

Lipoedema

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Lipoedema is a disease characterized by excessive bilateral and symmetrical accumulation of subcutaneous tissue in the lower extremities. It is a poorly understood condition, and low awareness of its existence often leads to incorrect diagnosis. Initially, lipoedema was considered to be completely independent of lifestyle. Currently, however, more and more cases of the coexistence of lipoedema and obesity are described in the literature as additionally affecting the severity of the disease.

Keywords: lipoedema ; lipedema ; obesity ; quality of life

1. Introduction

As a disease, lipoedema is still not fully understood^{[1][2][3][4]}. So far, the pathomechanism and the degree of its general prevalence have not been established^{[4][5][6]}. Currently, available data suggest that genetic factors play a very important role in the development of lipoedema^{[7][8]}. Many researchers have attempted to determine the aetiology and mechanism of the development of lipoedema, but the presented data still remain mere hypotheses^{[1][2][3][4][9][10][11]}. The prevalence of lipoedema in the general public is also unknown, and the data from many sources in this regard is widely divergent^{[9][12][13]}. There is also a lack of systematic knowledge of the diagnostic criteria, which often leads to incorrect diagnosis^[14]. Difficulties in diagnosis result in a delay or absence of targeted treatment, which results in a much more severe course of the disease leading to disability^{[1][4][15][16]}. Lipoedema is defined as the pathological multiplication of adipose tissue cells due to hormonal change^[17]. The disease affects mainly women, and usually begins during puberty, pregnancy or menopause^[9]. Isolated cases of lipoedema in men have been described in the literature and hormonal disturbances were present in all cases^[9]. Lipoedema is characterized by a bilateral and symmetrical distribution of adipose tissue, mainly around the lower extremities^{[16][17]}. Its specific feature is the presence of a visible disproportion between a slim upper body and thickened lower limbs^{[11][18]}. What is also very important is that attempts to lose weight through intense physical activity and restrictive diets fail to reduce lipoedema, resulting only in the increase in the existing disproportion between the upper and lower half of the body^{[2][16]}. Other features that significantly distinguish lipoedema from other conditions are increased tendency to bruising, heaviness in the legs and high tactile sensitivity of the tissue affected by lipoedema^{[11][18][19]}. Therefore, lipoedema is not only an aesthetic problem but also has a significant impact on the functioning and mobility of the patient^{[1][4]}. Currently, the complexity and multifactorial nature of this disease are more and more emphasized. A major obstacle in the correct diagnosis of this disease is its coexistence with obesity. Excessive body weight in this case may mask some characteristic features of lipoedema. Obesity or being overweight is believed to accompany a very large group of patients with lipoedema, and it significantly worsens the symptoms of lipoedema and the patient's general condition^{[1][9][20]}.

Another important issue is the influence of mental state, both on the development of the initial symptoms of the disease and its role in the severity of the experienced ailments. Patients with lipoedema often face a lack of understanding from their environment, which negatively affects their self-esteem, thus resulting in physical limitation of daily activities^{[15][16][21]}. Lipoedema, due to its chronic and progressive nature, has a significant impact on the quality of life of patients affected by it^[22]. Very low awareness of lipoedema among physicians and the public often leads to misdiagnosis. In many cases, proper diagnosis is formulated many years after the symptoms of lipoedema appear^{[23][24]}. Alongside long-term lipoedema lasting a number of years, a mixed form of lipo-lymphoedema may develop. It is an advanced stage of the disease where, in addition to the symptoms typical of lipoedema, the patient successively develops lymphatic insufficiency, lymphoedema and other complications such as erysipelas or lymph ulcer^[25].

2. Lipoedema

2.1. Lipoedema and Body Weight Relationship

Body weight is assessed using the BMI, which is the ratio of body weight in kilograms to height, expressed in meters and squared. According to WHO, obesity is found at values above 30 kg/m², overweight 25–29.9 kg/m² and normal body weight 18.5–24.9 kg/m².

Four studies reported on the BMI of patients, and in all studies the largest proportion were classified as obese^{[20][23][26][27]}. This was greatest in the study by Erbacher (*n* = 150, 76.7%) who also reported the smallest proportion of participants with BMI in the normal range (3.3%)^[23]. The most recent study by Dudek reported the largest proportion of patients in the obese category (*n* = 95, 50%) and the least proportion of normal body weight cases (20.4%)^[26]. The BMI of the patient in the earlier study by Dudek and the study by Romeijn fall between these ranges^{[23][27]}. All BMI values are summarised in **Table 1**.

Table 1. Description of articles initially included by PRISMA methodology.

Reference	Number of Subjects	Data not available	Normal Body Weight	Overweight	Obesity
[27]	n=329	n=8	14 (4.3%)	40 (14.4%)	267 (81.3%)
[26]	n=98	n=3	20 (20.4%)	26 (26.5%)	49 (50%)
[20]	n=150	n=0	5 (3.3%)	15 (10%)	130 (86.7%)
[23]	n=163	n=0	21 (12.9%)	41 (25.2%)	101 (61.9%)
Total	n=729	n=11	60 (8.23%)	122 (16.735)	547 (75.04%)

Thomas F. Wright and Karen L. Herbst present a case report of a young woman with lipoedema. The first symptoms in the form of accumulation of adipose tissue around the thighs, calves and ankles appeared in her at the age of 12, and despite normal BMI (17 kg/m²), the disturbance in proportion was clearly marked. The woman, thinking she was obese, tried to lose weight using very restrictive diets and intense physical activity. Despite a significant reduction in body weight (BMI 15 kg/m²), the disproportion was still visible, and the woman developed anorexia. When she regained normal body weight (BMI 21 kg/m²), other symptoms appeared in the form of pressure sensitivity and tendency to bruising ^[28].

2.2. Lipoedema Associated Comorbidities

In 2019, a study was conducted in Korea to investigate the relationship between obesity and the development of subclinical and clinical lymphoedema in patients with lipoedema. A total of 258 women with lipoedema participated in the study. The subjects were divided into 3 groups according to BMI. Group 1 had 98 women with BMI less than 30 kg/m², group 2 had 124 with BMI between 30 and 40 kg/m², and group 3 had 36 women with BMI over 40. The occurrence of lymphoedema was assessed using bioimpedance. Subclinical lymphoedema was found least in subjects from group 1 (16.3%) and increased with increasing BMI to 48.3% in group 2 and 72.3% in group 3. Likewise, clinical lymphoedema was found least in subjects from group 1 (6.1%) and increased with increasing BMI to 51.6% in group 2 and to 77.8% in group 3. This proves a significant relationship between the occurrence of obesity and the appearance of lymphoedema in patients with lipoedema^[25].

Four studies reported on the presence of comorbidities and all indicated the presence of hypothyroidism among their cohorts ^{[23][24][26][29]}. Overall, the largest proportion of patients included in these studies were obese (28%), and 27.5%, 22.7%, and 19.2% were affected by hypothyroidism, depression, and allergies respectively. Sleep disorders and migraines were present in 12.5% of subjects followed by hypertension (10%) and asthma (9.4%). Bowel disorders were reported by 8.7% of patients, and 6.25% of patients suffered from rheumatic diseases. Out of all respondents, 6.2%, 6%, and 5.56% were affected by lymphoedema, heart disease, and diabetes respectively. The least portion of subjects reported dyslipidemia (3.8%), polycystic ovary syndrome (3.5%), skin disorders (3%) and fibromyalgia (3.2%). One quarter of all subjects had no comorbidities (25.2%). **Table 2** presents the number of comorbidities in people with lipoedema.

Table 2. Body weight in people with lipoedema.

Comorbidity	Ghods M. ^[29] (n=106)	Dudek J.E. ^[26] (n=98)	Bauer A.T. ^[24] (n=209)	Romeijn J.R.M. ^[23] (n=163)	Total (n=576)
Allergy	39 (36.8%)	-	72 (34.4%)	-	111 (19.27%)
Obesity	39 (36.8%)	49 (50%)	-	81 (49.7%)	161 (28%)
Sleep disorders	27 (25.5%)	-	45 (21.5%)	-	72 (12.5%)
Hypothyroidism	33 (31.1%)	31 (31.6%)	75 (35.9%)	19 (11.65%)	158 (27.5%)
Depression	27 (25.5%)	56 (57.14%)	48 (23%)	-	131 (22.74%)
Hypertension	26 (25.5%)	4 (4.1%)	28 (13.4%)	-	58 (10%)
Migraine	24 (22.6%)	-	47 (22.5%)	-	71 (12.5%)
Skin disorders	20 (18.8%)	-	-	-	20 (3.5%)
Asthma	19 (18%)	-	27 (12.9%)	8 (4.9%)	54 (9.4%)
Bowel disorders	11 (10.4%)	4 (4.1%)	27 (12.9%)	8 (4.9%)	50 (8.7%)
Rheumatic diseases	9 (8.4%)	20 (20.4%)	7 (3.3%)	-	36 (6.25%)
Dyslipidemia	7 (6.6%)	-	15 (7%)	-	22 (3.8%)
Diabetes (type 1 and 2)	5 (4.7%)	13 (13.3%)	5 (2.4%)	9 (5.5%)	32 (5.56%)
Polycystic Ovary Syndrome	3 (2.8%)	5 (5.1%)	12 (5.7%)	-	20 (3.5%)
Lymphoedema	-	30 (30.6%)	-	5 (3%)	35 (6%)
Venous insufficiency	-	20 (20.4%)	-	-	20 (3.5%)
Fibromyalgia	-	4 (4.1%)	-	14 (8.5%)	18 (3.2%)
Heart disease	-	-	-	35 (21.5%)	35 (6%)
Lack of comorbidities	13 (12.3%)	18 (18.4%)	43 (20.6%)	71 (43%)	145 (25.17%)

2.3. Quality of Life

In order to assess the quality of life of the respondents, two publications used the WHOQOL-BREF (The World Health Organization Quality of Life) form, one used RAND 36, and one used EQ5 DL3 L^{[23][26][27]}.

J R.M Romeijn et al. conducted a study in the Netherlands to check the quality-of-life level among patients with lipoedema using the EQ-5 D-3 L and RAND-36 survey forms. EQ-5 D-3 L analyses quality of life from the viewpoint of health. The questionnaire consists of five parts, and assesses mobility, independence, daily activities, pain, and depression levels. The mean value of the EQ-5 D-3 L index was lower (66.1/100) in patients with lipoedema compared to the general Dutch population (85/100). Daily activities such as work, study, and household chores were difficult for 64.8% of the respondents, while 3.1% were completely unable to perform these tasks. Disorders of the musculoskeletal system occurred in 63% of the respondents, but only 9.9% reported difficulties with washing and dressing, and 1.2% of the

respondents were unable to get dressed without assistance. The occurrence of ailments involving pain was confirmed by 74.1% of patients, and 16.7% described the pain as severe. Depression was found in 42% of respondents^[23].

The same study also used another form to assess quality of life, namely RAND-36. It is a 36-item questionnaire assessing nine aspects of health: perception of general health; physical functioning; mental health; pain; impact of limitations stemming from emotional problems; and dysfunctions caused by physical limitations, social functioning, vitality, and changes in health status. The total RAND score differed significantly between patients with lipoedema (59.3/100) and the mean score in the Dutch population (74.9/100)^[23].

A study published by Dudek in 2018, which included 329 patients with lipoedema, showed a relationship between the quality of life and a more severe course of the disease, depression, and reduced mobility. An inverse relationship was found between quality of life and severity of symptoms of lipoedema ($r = -0.651$), severity of depression ($r = -0.75$), and stress level stemming from physical appearance ($r = -0.654$). It was also observed that the higher the mobility, the better the perception of quality of life ($r = -0.607$), where r is the relationship between two variables, i.e., the strength of the correlation^[27].

2.4. Time of Diagnosis

Table 3 presents average waiting time for diagnosis of lipoedema.

Table 3. Occurrence of comorbidities among people with lipoedema.

Reference	Average Age of Onset	Average Age of Diagnosis	Average Waiting Time for Diagnosis
^[23]	20 years of age	38.3 years of age	18.3 years
^[24]	16 years of age	31 years of age	15 years

2.5. Psychological Stress and Pain

Erbacher and Bertsch conducted a study to check the impact of psychological stress on the development of symptoms of lipoedema. Two interviews were conducted with each of the 150 respondents. For the purposes of the study, psychological stress was defined as the presence of a mental illness (according to ICD-10: eating disorders, depression, anxiety disorders, post-traumatic stress disorder, and panic attacks) or the presence of symptoms that may indicate a mental illness. The interview also included the severity of lipoedema symptoms and the severity of pain. Depressive disorders, eating disorders, post-traumatic stress disorder, and anxiety disorders occurred in 51.1% of the respondents. In addition, it was also noted that the above diseases were more common in patients with BMI higher than 40 kg/m² compared to those with a lower BMI. Pain intensity was measured using a 10-point VAS (Visual Analogue Scale), where 0 is no pain and 10 is maximum pain. No pain and very slight pain (1 point on the VAS scale VAS) were not indicated by any of the respondents. The value of 2 points on the VAS scale was indicated by 0.7% of the respondents, 3 by 2.7%, 4 by 13.3%, 5 by 14%, 6 by 18%, 7 by 17.3%, and 8 by 19.4%; pain intensity at 9 points on the VAS scale was indicated by 8.7% of the respondents, and the maximum level of perceived pain occurred in 6% of the respondents. After comparing the level of pain with the occurrence of psychological stress, it was shown that in patients with mental disorders, the level of perceived pain on the VAS scale was higher (on average, 6.95 points on the VAS scale in patients with mental disorders, 6.32 in patients with no mental disorders)^[20].

3. Conclusions

A majority of lipoedema patients is also overweight or obese and with the increase in BMI, the risk of lymphoedema in patients with lipoedema also increases. Lipoedema significantly reduces the level of quality of life, and there is a relationship between the level of perceived pain and the occurrence of psychological distress in lipoedema patients.

Further research should be carried out to increase knowledge about lipoedema and to establish specific diagnostic criteria, which would decrease the waiting time for diagnosis. There is a need to carry out more clinical trials in which patients with diagnosed lipoedema participate. Currently, the number of randomized controlled trials concerning lipoedema patients is low, and as mentioned before, the survey research and clinical observations are not absolutely objective.

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