in Patients with Venous Leg Ulcers Treated by Means of Local Hyperbaric Oxygen Therapy or Local Ozone Therapy—A Single Center Study

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Abstract: Venous leg ulcers still pose a significant medical problem worldwide. The complexity of the problem determines the need for further interdisciplinary activities that will improve the quality of life of treated patients. The study compared the quality of life of patients with venous leg ulcers who received local hyperbaric oxygen therapy or local ozone therapy procedures as a part of comprehensive treatment. The study included 129 patients (62 men and 57 women) with venous leg ulcers. Group I underwent local hyperbaric oxygen therapy (HBOT), group II - local ozone therapy (OZONE). In both groups, the patients' quality of life was assessed before the start of treatment cycle, as well as 10 weeks and 6 months after the completion of the treatment, by using the EQ-5D-5L questionnaire and the Polish shortened version of the SF-36 scale. After completing the respective therapeutic cycle, both groups showed a statistically significant ($p<0.001$) improvement the quality of life according to the EQ-5D-5L questionnaire and the SF-36 scale. Differences were noted between 1st examination (before treatment) and 2nd examination (10 weeks after treatment), as well as 3 examination (6 months after treatment). In the EQ-5D-5L assessment of anxiety and depression, self-care and activities of daily living 6 months after the end of treatment, better results were found in the group of patients treated with local hyperbaric oxygen therapy ($p<0.001$). In this group, 6 months after the end of the treatment, a statistically significantly higher result on the EQ-VAS scale was also obtained (73.09±19.8 points vs. 68.03±17.37 points, $p=0.043$). However, in the SF-36 assessment 6 months after the end of treatment better results - a statistically significantly lower value of the quality of life index - were recorded in the group of patients treated with local ozone therapy (103.13±15.76 points vs. 109.89±15.42 points, $p<0.015$). Hyperbaric oxygen therapy and local ozone therapy procedures have a beneficial effect on improving the quality of life of patients with venous leg ulcers.

Keywords: quality of life; ozone therapy; local hyperbaric oxygen therapy; venous leg ulcers; treatment; hard to heal wounds

Introduction

The assessment of quality of life (QoL), which is of interest for many fields of medicine, became popular only in the second half of the 20th century. Initially, it focused primarily on disability which concerned chronic diseases. Over time, additional aspects began to be taken into account during the assessment, such as the patient's emotional state, self-care, social activity and cognitive abilities. Currently, quality of life is a complex and interdisciplinary issue. This concept is most fully defined by the commonly cited definition of the World Health Organization (WHO) as: "*personal, individual perception of one's own life position in the cultural context, the value system in which a person lives and in*

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relation to the goals set, expectations, patterns and fears, the degree depending on the environment, social relations and environmental features'' [1,2].

Health Related Quality of Life (HRQoL) is a much narrower concept than the general quality of life. It concerns the patient's assessment of his or her current level of functioning and satisfaction in relation to his or her individual situation, depending on his or her current health condition. Health-related quality of life can be defined as "*the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient*" [3,4].

Despite the significant progress and intensive development of medicine, increasing expenditures made on preventive measures and treatment, chronic wounds still constitute a significant problem for health care systems. It is estimated that approximately 1.5-2 million patients in Europe struggle with problems with difficult-to-heal wounds [5]. In the United States, this problem affects approximately 2.4–4.5 million people [6]. In Poland, leg ulcers occur in approximately 17-20% of the population. In over 50% of cases, leg ulcers persist for more than 9 months, and in over 2/3 of them, recurrences occur [7]. Ulcers are primarily the cause of chronic pain and limited mobility, which significantly reduces the sense of quality of life of treated patients. The burdensome, painful nature of the disease, its chronicity and frequent relapses force patients to actively seek help [8,9].

Leg ulcers of the lower limbs most often have a vascular etiology (more than 80% of all chronic leg ulcers), which is associated with venous insufficiency and/or atherosclerosis of peripheral arteries. They are diagnosed more often in women, and their incidence increases with age. The increase in the incidence of leg ulcers is also related to the demographic situation and aging of societies, as well as the increased incidence of lifestyle-related diseases such as obesity, diabetes, hypertension, and hypercholesterolemia, which favor the development of chronic wounds and complicate their treatment [7,9,10].

The prevalence of the disease and the high costs of its treatment, often resulting from the inability to provide care for the ulcer and leading an inappropriate lifestyle, make clinicians very interested in searching for new, more effective treatment methods. However, proper care for patients with leg ulcers requires not only knowledge of clinical data, but also, for example: mobility options, material conditions, family ties, the ability to change dressings, assessment of observed changes, and, above all, appropriate selection of treatment methods that ensure effective improvement of the quality of life of these patients [11,12].

The aim of the study was to compare the quality of life of patients with venous ulcers of the lower limbs who received local hyperbaric oxygen therapy or local ozone therapy, using the EQ-5D-5L questionnaire and the shortened Polish version of the SF-36 scale.

Material and methods

The study included 129 patients (62 men and 57 women) aged 55 to 78 years (average age: 67 years) diagnosed with venous leg ulcers, qualified on the basis of the following inclusion criteria: venous ulcers in the lower limbs in the category C6 according to CEAP classification, ulcer surface over 5 cm^2, partial skin thickness damage (II° according to NPIAP), ulcer persistence exceeding 6 weeks, age > 55 and < 80 years, informed and voluntary consent to participate in the study.

Exclusion criteria were as follows: ulcer etiology other than venous one, ulcer surface less than 5 cm2, age <55 and >80 years, ulcer duration of less than 6 weeks, comorbidities (diabetes mellitus and hypertension), cognitive disorders, lack of voluntary and conscious–patient's consent to participate in the study.

The evaluation included patients hospitalized at the Department of Internal Diseases, Angiology and Physical Medicine in Bytom in the years 2019-2021, randomly divided into two groups differing in terms of the physical treatment method used - in group I local hyperbaric oxygen therapy was used, and in group II ozone therapy. In group I treated with hyperbaric oxygen therapy there were 36 men and 32 women (mean age 65.0±10.9 years), whereas in group II treated with local ozone therapy there were 36 men and 25 women (mean age 66.0± 13.2 years). The average duration of leg ulcers in group I, which amounted to 3.36±1.12 years, did not differ statistically significantly from the duration of leg ulcers in group II, which was 3.37±1.25 years.

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Local hyperbaric oxygen therapy procedures in group I were performed with the use of the LASEROBARIA-S device (FASSER S.A., Tarnowskie Góry, Poland) [13]. The treated limb was placed in the treatment chamber, which was sealed with an elastic collar at the thigh level. The concentration of oxygen introduced into the chamber was about 95%, at the pressure of 1.5 ATA and flow rate of about 5 L / min. The treatment cycle included 30 treatment procedures performed once a day, lasting 30 minutes each, applied in 2 series of 15 treatments (excluding Saturdays and Sundays). The interval between two series of hyperbaric oxygen therapy was 4 weeks. The total length of therapeutic cycle was 10 weeks.

Local ozone therapy procedures in group II were performed with the use of Ato-3 device (Metrum Cryoflex, Blizne Łaszczyńskiego, Poland) [14]. Ozone was applied to the surface of the ulcer in the form of oxygen-ozone mixture (5% ozone and 95% oxygen) with the concentration of 40 μg/ml, using the so-called "Ozone bag". The duration of a single procedure was 30 minutes. Treatment procedures were also performed daily for 30 days in two series of 15 treatments (except Saturdays and Sundays). The interval between two series of ozone therapy treatments was 4 weeks. The total length of therapeutic cycle was 10 weeks.

During the cycles of combined physical treatment procedures performed in both groups of patients, similar conventional pharmacological treatment was applied: micronized purified flavonoid fraction, pentoxifylline, and acetylsalicylic acid in standard doses. In addition, Allevyn Adhesive Ag dressing (Smith & Nephew Inc., Watford Hertfordshire, UK) was applied topically to wounds. It ensures adequate moisture content and sterility of the wound and it also has an antibacterial effect. After physical procedures, compression therapy was applied (compression class 3) for 17 hours a day.

Before starting the physical treatment cycle, after 10 weeks of therapy, and also 6 months after the end of treatment a clinical assessment, questionnaire assessments of the quality of life were performed in both groups.

The Polish version of the EQ-5D-5L questionnaire was used to assess the quality of life of the examined patients. The EQ-5D-5L survey is a standardized document and it did not require any validation. The survey assessed 5 dimensions of quality of life: moving around (1), self-care (2), performing ordinary everyday activities such as work, studying, household chores (3), feeling pain/discomfort (4) and feeling anxious/depressed (5). Dimensions were assessed using a 5-point Likert scale. The respondents marked with an "x" one of the following levels that best reflected their current health condition (1 – no problems, 2 – minor problems/slight severity, 3 – moderate problems/moderate severity, 4 – serious problems/severe severity, 5 – inability to perform activities/very severe intensity).

Additionally, an assessment was performed using the EuroQoL Visual Analogue Scale (EQ-VAS), with which the patient assessed his or her current health condition on a scale from 0 (worst imaginable state) to 100 (best imaginable state) [15].

The second research tool used was a shortened Polish version of the SF-36 quality of life questionnaire assessing 8 dimensions of health, i.e. physical functioning, social functioning, role limitation in relation to physical problems, role limitation in relation to emotional problems. roles, mental health, vitality, pain and general health assessment. The categories are grouped into two scales: physical one (PCS – Physical Component Summary – 1) and mental one (MCS – Mental Component Summary – 2). The quality of life index (QoL index – 3) is the sum of points assessing all 8 dimensions of quality of life and allows for an overall assessment of health status. According to the Polish version, the higher the point value, the more negative the subject's self-esteem in terms of his/her quality of life [16].

The assessment was performed by people with medical education (a doctor and a physiotherapist) with competences in assessing the health condition and the effectiveness of the wound treatment process.

The study was conducted in accordance with Declaration of Helsinki (1964) and its protocol has been accepted by the local bioethical committee at the Medical University of Silesia in Katowice,

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Poland (approval reference number: PCN/0022/KB1/102/III/16/19/21). All enrolled patients gave written informed consent for participation in the study and agreed to complete the questionnaire.

Statistical analysis

Statistica 13 software package (StatSoft, Poland) was used to analyze the collected results. Those results were presented using mean values, standard deviation, and 95% confidence intervals. The distribution of the variables studied was examined using the Shapiro-Wilk test. Due to the compliance with normal distribution, Student's t-test and one-way analysis of variance (ANOVA) were used to test the statistical significance of differences in the examined parameters. The level of statistical significance was assumed to be $p<0.05$.

Results

The assessment of the quality of life of the studied patients performed before the beginning of treatment, using the EQ-5D-5L questionnaire, showed high score values for all assessed dimensions of quality of life, which confirms the low sense of quality of life in these patients.

The analysis of results obtained in assessing the quality of life of the examined patients, made according to EQ-5D-5L questionnaire, showed a statistically significant improvement in quality of life assessment results ($p<0.001$) for all 5 assessed dimensions of quality of life, both in the group of patients who received local hyperbaric oxygen therapy and in the group of patients who received local ozone therapy. In both compared groups of patients, a statistically significant improvement (lower score) was noted between study 1 (before the start of treatment) and study 2 (after 10 weeks of treatment), as well as study 3 (6 months after the end of treatment) (Table 1).

Table 1. The assessment of quality of life according to the EQ-5D-5L [points] questionnaire in patients treated with hyperbaric oxygen therapy and local ozone therapy, along with statistical evaluation.

Quality of life dimension and assessment period	**Local hyperbaric oxygen therapy (n=68)**				**Local ozone therapy (n=61)**				**p**
	mean	confidence -95%	confidence 95%	SD	mean	confidence -95%	confidence 95%	SD	
EQ-5D-5L (1) before treatment	4.57	4.45	4.70	0.53	4.46	4.33	4.59	0.50	0.210
EQ-5D-5L (2) before treatment	3.82	3.58	4.07	1.02	3.82	3.62	4.02	0.76	0.981
EQ-5D-5L (3) before treatment	3.96	3.78	4.14	0.74	3.79	3.64	3.94	0.58	0.155
EQ-5D-5L (4) before treatment	4.44	4.31	4.57	0.53	4.31	4.17	4.45	0.53	0.169
EQ-5D-5L (5) before treatment	4.15	4.00	4.29	0.61	4.16	4.02	4.31	0.55	0.869
EQ-5D-5L total before treatment	4.18	4.08	4.29	0.42	4.10	4.03	4.18	0.28	0.220
EQ-5D-5L (1) 10 weeks	2.24	2.10	2.37	0.55	2.26	2.14	2.39	0.48	0.768

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after treatment									
EQ-5D-5L (2) 10 weeks after treatment	1.69	1.57	1.81	0.50	1.52	1.40	1.65	0.50	0.061
EQ-5D-5L (3) 10 weeks after treatment	1.62	1.50	1.74	0.49	1.57	1.45	1.70	0.50	0.615
EQ-5D-5L (4) 10 weeks after treatment	1.65	1.53	1.76	0.48	1.66	1.53	1.78	0.48	0.919
EQ-5D-5L (5) 10 weeks after treatment	1.50	1.38	1.62	0.50	1.67	1.55	1.79	0.47	**0.048**
EQ-5D-5L total 10 weeks after treatment	1.73	1.67	1.80	0.26	1.73	1.68	1.78	0.20	0.989
EQ-5D-5L (1) 6 months after treatment	3.18	2.93	3.43	1.04	3.33	3.13	3.52	0.77	0.352
EQ-5D-5L (2) 6 months after treatment	2.06	1.86	2.26	0.83	2.56	2.35	2.77	0.83	**0.001**
EQ-5D-5L (3) 6 months after treatment	2.07	1.89	2.26	0.76	2.57	2.35	2.80	0.88	**0.001**
EQ-5D-5L (4) 6 months after treatment	2.00	1.84	2.16	0.65	2.31	2.10	2.52	0.83	**0.018**
EQ-5D-5L (5) 6 months after treatment	1.93	1.79	2.06	0.55	2.28	2.04	2.52	0.93	**0.009**
EQ-5D-5L total 6 months after treatment	2.24	2.11	2.38	0.56	2.60	2.44	2.77	0.63	**<0.001**
EQ-VAS before treatment	40.27	37.07	43.57	21.33	38.10	37.2	39	22.71	0.569
EQ-VAS 10 weeks after treatment	66.19	62.69	69.69	24.79	63.62	61.82	65.42	21.08	0.122
EQ-VAS 6 months after treatment	73.09	71.79	74.49	19.80	68.03	64.93	71,13	17.37	**0.043**

(1) moving around, (2) self-care, (3) performing normal activities of daily living, (4) pain/discomfort, (5) anxious/depressed.

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Detailed analysis of the individual dimensions of quality of life, assessed according to EQ-5D-5L questionnaire study, conducted after 10 weeks of treatment showed a statistically significantly lower score regarding the feeling of anxiety and depression in the group of patients treated with local hyperbaric oxygen therapy, as compared to the group of patients treated with local ozone therapy (1.50±0.50 points vs. 1.67±0.47 points, p <0.048), which was associated with a greater degree of mood improvement in this group of patients (Table 1).

In turn, the analysis of individual dimensions of quality of life, assessed according to the EQ-5D-5L questionnaire, carried out 6 months after the end of treatment, in the group of patients treated with local hyperbaric oxygen therapy, when compared to the group of patients treated with local ozone therapy, showed a statistically significantly lower score regarding the overall assessment of quality of life (2.24 points vs 2.60 points, p<0.001), as well as statistically significantly lower scores regarding, respectively: self-service efficiency (2.06±0.83 points vs 2.56±0.83 points, p<0.001), performing ordinary everyday activities (2.07±0.75 points vs 2.57 ±0.88 points, p<0.001), feeling pain and discomfort (2.00±0.64 points vs 2.31±0.82 points, p=0.018), and feeling anxiety and depression (1.92±0.55 points vs 2.27±0.93 points, p=0.009), which indicates greater therapeutic effectiveness of hyperbaric oxygen therapy in terms of improving the assessment of the above dimensions of quality of life in treated patients (Table 1).

It should be emphasized that in both groups of patients that were compared, the scores for individual dimensions of quality of life 6 months after the end of treatment were higher than after 10 weeks of treatment, which indicates that the therapeutic effect obtained was not lasting and durable.

The analysis of the test results regarding pain symptoms assessed using the EQ-VAS scale, carried out after 10 weeks of treatment, showed a statistically significant reduction in the intensity of pain sensation in both groups of patients (p<0.001), while the results obtained in both compared groups did not differ statistically significantly (p=0.122). However, in the analysis conducted 6 months after the end of treatment, a statistically significantly higher score was recorded in the group of patients treated with local hyperbaric oxygen therapy, as compared to the group of patients treated with ozone therapy () (73.09±19.80 points vs. 68.03±17.37 points, p=0.043).

The assessment of the quality of life of the studied patients, carried out before the start of treatment, performed using the SF-36 questionnaire, showed high score values both in the physical and mental scales, and in the case of quality of life index, which confirms the low sense of quality of life in these patients.

The analysis of results of quality of life assessment of the examined patients, carried out according to the SF-36 questionnaire, also showed a statistically significant improvement in the results of the quality of life assessment (lower score) (p<0.001) in the assessed physical and mental sphere and in the quality of life index, both in the group of patients who received local hyperbaric oxygen therapy, as well as in the group of patients who received local ozone therapy. In both groups of patients that were compared, a statistically significant improvement (lower score) was noted between study 1 (before the start of treatment) and study 2 (after 10 weeks of treatment), as well as study 3 (6 months after the end of treatment) (Table 2).

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Table 2. The assessment of the quality of life according to the SF-36 [points] questionnaire in patients treated with hyperbaric oxygen therapy and local ozone therapy, along with statistical evaluation.

Quality of life scale and assessment period	Local hyperbaric oxygen therapy (n=68)				Local ozone therapy (n=61)				p
	mean	confidence -95%	confidence 95%	SD	mean	confidence -95%	confidence 95%	SD	
SF-36 (1) before treatment	81.21	78.56	83.86	10.95	84.25	81.92	86.57	9.08	0.091
SF-36 (2) before treatment	59.32	58.31	60.34	4.19	59.54	58.48	60.61	4.16	0.768
SF-36 (3) before treatment	144.21	140.83	147.58	13.93	146.20	142.99	149.40	12.51	0.397
SF-36 (1) 10 weeks after treatment	50.72	48.88	52.56	7.62	50.07	48.30	51.83	6.90	0.611
SF-36 (2) 10 weeks after treatment	40.24	38.46	42.01	7.33	39.75	38.10	41.41	6.46	0.694
SF-36 (3) 10 weeks after treatment	85.40	83.23	87.57	8.96	79.38	77.07	81.68	8.99	**0.001**
SF-36 (1) 6 months after treatment	58.99	56.78	61.19	9.11	61.11	59.11	63.12	7.82	0.159
SF-36 (2) 6 months after treatment	50.04	48.70	51.39	5.56	51.89	49.23	54.54	10.37	0.205
SF-36 (3) 6 months after treatment	109.90	106.16	113.63	15.42	103.13	99.09	107.17	15.76	**0.015**

1) – physical scale, (2) mental scale, (3) quality of life index.

A detailed analysis of the quality of life assessment using the SF-36 scale carried out after 10 weeks of treatment did not show statistically significant differences in the scores on the physical and mental scales between the groups of patients treated with both compared physical methods, but showed a statistically significantly lower value of the quality of life index scores in patients treated with local ozone therapy, as compared to patients treated with local hyperbaric oxygen therapy (79.37±8.99 points vs 85.39±8.96 points); ($p<0.001$), which indicates a higher therapeutic effectiveness of local ozone therapy in this respect (Table 2).

Similarly, the analysis of the quality of life assessment using the SF-36 scale, carried out 6 months after the completion of treatment, did not show statistically significant differences in the scores on the physical and mental scales between the groups of patients treated with both compared physical methods, but showed a statistically significantly lower value of the quality of life index scores in patients treated with local ozone therapy, compared to patients treated with local hyperbaric oxygen therapy (103.13±15.76 points vs 109.89±15.42 points, $p=0.015$), which indicates that the therapeutic effectiveness of local ozone therapy remains higher in this respect also in long-term observation (Table 2) .

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It should be emphasized that in both compared groups of patients, the values of the quality of life index 6 months after the end of treatment were higher than after 10 weeks of treatment, which indicates that the therapeutic effect obtained was not so durable lasting.

Discussion

The quality of life of patients has been the subject of many assessments and analyzes for several decades. The assumption of the therapeutic activities undertaken is meant to improve the quality of life of a sick person who has to struggle with the troublesome symptoms of the disease, i.e. pain, functional limitations and self-care. The quality of life is determined by viewing through the prism of various areas of life, although one of its most important determinants is the generally understood well-being, which is the result of assessing one's health, both physical and mental one [1,17,18].

When assessing the effects of treatment of venous leg ulcers (VLU), attention should be paid not only to the elimination of the symptoms of the disease, but also to the biopsychosocial sphere of the patient's functioning, including the ability to perform self-care and fulfill specific social roles, as well as the subjective assessment of the quality of life. When assessing the quality of life in the case of VLU, the authors have used a number of both general and disease-specific research tools. An aspect that has not yet been fully resolved is the determination of the features which are characteristic of VLU are the most decisive ones for the reduction of health-related quality of life (HRQoL). Most authors consider pain, the size of the wound surface, wound discharge, and unpleasant odor as the key factors reducing HRQoL in these patients. [4,19–21].

To assess whether the medical care provided to patients with VLU contributes to improving their overall quality of life, the first step should be, as mentioned above, to identify factors related to quality of life in relation to health [22]. So far, as indicated by the research conducted by Hsiao et al., in some countries (e.g. Taiwan) there have been no studies on the quality of life in patients with VLU [23].

It should be emphasized that patients with difficult-to-heal wounds face the following problems: reduced physical fitness, the need to change their current lifestyle, changes in their own preferences, as well as changes in the family and social environment; also a reduced quality of life related to the presence of wound exudate, unpleasant odor, pain, insomnia, depression and anxiety, which causes difficult functioning at home, work, community, deterioration of interpersonal relationships, lack of acceptance, confusion, lowered self-esteem and inability to perform current roles in social conditions, and in many cases it also forces the resignation from paid work and social isolation [24,25]. The occurrence of a decrease in the quality of life in patients with venous leg ulcers caused by the above factors was confirmed by our research results, which showed unfavorable scoring in both quality assessment questionnaires used to examine both groups of patients, regarding both the physical and mental sphere, including all assessed dimensions of quality of life.

The reduced assessment of the quality of life in patients with venous leg ulcers was also confirmed by the authors of numerous publications available.

Miertová et al. assessed selected aspects of quality of life in 61 patients with venous leg ulcers treated in outpatient settings, using the modified Freiburg Life Quality Assessment wound module (FLQA-w) questionnaire. The worst result was obtained in the category of everyday life (3.61±0.93 points), and a significant impact on the assessment of the quality of life, among others, was related to the duration of ulcer treatment [26].

Iglesias et al. assessed HRQoL in 387 patients with venous leg ulcers from 9 regions of the UK, using the SF-12, EQ-5D-5L, and Hyland questionnaires. According to the authors, the SF-12 and EQ-5D-5L questionnaires revealed good assessment properties and were responsive to changes in HRQoL assessment after ulcer healing [27].

Dias et al. compared the quality of life in 204 patients with chronic venous disease, using the SF-36 questionnaire and showed that in the group of patients with venous ulcers, the scores for all aspects of quality of life were significantly lower [24].

González et al. assessed HRQoL in 34 patients with venous leg ulcers lasting for 3-5 months, taking the stage of ulceration into account. They showed that venous ulcers have a negative impact,

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especially on the emotional state, and the presence of tissue incapable of regeneration, as well as poor control of exudate and infection determine the deterioration of HRQoL results [11].

Hareendran et al. assessed HRQoL in a group of 38 patients with venous leg ulcers. They found that significantly worse HRQoL assessment ($p<0.05$) occurred in elderly patients with pain and non-healing wounds. The factors contributing to the deterioration of HRQoL assessment results included: pain (80.5%); pruritus (69.4%); changed skin appearance (66.7%); sleeplessness (66.6%); functional limitations (58.3%), and disappointment with the effects of treatment (50%) [28].

Folguera-Alvarez et al., after conducting a cross-sectional study in 22 primary health care centers on a sample of 93 patients with VLU, showed that the severity of the ulcer, pain and symptoms of infection significantly reduce the perceived quality of life of the studied patients [29].

In turn, Van Korlaar et al., after conducting a query of 25 articles from available databases, which aimed to assess the quality of life of patients with chronic venous disease, showed that the quality of life of patients with chronic venous disease is disturbed, especially in the physical domain, mainly in relation to pain, physical functioning and mobility. The results also showed the occurrence of negative emotional reactions and social isolation of the respondents [30].

Szewczyk et al., based on research conducted in 2005, found that over 80% of patients with chronic leg ulcers give up developing their own interests and reduce the frequency of participating in social gatherings and making new friends due to troublesome symptoms. Moreover, pain associated with ulcers caused insomnia, fatigue, exhaustion, and lack of energy, which resulted in frequent occurrence of depression [31].

In another work, Jawień et al. assessed biopsychosocial functioning and the occurrence of limitations in people with varicose veins of the lower legs. The authors found a frequent occurrence of depression in the studied group of patients, a higher risk of falls, and malnutrition. Moreover, patients had an increased risk of impaired functioning in the social, emotional, and physical spheres [32].

In turn, Ścisło et al. assessed the quality of life of 61 patients with venous ulcers of the lower limbs. The surveyed patients rated their satisfaction with the quality of life higher than with their objective health status. They rated the quality of life the highest in the social area, and the lowest in the physical area [33].

In the presented study, the EQ-5D-5L questionnaire was used to assess the quality of life, which is characterized by high sensitivity, precision and, at the same time, it is understandable to patients. Most authors believe that increasing the number of levels from 3L to 5L in each dimension increased the "sensitivity" of the EQ-5D-5L questionnaire. Another advantage of the EQ-5D-5L questionnaire used in this study is its universality and applicability to any medical condition. On the other hand, the EQ-5D-5L questionnaire also has its limitations. First of all, it does not cover spiritual aspects, although this area is now considered very important in holistic patient care [15,34].

The aim of the study was to assess the quality of life of patients who received treatment in the form of two physical methods, namely local hyperbaric oxygen therapy or local ozone therapy. The quality of life of the study patients was assessed before the start of treatment, 10 weeks after the start of treatment, as well as 6 months after the completion of treatment. As shown by the obtained research results, in each of the evaluations positive results were obtained, showing the beneficial impact of the physical methods used on the quality of life of the examined patients, regarding both the physical and mental spheres, as well as all assessed dimensions of quality of life. Since in both groups of patients compared, the scores for all dimensions of quality of life assessed using the questionnaire and the quality of life index assessed using the SF-36 questionnaire were worse 6 months after the completion of treatment than immediately after the end of the 10-week treatment cycle, it should be assumed that therapeutic effect obtained with both compared therapeutic methods, in relation to the assessment of patients' quality of life, was not fully sustainable.

The analysis of long-term therapeutic effects achieved using both physical methods in the group of patients treated with local hyperbaric oxygen therapy compared to the group of patients treated with local ozone therapy, in the case of a detailed analysis of individual dimensions of quality of life according to the EQ-5D-5L questionnaire, showed a statistically significantly lower score regarding

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self-care efficiency, performing ordinary everyday activities, feeling pain and discomfort, as well as feeling anxiety and depression, and in the case of analysis using the SF-36 questionnaire, a statistically significantly higher score on the quality of life index, which indicates greater therapeutic effectiveness of local hyperbaric oxygen therapy in terms of improving quality dimensions life analyzed in the EQ-5D-5L questionnaire, and for local ozone therapy in terms of the quality of life index of patients treated for venous leg ulcers analyzed by means of the SF-36 questionnaire.

The available literature contains only single publications assessing the impact of the therapy on improving the quality of life of patients with venous leg ulcers.

In the study by Tiwary et al., the quality of life was assessed in 50 patients with venous leg ulcers using the SF-36, Charing Cross Venous Ulcer Questionnaire (CXVUQ) and the Chronic Venous Disease Clinical Severity Scale (VCSS). After endovascular treatment and compression therapy, the ulcers healed in most but 7 (12.5%) patients. Recurrence of ulcers was observed in 12 limbs (21.43%). However, the quality of life assessed after the completion of treatment showed a statistically significant improvement compared to the baseline values before the start of therapy $p<0.001$ [35].

In retrospective, in the single-center cohort study performed by Lalieu et al., 15 patients from an outpatient clinic with a VLU were treated with the use of HBOT and standard wound care. Patients received an average of 43±20 sessions of HBOT. The improvement in patient-related outcome measures (PROMs) was assessed by the EQ-5D-3L questionnaire and included quality of life (QoL) and pain score. Most of those patients reported improvement in all health aspects covered by the questionnaire - pain score decreased from 5.7 (±2.5) to 2.1 (±2.2) ($p<0.0001$), and health score increased from 57.2±15.6) to 69.9±18.9) ($p=0.02$) [36].

Morteza et al. evaluated the effect of ozone therapy on the health-related quality of life of 86 patients with chronic wounds. To measure the quality of life, the Cardiff wound impact questionnaire and the SF-36 questionnaire were used. As an effect of medical O_3 therapy, a significant improvement in the healing of chronic wounds, as well as a significant improvement in the health-related quality of life of patients were observed. According to the authors, this method of treatment could be a valuable therapeutic option in the treatment of chronic wounds [37].

Confirmation of the beneficial effect of therapy on the assessed quality of life was also obtained in the work of Solidade-Simoes et al., in which the quality of life was assessed in 171 patients with venous leg ulcers treated in primary health care entities in two cities in Brazil and Portugal. The quality of life scores using the short version of the SF-36 questionnaire were significantly better in Portugal as concerned physical aspects, pain and social functioning in different domains, as well as the physical health dimension and total QoL score [38].

The results of the studies presented above confirm the beneficial effect of treatment with physical methods, such as local hyperbaric oxygen therapy and local ozone therapy, on the assessment of the quality of life of patients with venous leg ulcers, which was made in our study.

The basis for proper care of patients with leg ulcers (regardless their etiology) is to minimize the loss of functionality, maintain the ability to independently perform basic daily activities, and protect against deterioration of the quality of life as a result of the disease. An important aspect of that is also individual planning of the educational process. It is also vital that the psychosocial costs associated with venous leg ulcers are relatively high. The association of venous leg ulcers with anxiety, pain, depression, social isolation, and sleep disorders invariably manifests itself in a reduced quality of life. Hence, conducting research in this area is becoming increasingly important. The data obtained from quality of life studies can help take clinical decisions and determine health strategies for the treatment of patients with difficult-to-heal wounds, and the results of these studies will allow medical care providers to focus not only on factors influencing ulcer healing, but also on factors affecting patients' HRQoL, as a holistic assessment of the needs of patients with VLU is currently recommended in order to conduct optimal and cost-effective treatment [39].

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Limitations of the study

With the above in mind, it is also important to acknowledge the limitations of the study, such as the non-representative and relatively small sample size, and the recruitment of participants only from one health center. The study also did not include the analysis of previous standards of care.

Conclusions

Therapy using local hyperbaric oxygen therapy as well as local ozone therapy has a positive effect on improving the quality of life of treated patients suffering from venous leg ulcers, in the 6-month observation period. This improvement concerns in particular the mental sphere, self-service and performing everyday activities, as well as the feeling of pain and mobility. The conducted research shows that none of the physical methods compared shows a clear advantage in terms of therapeutic effectiveness in this area, and the observed differences result from the very method used to assess the quality of life. Developing and implementing wound care strategies that also focus on improving health-related quality of life is a challenge for modern healthcare systems around the world. Therefore, it seems reasonable to continue research on the analysis of the assessed quality of life parameters using a larger group of studied patients.

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Institutional Review Board Statement: The study was conducted in accordance with Declaration of Helsinki (1964) and its protocol has been accepted by the local bioethical committee at the Medical University of Silesia in Katowice, Poland (approval reference number: PCN/0022/KB1/102/III/16/19/21). All enrolled patients gave written informed consent for participation in the study and agreed to complete the questionnaire.

Data Availability Statement: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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