



Article Characteristics and Patient Reported Outcome Measures in Lipedema Patients—Establishing a Baseline for Treatment Evaluation in a High-Volume Center

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Abstract: Lipedema patients suffer not only from visual stigma but also reduction in their quality of life through pain and performance loss in daily life. In clinical practice, it is still difficult to reliably diagnose the disease. This study aims to provide further insights into the characteristics of lipedema patients of all stages and provide a baseline prior to surgery for a surgical treatment evaluation by means of patient-reported outcome measures. Methods: Patients completed a lipedema-specific questionnaire containing 50 items, the World Health Organization Quality of Life BREF (WHOQOL-BREF) and the Patient Health Questionnaire 9 (PHQ-9). The data were analyzed using SPSS statistics 27. Patients who had already received liposuction were excluded. Results: Five hundred and eleven patients were included, of whom 337 completed the PHQ9 and 333 completed the WHOQOL-BREF questionnaires. The general characteristics of lipedema patients, especially the daily symptoms, are described. Previous observations, such as the frequent occurrence of hypothyroidism and the low rate of type 2 diabetes, were confirmed. Over 49% suffer from severe impairments in their jobs, whereby the disease shows a familial accumulation. The results of the WHOQOL-BREF and the PHQ-9 suggest a high level of mental stress. Discussion: As surgical intervention in lipedema patients is gaining traction, its effects should be well-documented. Therefore, a comprehensive baseline needs to be established prior to surgical treatment. The psychological components are just as important as the inclusion of daily impairments.

Keywords: lipedema; liposuction; QoL; depression; obesity; restrictions in daily life

1. Introduction

Lipedema is a potentially widespread disease appearing almost exclusively in women. It is often misdiagnosed as obesity [1,2] while leading to high depression levels and significant impairment on their quality of life (QoL) [3].

The reported prevalence varies between 5 and 15% in women [4–6]. Patients frequently have to visit more than three doctors, and often, more than 15 years pass prior to a correct diagnosis [7,8]. In a study from the United Kingdom, 54% of district general hospital consultants did not recognize or had even seen this disease in their everyday professional life [9].

A symmetric accumulation of painful adipose tissue, especially in the limbs, is characteristic and leads to a disproportionate tissue distribution [1,2,10]. While the legs are almost



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Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). always affected, the arms are more often affected in higher stages [4,11,12]. Pain in the adipose tissue is one of the most common symptoms, which causes a lot of limitation in everyday and professional life [12]. Patients report additional symptoms in the affected areas, such as bruising, sensitivity to touch, feeling of tension, heavy and tired limbs and aesthetic impairment (Table 1) [13–16]. Affected patients usually recognize the first symptoms like enlargement of the legs during adolescence [3,7,8,17].

In 2004, Meier-Vollrath and Schmeller developed a systematic classification by subdividing the disease into three stages, depending on the visual and haptic findings of adipose tissue [11,12,18]. In addition, lipedema is divided into five subtypes, depending on the primary affected region [4,19] (Table 1).

Diagnostic Criteria	Type of Lipedema	Location of Onset
Almost exclusive occurrence in women	1	Hips
Bilateral and symmetrical manifestation with minimal involvement of the feet	2	Hips and thighs
Persistent enlargement after elevation of the extremities or weight loss Arms are affected	3	Hips, thighs and shanks
Minimal pitting edema	4	Arms
Negative Kaposi–Stemmer sign Pain, tenderness on pressure	5	Shanks

Table 1. Types of lipedema and diagnostic criteria of lipedema [1,2,19].

Most lipedema patients receive a noninvasive, conservative therapy [20]. Complex decongestive therapy (CDT) consists of manual lymphatic drainage (MLD), intermittent pneumatic compression (IPC) and a compression garment.

Not only during hospitalization but also in outpatient treatment, patients benefit from CDT through leg volume and pain reduction [4,21,22]. However, these outcomes are frequently diminished during the outpatient periods. Some patients overcompensate for these effects so that their leg volume increases overall [21]. The compression garment needs to be worn as much as possible in order to reduce edema and pain in everyday life in over 50% of patients [20].

The current literature suggests that liposuction may be a promising approach as an invasive treatment modality in terms of pain reduction and increase in the quality of life [13–16,23].

Overall, the outcome data of liposuction in lipedema are sparse, and studies in patients with a confirmed lipedema diagnosis are rare.

With this study, we aim to gain further insight into the characteristics of lipedema patients of all stages. In addition, to evaluate surgical treatment, we provide a baseline before surgery for patient-reported outcomes (PROMs).

2. Methods

This study was approved by the local ethics committee. Ethic Committee Name: Ethics Committee of the Medical Association Westphalia-Lippe and Westphalian Wilhelms University. Approval Code: 2021-684-f-S. Approval Date: 9 March 2022.

2.1. Patient Selection

All patients visiting our institution with the suspected diagnosis of lipedema were included in the study. Each patient was asked to fill in an individually designed questionnaire prior to their consultation (Appendix A). Patients who already received a liposuction or any bariatric surgery prior to consultation, were a minor or who turned out to not be suffering from lipedema were excluded.

2.2. Structure of Questionnaire

General information such as height, weight, age of symptom onset, age at diagnosis, location of pain and family history of lipedema were evaluated. Patients were asked to give information about their impairment in professional life and which therapies they had undergone so far. Further, comorbidities and smoking behavior were assessed.

Twenty questions referred to the patients' pain symptoms using a numeric rating scale from one to ten. The subjects were: exact location of pain, bruising, swelling, heat and coldness of extremities, muscle cramps, heaviness or fatigue of the legs, skin problems, pruritus, limitations while walking and in quality of life and satisfaction with optical appearance of the legs.

The QoL and level of depression were monitored via the World Health Organization Quality of Life-BREF (WHOQOL-BREF) and the Patient-Health-Questionnaire-9 (PHQ-9).

The WHOQOL-BREF is a patient-reported outcome measurement tool to monitor their overall health. It contains twenty-four items divided into four domains to measure every facet of their quality of life using a Likert scale from one to five. These health domains are physical health, psychological health, social relationships and environment. Further, two single "benchmark" items are given to monitor the general aspects of general health and overall QoL. This questionnaire shows high validity in studies to map the quality of life [24–27].

The PHQ-9 was applied for the depression severity evaluation. It consists of nine different items assessing depression. Participants were asked to provide the frequency of symptom appearance during the last 28 days via a four-point-Likert-scale (from zero (=not at all) to four (=nearly every day)). The higher the score, the higher the depression severity. A score of five to nine equals "minimal symptoms", while 20 and more points demonstrate "serve depression" [28,29].

2.3. Data Collection

Data were collected in an individually designed database in SPSS statistics 27. A retrospective analysis was performed. Spearman's correlation coefficient was determined to show positive and negative correlations. For a confirmatory analysis, an analysis of variance (ANOVA) was performed to show differences between groups due to continuous outcome variables. Due to multiple testing, a Bonferroni correction was used to adjust the global significance of 5%. Each test was performed to a local significance level of 1%.

3. Results

3.1. General Information

Five hundred and eleven patients met the eligibility criteria and were included in this study. Patients had a mean age of 40.16 (\pm 12.45) years and a BMI of 33.31 kg/m² (\pm 7.8) across all stages. The lipedema stage and BMI demonstrated a positive correlation (Spearman r = 0.566, ANOVA *p* < 0.001) (Table 2). On average, 16.11 (\pm 11.39) years elapsed between the symptom onset and diagnosis. Table 2 presents detailed information on the patient characteristics.

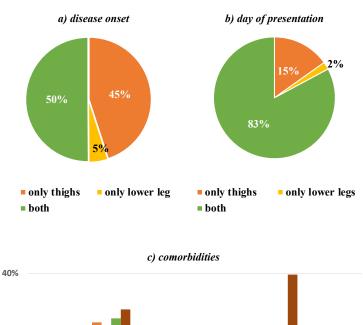
Over 80% of patients noticed the first increased tissue proliferation during hormonal changes, such as puberty (67.3%), pregnancy (9.5%) and during menopause (4.0%).

At disease onset, 50.1% of patients had both thighs and lower legs affected, i.e., the entire leg. On the day of presentation in our institution, the entire leg was affected by increased fat accumulation in 82.4% of patients (Figure 1).

If we look at the dietary behaviors of the patients, we see that only 7% had never tried to lose weight by changing their diet. In contrast, 25% said that their efforts of dietary changes did not show any affect, whereby 44.5% had little success. About 41% declared that they were able to lose up to five kilograms of body weight.

Age at Presentation	Mean 40.16 (±12.45)
Weight at presentation	mean 96.16 kg (±23.11)
BMI at presentation	mean 33.13 (±7.8)
BMI < 18.5	0.0%
BMI 18.5 to 24.99	11.7%
BMI 25 to 29.99	23.2%
BMI 30 to 34.99 (obesity I°)	24.2%
BMI 35 to 39.99 (obesity II°)	19.6%
BMI > 40 (obesity III°)	20.2%
Age at onset of symptoms	mean 19.66 (± 10.00)
5 J I	mean 36.69 (± 10.00)
Age at diagnosis	
years between onset and diagnosis	mean 16.11 (\pm 11.39)
BMI stage I	mean 24.71 ± 3.61
BMI stage II	mean 32.11 ± 6.00
BMI stage III	mean 39.33 ± 7.53
Stage I legs (at presentation)	8.6%
Stage II legs	57.8%
Stage III legs	33.6%
Stage I arms	11.8%
Stage II arms	36.0%
Stage III arms	9.9%
Stage 0 arms	42.3%
-	87.2%—nonsmoker
	6.4%—<5 per day
Smoking behavior	3.4%—5–10 per day
0	1.8%—11–15 per day
	1.2%—16–20 per day
Comorbidities	75.9%
hypothyroidism	31.3%
joint pain	27.3%
Skin problems	19.2%
Hypertonia	18.5%
Typertoina	
the second second	10.2% patient
thrombosis	9.3% only family member
Type 2 diabetes	3.0%
Symptoms	mean (\pm SD) (<i>n</i> = 511)
Feeling of "heavy" legs	8.21 (±1.95)
Feeling of tired legs	7.79 (±2.17)
Bruising (hematomas)	7.63 (±2.31)
Feeling of tension in the legs	7.49 (±2.19)
Hypersensitivity to touch	7.32 (±2.42)
Swelling	7.04 (±2.41)
Pain in the affected areas	6.68 (±2.32)
Impairment in walking	6.45 (±2.78)
Pain in thighs:	6.34 (±2.5)
Pain in lower legs:	6.18 (±2.53)
Pain in arms:	$5.33 (\pm 2.72)$
Feeling of cold in the legs	$5.35 (\pm 2.72)$ $5.11 (\pm 3.21)$
Feeling of warmth in the legs	
0	$4.92 (\pm 3.01)$ $4.78 (\pm 2.00)$
Itching Dain in hette du	$4.78 (\pm 3.00)$
Pain in buttock:	4.65 (±2.62)
muscle cramps	$4.63 (\pm 2.86)$
Skin complications	$4.11(\pm 2.98)$
Pain in belly:	4.00 (±2.72)

Table 2. Patient characteristics (population n = 511).



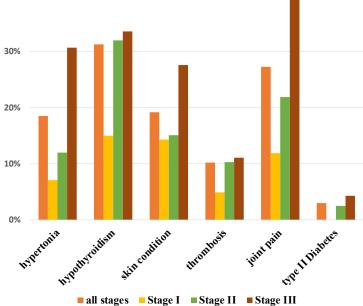


Figure 1. Patient characteristics: (a) shows the affected regions at the time of disease onset. In comparison, (b) shows the affected regions at the time of presentation to our clinic. (c) illustrates the comorbidities of lipedema patients, differentiated according to their present stage.

3.2. Comorbidities

Table 2 gives detailed information about the occurring concomitant diseases. There was shown that 31% of patients suffered from hypothyroidism. Adiposity-associated diseases like hypertonia and type 2 diabetes occurred with a frequency of 18.5 and 3%. In Figure 1, the concomitant diseases are also differentiated according to stage. The number of patients with hypertension increased to 30.7% at stage 3.

In addition, joint problems were more prevalent in stage 3 patients (39.8%, n = 64 of 161) than in stage 1 patients (11.9%).

Thrombosis also occurred less often in patients with stage 1 (4.9%) than with stage two (10.3%) or three (10.1%).

3.3. Familial Clustering

Patients were asked if any family members suffered from lipedema or remarkably "thick legs".

In 33.6% of cases, the patient's mother was also suspected to be affected by lipedema. With 28.4%, grandmothers were suspected to be affected in the previous generation (maternal 15.4%, paternal 10.3%). Further detail is shown in Table 3 and visualized in Figure 2.

Table 3. Family history of lipedema or noticeably thick legs.

Family Member	Affected ($n = 511$)
mother	33.6%
grandmother (in general)	28.4%
grandmother maternal	15.4%
sister	14.6%
grandmother paternal	10.3%
aunt paternal	9.8%
aunt maternal	9.2%
daughter	2.3%

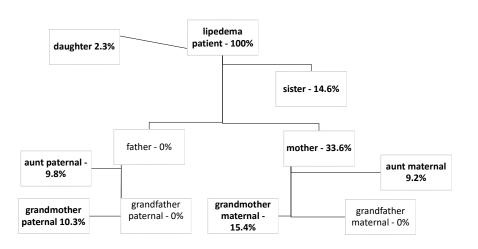


Figure 2. The pedigree of familial occurrence of enlarged legs shows the frequency within the immediate family.

3.4. Symptoms

Eighteen different items were asked by means of a numerical rating scale from one (none) to ten (very serve/strong) to establish a daily symptom overview (Table 2). The highest mean scores were not for leg pain (6.68 (\pm 2.32)) but for tiredness (7.79 (\pm 2.17)) and heavy legs (8.21 (\pm 1.95)). Likewise, hematomas (7.63 (\pm 2.31)) and the feeling of tension (7.49 (\pm 2.19)) were prominent in the affected regions (Table 2).

3.5. Effects on Daily Life

During work 96% of patients suffered from leg impairment, while 64% also had problems in their arms. Figure 3 illustrates the restrictions in detail. These complaints led to occupational restrictions of varying severity. Over all the stages, 49% suffered from severe impairment in their jobs or were even completely unable to work. Figure 3 shows a differentiation by the stages.

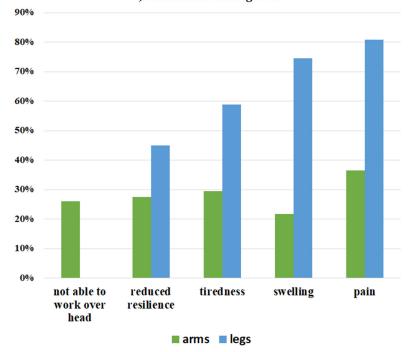
On a numeric rating scale from one to ten regarding the quality of life reduction (one = no reduction, ten = very severe reduction) across all stages, the most picked single score (25.33%) was the maximum score of ten (Figure 4).

There was a statistically significant, positive correlation between the stage of lipedema and the level of the numerical rating scale score (Spearman r = 0.55, ANOVA p < 0.001) (Figure 5a).

3.6. Mental State

The PHQ-9 was fully completed by 337 patients. In total, the mean value was 10.84 (± 6.39). In sum, the test suggested that 54.01% of lipedema patients were at risk of

suffering from a moderate to severe depressed mood. The higher the lipedema stage was, the higher the PHQ-9 score was (Spearman r = 0.2, ANOVA p = 0.002) (Figure 5b).



a) Restrictions during work

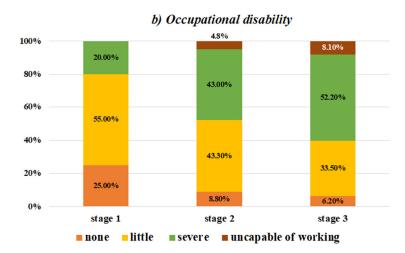


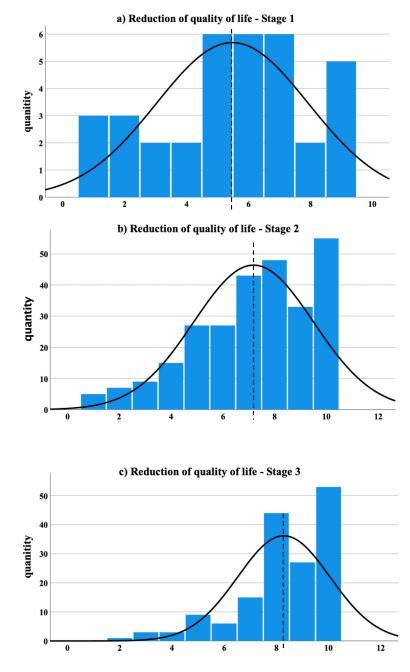
Figure 3. Restrictions and disability at work: (**a**) gives a detailed look at the restrictions during work, distinguishing whether arms or legs are affected, and (**b**) shows the degree of occupational disability differentiated by stage.

There was a highly significant positive correlation between the degree of occupational disability and the PHQ-9 score (Spearman r = 0.413, ANOVA p = <0.001) (Figure 5d).

Three hundred and thirty-three patients completed the WHOQOL-BREF questionnaire. The mean value of all the domains was 60.5 (\pm 16.02). The lowest scores were obtained in the physical (mean 54.54 \pm 20.1) and mental (mean 51.91 \pm 18.67) health domains, while the highest mean score was obtained in the environment domain (mean 71.85 \pm 16.00).

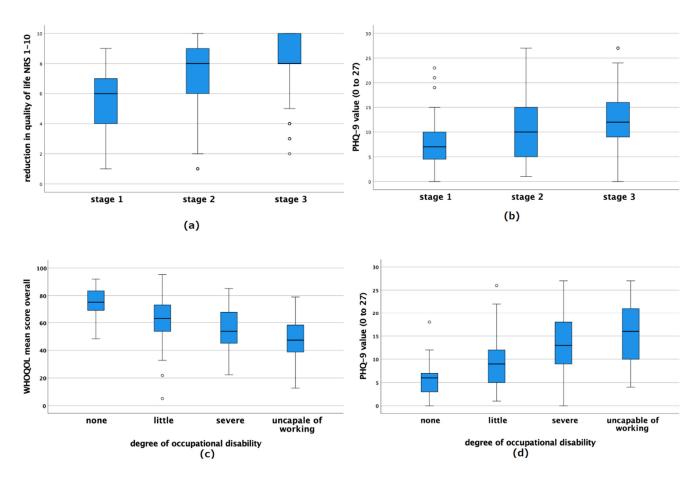
The WHOQOL-BRREF score had a highly significant negative correlation with the degree of occupational limitation (Spearman r = -0.406, ANOVA test *p* < 0.001) (Figure 5c).

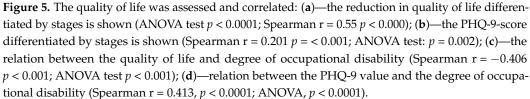
Patients who had a higher BMI also showed significantly lower scores in the WHOQOL-BREF questionnaire (r = -0.353, ANOVA p = 0.016).



There was a significant negative correlation between the PHQ-9 and the WHOQOL-BREF scores (Spearman r = -0.775, ANOVA p < 0.0001).

Figure 4. The reduction of the quality of life, by means of a numerical rating scale from one to ten, is differentiated by stage. The results for Stage 1 are shown in (a) (mean 5.49 ± 2.55), whereby Stage 2 is shown in (b) (mean 7.19 ± 2.13), and Stage 3 is shown in (c) (mean 8.29 ± 1.78). The dashed line illustrates the mean value. The solid curved line represents the normal distribution.





4. Discussion

Lipedema is a multifaceted disease that affects patients' lives in multiple ways. This study characterizes a large monocentric lipedema patient cohort prior to surgery, combining clinical data with validated HRQOL and depression questionnaires. The presence of the disease was confirmed by clinicians, and the stage was professionally determined according to the valid criteria.

Setting this baseline is crucial in order to accurately record and evaluate the effectiveness of liposuction for lipedema treatment, especially from the patient-reported outcome perspective.

The often-publicized observations that the disease initially becomes symptomatic during hormonal upheavals and multiple years pass from disease onset until correct diagnosis are supported by our findings [7,8,17,30].

One of the most serious symptoms of lipedema patients in our study, besides pain, was the tendency for frequent hematomas in the affected regions. As a possible explanation for this, a higher capillary fragility (CF) was observed with angiosterrometry using the Parrot's Angiosterrometer in 2008 [22].

The most commonly reported comorbidities, according to the current literature, is hypertension (13–27%) and hypothyroidism (20–35% or higher) [8,11,17,31]. Additionally, these observations were confirmed by our data. The clustered occurrence of hypothyroidism is particularly interesting, as this may promote obesity [32,33]. As demonstrated,

the BMI showed a highly significant positive correlation with lipedema progression. The increased accumulation of fatty tissue on the legs makes this a logical consequence. It should be critically questioned whether the sole determination of the BMI can provide a valid statement about the obesity status. Compared with obese populations, lipedema patients showed a lower prevalence of type 2 diabetes and hypertension [34,35].

The disease may be masked by concomitant obesity, making it difficult for the clinician to differentiate. Further studies may also elucidate the causal relationship between lipedema and patients' hormonal status. Here, another discriminant could be determined to increase the discriminatory power between lipedema and obesity.

As our data showed, more than a quarter of patients already unsuccessfully tried to lose weight. By losing about five kilograms of body weight, 40% had only limited success.

Recent publications have discussed the positive effects of special diets, such as Ketogenic or Mediterranean diets, on the body composition of lipedema patients [36,37]. As part of a multimodal treatment concept, more intensive nutritional medical consultations and individual discussions of the appropriate dietary form seem necessary. Patients should be offered professional sports counseling to reduce adipose tissue that is still reactive to dietary changes and exercise. Likewise, it could be necessary to analyze the body composition in a more detailed way. By using a bioimpendance analysis (BIA) quantification of fat accumulation, distribution, as well as monitoring it over the course of the therapy, is possible. In addition, it may be possible to identify differences between lipedema and obesity patients, which could be a diagnostic criterion and a distinctive feature in the future. This method is already widely used and could be applied in practice with little effort [38–41].

The current literature has already reported a familial clustering of the disease and suggested a genetic disposition [8,42,43]. Our data confirmed this clustering, especially among the patients' mothers and grandmothers. A bias in self-reporting cannot be excluded, because there may be an increased awareness for this disease in families where lipedema occurs. Nevertheless, it may be possible that the frequent occurrence in families offers a further diagnostic criterium to distinguish lipedema from obesity.

Lipedema patients show a high potential to develop depression or already suffer from depression. This is shown by increased scores in the PHQ-9 index and is also reflected in a significant quality of life reduction in lipedema patients. An increased 12-month prevalence for depression at 25% compared to about 8% in the general population has already been demonstrated [11,15,30]. We confirmed these findings with data from our large heterogeneous lipedema population.

The common practice of assessing the QoL or personal well-being with single-item questionnaires should be abandoned in future publications and clinical practice. By assessing the mental state of patients with valid and multimodal questionnaires, a comprehensive documentation can be obtained, with the QoL and the valid evaluated level of depression as valuable parameters.

Concerning surgical treatment options, not only with regards to the near-term reduction of adipose tissue and body weight but also with the long-term results, liposuction offers promising results so far. It may reduce the level of pain and general limitations in everyday or professional life and increase the quality of life and even the subjective quality of patients' sex lives [8,11,13–16,23,31,44–46]. Furthermore, it reduces the need for CDT in about 46% of patients, and a significant reduction (p = 0.0002) of the number of migraine attacks per month was observed after liposuction [11,14].

However, to date, there has been only one data series that monitored the same patient population several times over a long period of time [14]. In addition, some of the current data were collected retrospectively, meaning that patients had to recall their condition before their surgery [15]. A recall bias was excluded in our data, since patients self-reported their complaints prior to their first liposuction. In addition, the current literature lacks validated questionnaires on the quality of life and the psychological state of the patients. With a standardized procedure for PROMs, it will further be possible to determine whether

WAL or TLA is the best method for treating lipedema. Taking this into consideration, we will be able to adequately monitor our treatment progress and be able to present the effectiveness of liposuction with high-quality data. As the socioeconomic impact of lipedema has been underrated for a long time, providing extensive high-quality data will not only serve to provide best possible treatment for patients but also ensure the recognition of the surgical treatment concept and its compensation.

In conclusion, lipedema remains a poorly understood disease. This study provided insight on family clustering, clinical characteristics and health-related quality of life in patients prior to surgical treatment and thus provided a baseline for the outcome assessment. This evaluation will be crucial for the improvement of multimodal treatment concepts and thus sustainably improve the quality of treatment for patients.

Author Contributions: Conceptualization, M.H., H.K. and M.K.; Formal analysis, M.H.; Investigation, M.H.; Methodology, M.H.; Project administration, H.K. and M.K.; Resources, T.H. and M.K.; Supervision, H.K., M.-L.K., P.W., M.A., T.H. and M.K.; Visualization, M.H.; Writing—original draft, M.H.; Writing—review & editing, H.K., M.-L.K., P.W., M.A. and M.K. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: Ethic Committee Name: Ethics Committee of the Medical Association Westphalia-Lippe and the Westphalian Wilhelms University. Approval Code: 2021-684-f-S. Approval Date: 9 March 2022.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Conflicts of Interest: The authors declare no conflict of interest.

Appendix A

Fachklinik Hornheide

Figure A1. Shows the self-designed questionnaire, which is filled out by each lipedema patient at her first presentation for anamnestic and treatment planning reasons before the doctor's consultation at the Hornheide specialized clinic.

Dear patient, we would like to ask for your assistance. To get an overview of your individual case, please answer the following questions:

Table A1. Questionnaire for initial examination (Lipedema).

Name:						
Date of Birth:						
Date:						
Body size (in cm):						
Body weight currently (in kg):						
Former maximum weight (kg):						
Former minimum weight (kg):						
At what age were the first signs of increased fatty tissue on the legs?	0 0 0 0	puberty, age: pregnancy, age: Menopause, age: other:				

Table A1. Cont.

At what age was the diagnosis of lipedema made?	
Which areas were affected first?	 Only thigh only lower legs Whole leg arms buttocks
Which areas are affected now?	 Only thigh only lower legs Whole leg arms buttocks others:
Who in your family suffers from lipedema or noticeably thick legs?	 nobody mother Paternal grandmother Maternal grandmother Paternal aunt Maternal aunt siblings others:
what do you do professionally?	
What discomfort do your legs give you during work?	 none pain swelling tiredness reduced resilience
What discomfort do your arms give you during work?	 none pain swelling tiredness reduced resilience no overhead work possible
How would you rate the limitation of your ability to work due to lipedema? It affects me:	 none a bit very severe unable to work Since:
Have you tried any dietary changes or diets?	 no yes, with success yes with little success yes, but without success
If so, how many kg of weight did you lose:	 0-5 kg 6-10 kg 11-15 kg 16-20 kg Own value

Table A1. Cont.

	\sim	20
	0	no
	0	Dietician
Has help been sought for this?	\bigcirc	Nutritionist
	0	Nutritional doctor
	0	WeightWatchers
	Õ	others:
	0	outers
	0	no
	0	Gymx/week
		Nordic Walkingx/week
Do you do any kind of sport?	0	
Do you do any kind of sport.	0	swimmingx/week
	0	bikingx/week
	0	joggingx/week
	\bigcirc	others:
	~	
Did you receive manual lymphatic drainage?	0	yes
	0	no, never
	0	1×/wook
If yes, since when or in what period? How many times a week?	0	$1 \times / \text{week}$
if yes, since when of in what period: flow many times a week?	0	$2 \times / \text{week}$
	0	more than $2 \times / \text{week}$
	0	no notatall
	0	no, not at all
If so, does lymphatic drainage help or did it help?	0	a bit
, , , , , , , , , , , , , , , , , , , ,	\bigcirc	satisfactorily
	0	very good
	0	no
Do you wear flat knit compression garments?	0	yes, sometimes
	0	yes, regularly
	\bigcirc	mainly during the day
	0	mainly during the night
If yes, since when or during what period?	Õ	<8 h/Tag
	0	9–12 h/Tag
	0	24 h/Tag
	0	no
	0	yes
		5
Have you already had liposuction?If yes, on which body region and	0	Thighs
	0	Lower legs
how much? (Amount in liters)	\bigcirc	Upper arms
	\bigcirc	belly
	0	buttocks
	Õ	others:
	\bigcirc	No other disease known
	\bigcirc	hypertonia
	0	Diabetes mellitus
	Õ	Hyperthyroidism
Please provide information about your personal medical history.	0	Hypothyroidism
1 Jone Personal address of the second s		Hashimoto
	0	
	0	Joints problems
	\bigcirc	Skin problems
	0	others:

Have you had a thrombosis or is thrombosis known to occur in relatives?	0	no yes, following region:
Do you take medications regularly, if so, which ones?		
Do you need to take pain medication due to pain from your lipedema?	0 0 0 0	no yes, somtimes yes, every week yes, every day name of painkillers:
Are allergies known? (especially to antibiotics and local anesthetics).		
Do you smoke? If yes, how much daily?	0 0 0 0	No 5–10/Tag 11–15/Tag 16–20/Tag >20/Tag

Table A1. Cont.

Table A2. Please indicate the intensity of your discomfort on the following scales from 1 to 10.

	Mark Applicable Intensity with X									
Do you have pain in the affected areas?	none v 1	very stro 2	ong D 3	\square 4	\square 5	6	— 7		9	□ 10
Pain in the lower legs: (leave blank if none)	none v 1	very stro 2	ong D 3	\square 4	\square 5	6	— 7		9	□ 10
Pain in the thighs: (leave blank if none):	none v 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7		9	□ 10
Pain in the buttock: (leave blank if none):	none v 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7		9	□ 10
Pain in the belly: (leave blank if none):	none v D 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7	8	9	□ 10
Pain in the arms: (leave blank if none):	none v 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7		9	□ 10
Is there sensitivity to touch or pressure pain?	none v 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7		9	□ 10
Are you prone to bruising (hematomas)?	none v 1	very stro 2	ong D 3	\square 4	□ 5	6	— 7		9	□ 10

	Marile	A	hla Inta		uh V					
Mark Applicable Intensity with X										
Is there a feeling of tension in the legs?	none 1	very stro 2	ong 3	\square 4	 5	6	— 7	□ 8	9	□ 10
Is there a feeling of warmth in the legs?	none 1	very stro 2	ong 3	\square 4	\square 5	□ 6	 7	$\frac{1}{8}$	9	□ 10
Is there a feeling of cold in the legs?	none 1	very stro 2	ong 3	4	5	6	 7		9	□ 10
Do you have muscle cramps?	none 1	very stro 2	ong 3	 4	□ 5	6	 7		9	□ 10
Is there a feeling of heavy legs?	none 1	very stro 2	ong 3	 4	□ 5	6	— 7	8	9	□ 10
Is there a feeling of tired legs?	\square 1	very stro 2	3	\square 4	□ 5	□ 6	 7		9	□ 10
Does swelling occur?	none 1	very stro	ong 3	\square 4	5	6	— 7	$\boxed{8}$	9	□ 10
Do skin complications occur?	none 1	very stro 2	ong 3	\square 4	\square 5	□ 6	— 7		9	□ 10
Is there itching?	none 1	very stro 2	ong 3	\square 4	\square 5	6	\Box	$\frac{1}{8}$	9	□ 10
Are there any restrictions on walking?	none 1	very stro 2	ong 3	\square 4	 5	6	— 7		9	□ 10
How would you rate the reduction in your quality of life?	none 1	very stro 2	ong 3	\square 4	□ 5	□ 6	 7		9	□ 10
How satisfied are you with the appearance of your legs?	Very s	satisfied	very uns	safisfied 4	5	 6	— 7		9	□ 10

Table A2. Cont.

References

- Wold, L.E.; Hines, E.A., Jr.; Allen, E.V. Lipedema of the legs; a syndrome characterized by fat legs and edema. *Ann. Intern. Med.* 1951, 34, 1243–1250. [CrossRef] [PubMed]
- Allen, E.V.; Hines, E.A. Lipedema of the Legs: A Syndrome Characterized by Fat Legs and Orthostatic Edema. Lipedema Project. 1940. Available online: https://lipedemaproject.org/mayo-clinic-staff-meetings-vascular-clinics-x-lipedema (accessed on 16 August 2020).
- 3. Dudek, J.E.; Białaszek, W.; Ostaszewski, P.; Smidt, T. Depression and appearance-related distress in functioning with lipedema. *Psychol. Health Med.* **2018**, 23, 846–853. [CrossRef] [PubMed]
- 4. Herpertz, U. Krankheitsspektrum des Lipödems an einer lyphologischen Fachklinik. Vasomed. *Lymphologie* **1997**, *5*, 301–307.

- 5. Herpertz, U. Lipedema. Z Lymphologie **1995**, *19*, 1–7.
- 6. Marshall, M.; Schwahn-Schreiber, C. Prävalenz des Lipödems bei berufstätigen Frauen in Deutschland: (Lipödem-3-Studie). *Phlebologie* **2011**, *40*, 127–134.
- 7. Romeijn, J.R.M.; de Rooij, M.J.M.; Janssen, L.; Martens, H. Exploration of patient characteristics and quality of life in patients with lipoedema using a survey. *Dermatol. Ther.* **2018**, *8*, 303–311. [CrossRef]
- 8. Bauer, A.T.; von Lukowicz, D.; Lossagk, K.; Aitzetmueller, M.; Moog, P.; Cerny, M.; Erne, H.; Schmauss, D.; Duscher, D.; Machens, H.G. New insights on lipedema: The enigmatic disease of the peripheral fat. *Plast Reconstr Surg.* **2019**, *144*, 1475–1484. [CrossRef]
- Tiwari, A.; Myint, F.; Hamilton, G. Management of lower limb lymphoedema in the United Kingdom. *Eur. J. Vasc. Endovasc. Surg.* 2006, *31*, 311–315. [CrossRef]
- 10. Herbst, K.L. Rare adipose disorders (RADs) masquerading as obesity. Acta Pharmacol. Sin. 2012, 33, 155–172. [CrossRef]
- 11. Ghods, M.; Georgiou, I.; Schmidt, J.; Kruppa, P. Disease progression and comorbidities in lipedema patients: A 10-year retrospective analysis. *Dermatol. Ther.* **2020**, *33*, e14534. [CrossRef]
- 12. Herbst, K.L.; Mirkovskaya, L.; Bharhagava, A.; Chava, Y.; Te, C.H.T. Lipedema fat and signs and symptoms of illness, increase with advancing stage. *Arch. Med.* 2015, 7, 8.
- Witte, T.; Dadras, M.; Heck, F.-C.; Heck, M.; Habermalz, B.; Welss, S.; Lehnhardt, M.; Behr, B. Water-jet-assisted liposuction for the treatment of lipedema: Standardized treatment protocol and results of 63 patients. *J. Plast. Reconstr. Aesthetic Surg.* 2020, 73, 1637–1644. [CrossRef] [PubMed]
- 14. Baumgartner, A.; Hueppe, M.; Meier-Vollrath, I.; Schmeller, W. Improvements in patients with lipedema 4, 8 and 12 years after liposuction. *Phlebol. J. Venous Dis.* **2020**, *36*, 152–159. [CrossRef] [PubMed]
- 15. Dadras, M.; Mallinger, P.J.; Corterier, C.C.; Theodosiadi, S.; Ghods, M. Liposuction in the treatment of lipedema: A longitudinal study. *Arch. Plast. Surg.* 2017, 44, 324–331. [CrossRef] [PubMed]
- 16. Rapprich, S.; Dingler, A.; Podda, M. Liposuction is an effective treatment for lipedema-results of a study with 25 patients: Liposuction in lipedema. *JDDG J. Dtsch. Dermatol. Ges.* **2011**, *9*, 33–40. [PubMed]
- Dudek, J.E.; Białaszek, W.; Gabriel, M. Quality of life, its factors, and sociodemographic characteristics of Polish women with lipedema. *BMC Womens Health* 2021, 21, 27. [CrossRef] [PubMed]
- Meier-Vollrath, I.; Schneider, W.; Schmeller, W. Lipödem: Verbesserte Lebensqualität durch Therapiekombination. *Dtsch. Ärztebl.* 2005, 7, A1061–A1067.
- Schmeller, W.; Meier-Vollrath, I. Lipödem—Aktuelles zu einem weitgehend unbekannten Krankheitsbild. Aktuelle Dermatol. 2007, 33, 251–260. [CrossRef]
- Paling, I.; MacIntyre, L. Survey of lipoedema symptoms and experience with compression garments. Br. J. Community Nurs. 2020, 25, S17–S22. [CrossRef]
- 21. Deri, G.; Weissleder, H. Vergleichende prä-und posttherapeutische Volumenmessungen in Beinsegmenten beim Lipödem. *Lymph Forsch.* **1997**, *1*, 35–37.
- Szolnoky, G.; Borsos, B.; Bársony, K.; Balogh, M.; Kemény, L. Complete decongestive physiotherapy with and without pneumatic compression for treatment of lipedema: A pilot study. *Lymphology* 2008, 41, 40–44. [PubMed]
- Schlosshauer, T.; Heiss, C.; von Hollen, A.; Spennato, S.; Rieger, U.M. Liposuction treatment improves disease-specific quality of life in lipoedema patients. *Int. Wound J.* 2021, 18, 923–931. [CrossRef] [PubMed]
- 24. Berlim, M.T.; Pavanello, D.P.; Caldieraro, M.A.; Fleck, M.P.A. Reliability and validity of the WHOQOL BREF in a sample of Brazilian outpatients with major depression. *Qual. Life Res.* 2005, 14, 561–564. [CrossRef] [PubMed]
- 25. Kalfoss, M.H.; Reidunsdatter, R.J.; Klöckner, C.A.; Nilsen, M. Validation of the WHOQOL-BREF: Psychometric properties and normative data for the Norwegian general population. *Health Qual. Life Outcomes* **2021**, *19*, 13. [CrossRef] [PubMed]
- Whoqol Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol. Med.* 1998, 28, 551–558. [CrossRef] [PubMed]
- Gunzelmann, T.; Brähler, E.C.; Angermeyer, R.K.; Matschinger, H. Deutschsprachige Version der WHO Instrumente zur Erfassung von Lebensqualität WHOQOL-100 und WHOQOL-BREFM. 2002. Available online: https://www.semanticscholar.org/paper/C. -Angermeyer%2C-R.-Kilian-%26-H.-Matschinger%3A-Version-Gunzelmann-Br%C3%A4hler/725ce6eb69e18a7c5d1835cee5 8cf16e43ab26ea (accessed on 20 December 2021).
- Kroenke, K.; Spitzer, R.L.; Williams, J.B. The PHQ-9: Validity of a brief depression severity measure. J. Gen. Intern. Med. 2001, 16, 606–613. [CrossRef] [PubMed]
- 29. Arroll, B.; Goodyear-Smith, F.; Crengle, S.; Gunn, J.; Kerse, N.; Fishman, T.; Falloon, K.; Hatcher, S. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. *Ann. Fam. Med.* **2010**, *8*, 348–353. [CrossRef]
- Dudek, J.E.; Białaszek, W.; Ostaszewski, P. Quality of life in women with lipoedema: A contextual behavioral approach. *Qual. Life Res.* 2015, 25, 401–408. [CrossRef]
- Wollina, U.; Heinig, B. Treatment of lipedema by low-volume micro-cannular liposuction in tumescent anesthesia: Results in 111 patients. *Dermatol. Ther.* 2019, 32, e12820. [CrossRef]
- Sanyal, D.; Raychaudhuri, M. Hypothyroidism and obesity: An intriguing link. *Indian J. Endocrinol. Metab.* 2016, 20, 554–557. [CrossRef]
- Taylor, P.N.; Albrecht, D.; Scholz, A.; Gutierrez-Buey, G.; Lazarus, J.H.; Dayan, C.M.; Okosieme, O.E. Global epidemiology of hyperthyroidism and hypothyroidism. *Nat. Rev. Endocrinol.* 2018, 14, 301–316. [CrossRef]

- Gouda, P.; Zheng, S.; Peters, T.; Fudim, M.; Randhawa, V.K.; Ezekowitz, J.; Mavrakanas, T.A.; Giannetti, N.; Tsoukas, M.; Lopes, R.; et al. Clinical phenotypes in patients with type 2 diabetes mellitus: Characteristics, cardiovascular outcomes and treatment strategies. *Curr. Heart Fail. Rep.* 2021, *18*, 253–263. [CrossRef] [PubMed]
- 35. Al-Goblan, A.S.; Al-Alfi, M.A.; Khan, M.Z. Mechanism linking diabetes mellitus and obesity. *Diabetes Metab. Syndr. Obes. Targets Ther.* **2014**, *7*, 587–591. [CrossRef] [PubMed]
- Keith, L.; Seo, C.; Rowsemitt, C.; Pfeffer, M.; Wahi, M.; Staggs, M.; Dudek, J.; Gower, B.; Carmody, M. Ketogenic diet as a potential intervention for lipedema. *Med. Hypotheses* 2020, 146, 110435. [CrossRef]
- Di Renzo, L.; Cinelli, G.; Romano, L.; Zomparelli, S.; De Santis, G.L.; Nocerino, P.; Bigioni, G.; Arsini, L.; Cenname, G.; Pujia, A.; et al. Potential effects of a modified mediterranean diet on body composition in lipoedema. *Nutrients* 2021, *13*, 358.
 [CrossRef]
- Macias, N.; Alemán-Mateo, H.; Esparza-Romero, J.; Valencia, M.E. Body fat measurement by bioelectrical impedance and air displacement plethysmography: A cross-validation study to design bioelectrical impedance equations in Mexican adults. *Nutr. J.* 2007, *6*, 18. [CrossRef] [PubMed]
- Sartorio, A.; Malavolti, M.; Agosti, F.; Marinone, P.G.; Caiti, O.; Battistini, N.; Bedogni, G. Body water distribution in severe obesity and its assessment from eight-polar bioelectrical impedance analysis. *Eur. J. Clin. Nutr.* 2004, 59, 155–160. [CrossRef]
- Utter, A.C.; Lambeth, P.G. Evaluation of multifrequency bioelectrical impedance analysis in assessing body composition of wrestlers. *Med. Sci. Sports Exerc.* 2010, 42, 361–367. [CrossRef] [PubMed]
- Gibson, A.L.; Holmes, J.C.; Desautels, R.L.; Edmonds, L.B.; Nuudi, L. Ability of new octapolar bioimpedance spectroscopy analyzers to predict 4-component-model percentage body fat in Hispanic, black, and white adults. *Am. J. Clin. Nutr.* 2008, *87*, 332–338. [CrossRef]
- 42. Child, A.H.; Gordon, K.D.; Sharpe, P.; Brice, G.; Ostergaard, P.; Jeffery, S.; Mortimer, P.S. Lipedema: An inherited condition. *Am. J. Med. Genet. Part A* 2010, 152, 970–976. [CrossRef]
- Michelini, S.; Chiurazzi, P.; Marino, V.; Dell'Orco, D.; Manara, E.; Baglivo, M.; Fiorentino, A.; Maltese, P.E.; Pinelli, M.; Herbst, K.L.; et al. Aldo-Keto reductase 1C1 (*AKR1C1*) as the first mutated gene in a family with nonsyndromic primary lipedema. *Int. J. Mol. Sci.* 2020, 21, 6264. [CrossRef] [PubMed]
- 44. Baumgartner, A.; Hueppe, M.; Schmeller, W. Long-term benefit of liposuction in patients with lipoedema: A follow-up study after an average of 4 and 8 years. *Br. J. Dermatol.* **2015**, *174*, 1061–1067. [CrossRef]
- Schmeller, W.; Hueppe, M.; Meier-Vollrath, I. Tumescent liposuction in lipoedema yields good long-term results: Tumescent liposuction in lipoedema. *Br. J. Dermatol.* 2012, 166, 161–168. [CrossRef] [PubMed]
- Schmeller, W.; Meier-Vollrath, I. Tumescent liposuction: A new and successful therapy for lipedema. J. Cutan. Med. Surg. 2006, 10, 7–10. [CrossRef]