GŁOWACKA, Justyna, TEKIELA, Natalia, PAPACHRISTOFOROU, Natalie, MICHAŁKA, Daria, GAŁUSZKA, Zuzanna, MAKAR, Monika, BARTUŚ, Tomasz, BĄK, Emilia, KOCJAN, Aleksandra and CHMIEL, Radosław. Lipedema: diagnosis, treatment and the vicious cycle - a review of the literature. Quality in Sport. 2025;38:57746. eISSN 2450-3118.
https://doi.org/10.12775/QS.2025.38.57746
https://apcz.umk.pl/QS/article/view/57746

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 12.01.2025. Revised: 05.02.2025. Accepted: 05.02.2025. Published: 05.02.2025.

Lipedema: diagnosis, treatment and the vicious cycle - a review of the literature

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Abstract

Introduction

Lipedema is a chronic condition that affects the majority of women. It involves swelling in fatty parts of the body such as the buttocks, hips, thighs and calves. It usually develops during a period of hormonal changes (puberty, pregnancy or menopause) and is often confused with lymphoedema or obesity, leading to a delay in correct diagnosis and the introduction of effective treatment. Fat oedema is estimated to affect 1 in 72,000 people. However, these figures, according to many sources, are much underestimated compared to the actual occurrence of the condition due to misdiagnosis. [1]

Purpose of Research

The aim of this work is to commonize the knowledge around the problem of lipedema, presenting the current diagnosis and treatment.

State of knowledge

Lipaemia is a chronic disease characterised by the development of fatty oedema in the lower extremities (in some cases also in the upper extremities), which is resistant to exercise. The pathogenesis of the disease is unclear and diagnosis and treatment still require much research.

Review Methods

The literature review was based on the most recent studies. PubMed and Google Scholar open databases were used in the research. The focus was put on literature published between 2013 and 2024.

Summary

Lipedema hinders women's physical, psychological and social functioning. Current diagnosis and treatment is not sufficient to be certain of an accurate diagnosis and to apply appropriate treatment. However, knowledge about this disease is becoming more publicised, through media, among other means, and research is being conducted at a larger scale.

Keywords: lipedema, liposuction, ketogenic diet, vicious cycle in lipedema, lipid oedema.

Background information

Lipid oedema makes it difficult for a person to function. The characteristic symptoms of lipedema are: a silhouette with a narrow waist and a large lower body; typical distribution of fat deposits on the lower limbs; pain and tenderness of the fatty tissue; feet are not affected by oedema (cupping phenomenon); increased tendency to hematoma formation, bruising [2].

In the advanced stages of the disease, swelling and reduced mobility may occur. [3], [4]

Complications that may occur in the course of this disease include joint problems, obesity-related diseases and psychological problems. [5]

In 2022, Johanna Falck and her team published the results of a survey on the relationship between lipedema and quality of life, in which 245 women took part. The findings showed that the disease was associated with a reduced quality of life. Additionally, the greatest limitations and the worst physical health were recorded in women in the advanced stage of the disease. [6]

Lipedema can also affect a person's psychosocial functioning. It causes low self-esteem, feelings of hopelessness and self-blame, exacerbate depression, anxiety, eating disorders, social isolation and appearance-related stress. [7], [8], [9], [10]

In 2021, an online survey was conducted by Joanna E. Dudek, Wojciech Białaszek and Marcin Gabriela on the severity of depressive symptoms in patients with fat oedema. This was a cross-sectional survey, with 98 women participating. The results indicated that as the severity of the disease increased and the symptoms became more apparent, the greater the severity of depression. [11]

The pathophysiology of lipedema is still not fully known. There are several theories on the origin of lipedema. One is that genetic predisposition and potential estrogen changes play a major role in the onset of lipedema.[12], [13] Another theory suggests that lipid oedema results from loss of tissue elasticity and vascularization disorders. Loose connective tissue, containing elastin, supports the function of blood and lymphatic vessels. The increase in adipose tissue in lipoid oedema impairs elasticity, hindering lymphatic vessel function and leading to capillary leakage. Hypoxia then triggers VEGF activation, promoting adipose tissue proliferation. Unfortunately, research supporting these theories is limited by the difficulty of obtaining samples and the lack of suitable research models. [1], [14], [15]

Adipose tissue in lipedema disease is characterized by being resistant to common weight loss methods such as diet and exercise, and therefore requires specialized treatment.[16]

Further research is needed to develop effective diagnostic criteria and therapeutic strategies.

Diagnostics

Lipedema is still little known among doctors. Only 9% of respondents received a correct diagnosis at their first visit. In 46% of people, symptoms appeared in adolescence, but the average age of diagnosis was 44 years. Many people noted that their complaints were mistakenly attributed to being overweight, unhealthy eating habits or lack of exercise. [17]

In 2018, S. Reich-Schupke, E. Mohren & M. Stücker in Germany conducted a survey on the diagnosis and therapy of patients with lipedema. They analyzed the data of 72 patients, most of which were women. The main symptoms included leg swelling and a feeling of heaviness, and the diagnoses were most often made by specialists. The study identified discrepancies in the diagnosis and therapy of lymphatic diseases, requiring further education for doctors, physiotherapists, medical equipment suppliers and patients. [18]

Diagnosis of lipoid oedema begins with a detailed medical history and clinical examination. [19], [20] During the interview, the duration and course of symptoms, factors that exacerbate them and the response to previous treatments such as lymphatic drainage or compression garments should be considered. It is also important to consider family history, as lipoid oedema often occurs in women in the same family. [20] The characteristic symptom is a symmetrical increase in the amount of fatty tissue in the limbs while remaining disproportionate to the torso. It is often accompanied by swelling, a tendency to bruise and hypersensitivity to touch. [19]

Diagnosis requires assessment of limb asymmetry, scarring, location of the oedema and tissue quality, including response to toe pressure. The fatty hypertrophy typical of lipedema spares the feet, resulting in visible narrowing at the ankles. [20]

Figure 1. 5 types of lipedema distribution. [20]

Type I	Type II	Type III	Type IV	Type V
Lipedema fat accumulates around the hips and buttocks	Lipedema fat accumulates in the area from the waist to the knees, resembling breeches	Lipedema fat accumulates from the waist to the ankles	Lipedema fat accumulates on the arms. Approximately 80% of women with lipedema have this type together with fatty oedema on the legs.	Lipedema fat accumulates on the calves. This type is rare.

Fatty oedema is divided into three stages:

Stage I: smooth skin with small nodules and reversible oedema;

Stage II: walnut-sized nodules, uneven skin;

Stage III: thickened skin with macro nodules and accompanying lymphoedema. [21]

In the diagnosis of lipidemia,the differentiation in diagnosis between lymphoedema and obesity is important. It is made difficult by the fact that there are few hard diagnostic criterias. However, there are exclusion criteria for lipidemia by which oedema can be excluded.[22]

Figure 2. Exclusion criteria in lipidemia. [22]

Exclusion criteria
- Lack of disproportion between upper and lower body - Asymmetrical fat distribution in the legs or arms, - Symptoms appear in late adulthood, - Patients have a waist-to-hip ratio greater than 0.85 in women and 1.0 in men - A pathological waist-to-height ratio of more than 0.5 in those under 40 years of age, 0.5-0.6 in those 40-50 years of age and more than 0.6 in the elderly. - There are no characteristic folds in the ankle area, - The tissues are not painful upon pressure, - There is no tendency to bruise easily - The thickness of the subcutaneous tissue measured 6-8 cm above the ankle is less than 12 mm.

The diagnosis of lipedema relies heavily on differentiating it from lymphoedema. The key difference between the two conditions is that lipedema usually causes symmetrical oedema, whereas lymphoedema causes asymmetrical oedema. In lipedema, the feet and hands are not occupied by oedema.[21] Additionally, lymphoedema with lipid oedema can occur at any stage of the disease. After years of the disease, the lymphatic vessels become inefficient, leading to increased oedema. In advanced stages, joint deformities often occur due to excess soft tissue. [23], [24]

In the differential diagnosis, Stemmer's sign is an important indicator. It involves pinching the top of the dorsum of the foot. If the patient cannot do this then the result is positive and indicates the presence of lymphoedema. [24], [25]

In contrast to lipoid oedema, in obesity there is a uniform distribution of fat throughout the body. In addition, lipoid oedema is often associated with pain and frequent bruising.[4], [26]
The table below shows the differences between fatty oedema (lipedema), lymphoedema and obesity. [39]

Figure 3. Differences in lipedema, lymphoedema and obesity. [39]

	lipedema	lymphoedema	obesity
Difference between waist and legs	Yes	Possible	No
Symmetrical occurrence on both legs	Yes	Possible	Yes
Pain	Yes	Yes	No
Involvement of feet and ankles	No	Yes	No

Additional ancillary investigations are carried out only in exceptional cases. The disease is chronic and progressive, with individual variations in its course, making it difficult to predict its progression.[19]
Increasingly, the use of diagnostic imaging is being attempted in the diagnosis of fat oedema. In 2021 Marina Cestari conducted a study on 40 patients. It showed that 3D ultrasound allows an accurate assessment of changes in the subcutaneous tissue, such as hypertrophy of fatty lobules, fibrosis and the presence of fluid along the fascia. [27]
In 2023, Raquel F. D. van la Parra and his team conducted a study to characterize lipedema and test the usefulness of imaging in diagnosis. The experiment involved 1154 patients with lipedema. Thirty-two studies were analyzed. However, the results showed the limited effectiveness of this method. [28]

Patient education

The diagnosed patient should be given reliable information about the disease. They should be informed about all treatment options. In addition, psychological support should be offered and contact to self-help organisations should be provided. The patient should be carefully informed about the complex decongestive therapy. This involves the use of various methods aimed at improving lymph flow and reducing fluid retention in the body. This is important in the treatment of conditions associated with oedema. [21]

Treatment

The treatment of lipedema remains a challenge as there is no causal therapy available. The main aim is to reduce symptoms, improve lower limb function, increase patients' quality of life and halt disease progression. Therapy includes both conservative and surgical approaches. Conservative treatment includes manual lymphatic drainage, compression therapy using a flat compression knit, physiotherapy, dietary advice (weight control) and educating the patient on self-treatment.

The patient should be informed that conservative treatment serves to alleviate symptoms and also prevents complications, however, it has little effect on the appearance of the legs. [21]

In 2022, a pilot study was conducted by Monika Czerwińska, Jacek Teodorczyk, Dawid Spychała, Rite Hansdorfer-Korzon to test the usefulness of compression therapy. Six women took part in the study. The qualification consisted of an interview with the participants to verify that they met certain criteria, such as female sex, age between 18 and 60 years, no contraindications to physical activity and the use of compression therapy, and the presence of symptoms typical of fat oedema: disproportion between the torso and lower limbs, a feeling of heaviness in the legs, pain during physical examination, easy bruising or difficulty in reducing body weight. Half of the women used only exercise for 6 weeks, while the remainder used compression therapy with flatware in addition to exercise. The effects of treatment were assessed by measuring body circumference and weight, analysing subjective symptom severity using a special questionnaire, examining skin and fat thickness using ultrasound, and assessing quality of life. The results showed a significant effect of compression therapy in reducing symptoms and improving quality of life. [29]

In 2023, a study was published to test whether body composition changes (physical activity) affect quality of life in patients with lipedema. Twenty-two women aged 18-65 years with a BMI corresponding to overweight and grade I obesity took part in this test. They did high

intensity interval training for 8 weeks. Weight reduction and reduction in hip circumference were observed, with no change in body composition. Physical exercise appeared to have a positive impact on quality of life in lipidemic subjects. [30]

Diet

Fat tissue formed in lipedema is resistant to weight loss. Studies have shown that a very low-calorie ketogenic diet reduces inflammation caused by the disease more than other weight-loss diets. [1], [31]

In 2021, Robert Cannataro's study was conducted. The 22-month experiment involved a 32-year-old woman diagnosed with lipid oedema. She was fed a ketogenic diet with a deficit of 250 kcal. The patient lost 41 kg of weight and the circumferences decreased in all areas, including those occupied by lipedema. In addition, a reduction in CRP was observed in laboratory tests, which may indicate a reduction in inflammation. [1], [32]

There are several theories according to which the ketogenic diet reduces symptoms and improves the quality of life of lipedemic patients while traditional diets do not. The first possible reason is that adipocytes in lipedema may require lower levels of insulin to activate lipolysis, the second that they have impaired sensitivity to glucagon, the third that they may be resistant to insulin despite systemic insulin sensitivity. [8] The effect of the ketogenic diet on lipedemic patients requires further study.

Nutritional supplements

People at present are increasingly turning to dietary supplements of various kinds. Their current use in the treatment of fat oedema is unproven. However, there are micronutrients and molecules that are worth looking out for.

Vitamin C

It has an antioxidant effect and can therefore have a positive impact on inflammation in lipedema. In addition, it supports collagen synthesis.

Polyphenols

Similarly to vitamin C, they have antioxidant effects. They have been shown to be effective in the treatment of inflammation and pain, and have been confirmed in studies on rheumatic diseases, fibromyalgia and polycystic ovary syndrome.

Omega 3 fatty acids

These have proven anti-inflammatory effects, particularly docosahexaenoic acid and eicosapentaenoic acid . Consumption of these two acids promotes adipocyte health, reduces macrophage activation, pro-inflammatory cytokine secretion and the synthesis of mediators that modulate inflammation and pain. To alleviate the symptoms of lipedema, it is recommended to consume at least 1 g, and in the initial phase up to 2 g of these acids per day.

Serratiopeptidase

Lipidemia can be used in the treatment of oedema through its fibrinolytic and proteolytic properties. It is sensitive to gastric acid, so high doses of up to 2 g per day are used. Liposomal and sublingual formulations are being developed. However, its best effects are observed when applied topically.

Bromelain

Studies on this enzyme have shown that it has fibrinolytic and clot-draining effects. It has the added advantage of being safe to use. However, there are no specific studies with its use in lipid oedema.

Vitamin D

Numerous studies show its negative correlation with adipose tissue. Its levels also influence the proper functioning of adipose tissue.

Vitamin B12

It has positive effects on nervous system function. In lipaemia, neuropathic soreness is increasingly highlighted by which vitamin B12 may be beneficial. Based on plasma values, supplementation of 500-1000 mcg is suggested. [40]

Surgical treatment – liposuction

In advanced stages of the disease. When conservative treatment is unsuccessful, surgical treatment, e.g. liposuction, should be considered. In order to spare the lymphatic vessels as much as possible, it should be performed using a wet technique. The most common technique

is tumescent liposuction, in which the solution used reduces pain and bleeding. Water-assisted liposuction and energy-assisted liposuction are also used. This is the only treatment method in which the fat tissue causing the disease is removed. [4], [21] In studies, this method shows good results. A great improvement in quality of life, a reduction in pain and a decrease in the tendency to develop haematomas are observed.[21]

In 2016-2017, a study was conducted by Thomas Witte and his team, in which 130 operated patients were given questionnaires before surgery. In them, they assessed the symptoms of the disease. They were then followed up in January 2019. The study showed a high treatment success rate. The surgery resulted in a reduction in symptoms and a reduction in the need for conservative treatment. [33]

There is also a study showing the longer-term impact of liposuction on lipedema patients. In 2022, the results of an analysis by Krupp and his team were published. They included patients who underwent liposuction between July 2009 and 2019, with patients completing questionnaires six months after surgery. This study also showed a beneficial effect on patients with fat oedema. Decreased symptoms of the disease and a reduced need for conservative treatment were observed. [34]

The vicious cycle

There is a growing body of research showing a link between pain, physical activity and mental health. Pain in patients with lipedema reduces their quality of life and exacerbates depression, so a susceptible therapeutic goal for lipedema is to reduce it. [35] In addition, physical activity is an important factor in mental health. It also results in reduced sensitivity to pain. A common cause of mental deterioration in lipedema is pain and physical and aesthetic impairment. [36] People with fat bingeing have an increased level of depression, which provokes reduced physical activity. Lack of physical activity and ongoing pain provoke increased depression. [37]

Increased depression lowers the threshold of sensitivity to pain by reducing physical activity. This creates a vicious cycle.

A study was conducted in 2022 with 3 hypotheses:

1. the increased pain increasing depression
2. high levels of physical activity leading to good mental health
3. the association of the combination of high pain and low physical activity with poor mental health.

The study included 511 women not undergoing surgical treatment. They completed questionnaires assessing quality of life, depression, physical activity and symptoms of illness. The results showed a significant impact of pain and physical activity on mental health.[36] In addition, it has been shown that regular physical activity can reduce sensitivity to pain. [38]
The problem for regular physical activity in lipedema is also reduced mobility and pain.
This study therefore shows that the synergistic effect of pain and low physical activity has a major impact on the treatment of patients with lipedema.[36]

Summary

Lipedema is a rarely diagnosed condition that significantly reduces quality of life. Unfortunately, we currently do not know its cause with certainty, so we can only reduce the discomfort and counteract the symptoms. It is often mistaken by doctors for lymphoedema or obesity, and the treatment given is inappropriate. It often leads to psychiatric disorders such as depression, which is why it is so important to commonize the knowledge about this disease. Today's diagnosis mainly involves a physical examination and history. Treatment includes conservative therapy with compression therapy, physiotherapies and weight management, and surgical treatment with liposuction. A great improvement in patients' function has also been observed with the inclusion of a ketogenic diet. Lipedema requires further research into the pathophysiology and effective diagnostic and therapeutic criteria.

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All authors have read and agreed with the published version of the manuscript.

Conflict of interest: The authors confirm no conflict of interest.

Funding Statement: No external funding was received to perform this review.

Statement of Institutional Review Committee: Not applicable.

Statement of Informed Consent: Not applicable.

Statement of Data Availability: Not applicable.

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