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Major clinical outcomes of dietary therapy in patients with lipedema in the preoperative period of plastic surgery: a systematic review

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Abstract

Introduction: The first clinical study on dietary therapy in lipedema showed improvement in general body composition and in specifically affected areas (upper and lower limbs) with the consumption of a low-carbohydrate diet and foods high in antioxidants inspired by the Mediterranean diet. **Objective:** It was to explore the main directions of dietary therapy in patients with lipedema as a pre-operative management tool for plastic surgery. **Methods:** The PRISMA Platform systematic review rules were followed. The research was carried out from August to September 2025 in the Scopus, PubMed, Science Direct, Scielo, and Google Scholar databases. The quality of the studies was based on the GRADE instrument and the risk of bias was analyzed according to the Cochrane instrument. **Results and Conclusion:** A total of 127 articles were found, and 33 articles were evaluated in full, and 23 were included and developed in the present systematic review study. Considering the Cochrane tool for risk of bias, the overall assessment resulted in 15 studies with a high risk of bias and 29 studies that did not meet GRADE and AMSTAR-2. Most studies showed homogeneity in their results, with X^2=71.5%>50%. It was concluded that in the pre-operative phase of plastic surgery for lipedema, the ketogenic diet effectively induced weight loss and fat mass, including in the limbs, areas considered unresponsive to dietary therapy in patients with lipedema. The best results were obtained with the combination of the ketogenic diet and carboxytherapy, which showed both an improvement in body composition and a reduction in pain, as well as an improvement in sleep quality. Healthy eating patterns for lipedema can be whole foods, enzyme-rich, plant-based, or ketogenic. Research favors plant-based low-carb diets, which correlate with decreased all-cause mortality relative to animal-based diets. Furthermore, vitamin D levels must be monitored and normalized in people with lipedema. A low-calorie diet based on foods rich in anti-inflammatory and antioxidant nutrients could contribute to the well-being of patients with lipedema, improving quality of life, and reducing asthenia, pain,

and anxiety. Selenium can reduce oxidative stress, which plays an important role in lipedema. MicroRNAs produced by the stromal vascular fraction of lipedema represent important therapeutic targets for the treatment of lipedema. Precision nutrition is an emerging branch of nutrition science that aims to use omics technologies (metabolomics) to better target the nutritional treatment of lipedema.

Keywords: Plastic surgery. Lipedema. Diet therapy. Nutrology. Pre-operative.

Introduction

Lipedema is a progressive, multifactorial, and disabling autosomal dominant inherited disease characterized by the accumulation of pathological subcutaneous adipose tissue in the superficial area, microangiopathy, chronic tissue inflammation, and pain [1]. Symptoms usually occur during puberty, pregnancy, or menopause, with estrogens playing a role in the pathophysiological process. Diagnosis is clinical; adipose tissue develops symmetrically and bilaterally in a descending manner, with the lower limbs being the most affected areas. It is classified into five types based on the distribution of lipedematous adipose tissue and into four stages based on the severity of the disease [2].

In this context, the first clinical study on dietary therapy, as a preoperative management of plastic surgery, in patients with lipedema showed improvement in overall body composition and in specifically affected areas (upper and lower limbs) with the consumption of a low-carbohydrate diet and foods high in antioxidants inspired by the Mediterranean diet [3]. The ketogenic diet is characterized by a low carbohydrate intake of <30 g/day, shifting from cellular glucose metabolism to lipid metabolism, thus inducing fat oxidation and ketosis (defined as a blood concentration of beta-hydroxybutyrate >0.5 mmol/L) [4-7].

In this sense, the authors Keith et al. (2021) [8] published a review article encouraging the ketogenic diet in patients with lipedema as the most effective therapy, even as a preoperative treatment. The hypothetical mechanisms involved are the reduction of insulin and therefore lipogenesis and lipohypertrophy promoted by hyperinsulinemia, increased satiety, both by the intake of a greater amount of lipids and by the improvement of brain sensitivity to leptin, modulation of inflammation, reduction of oxidative stress, carried out by beta-hydroxybutyrate [9], reduction in sensitivity to mechanical, thermal and/or neuropathic pain after several weeks of ketosis [10].

The authors Susan et al. (2008) [4] hypothesized that carbohydrate restriction reduces neuronal excitability, suppressing pain perception, reducing inflammation, and increasing adenosine levels, a natural analgesic. In addition, a decrease in discomfort and depression related to appearance was highlighted after a reduction in weight and body fat, particularly in the most affected areas [11,12].

Therefore, the present study aimed to conduct a systematic review to explore the primary directions of dietary therapy in patients with lipedema as a preoperative management strategy for plastic surgery.

Methods

Study Design

This study followed an international model for systematic review, adhering to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Available at: http://www.prisma-statement.org/?AspxAutoDetectCookieSupport=1. Accessed on: 09/16/2025. The methodological quality standards of AMSTAR-2 (Assessing the methodological quality of systematic reviews) were also followed. Available at: https://amstar.ca/. Accessed on: 09/16/2025.

Data Sources and Search Strategy

The literature search process was conducted from August to September 2025 and developed using Scopus, PubMed, Lilacs, Ebsco, Scielo, and Google Scholar, encompassing scientific articles from various periods up to the present day. The following descriptors were used (DeCS/MeSH Terms): *"Plastic surgery. Lipedema. Diet therapy. Nutrology. Pre-operative",* and the Boolean operator "and" was used between MeSH terms and "or" between historical findings.

Study Quality and Risk of Bias

Quality was classified as high, moderate, low, or very low regarding the risk of bias, clarity of comparisons, precision, and consistency of analyses. The most evident highlight was for systematic review articles or meta-analyses of randomized clinical trials, followed by randomized clinical trials. Low-quality evidence was attributed to case reports, editorials, and brief communications, according to the GRADE instrument. The risk of bias was analyzed according to the Cochrane instrument through the analysis of the Funnel Plot (Sample size versus Effect size), using Cohen's d test.

Results and Discussion

Summary of Findings

A total of 127 articles were submitted to eligibility analysis, with 23 final studies selected to compose the

results of this systematic review. The listed studies presented medium to high quality (Figure 1), considering the level of scientific evidence of studies such as meta-analyses, consensus, randomized clinical trials, and prospective and observational studies. Biases did not compromise the scientific basis of the studies. According to the GRADE instrument, most studies showed homogeneity in their results, with X^2=71.5%>50%. Considering the Cochrane tool for risk of bias, the overall evaluation resulted in 15 studies with a high risk of bias and 29 studies that did not meet the GRADE and AMSTAR-2 criteria.

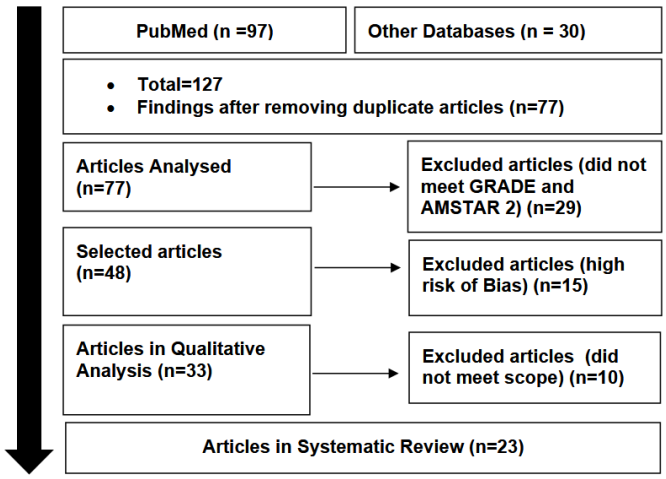

Figure 1. Flowchart - Article selection process. Source: Own authorship.

Figure 2 presents the results of the risk of bias of the studies using the Funnel Plot, showing the calculation of the Effect Size (Magnitude of the difference) using Cohen's d test. Precision (sample size) was determined indirectly by the inverse of the standard error (1/Standard Error). This graph showed a symmetrical behavior, not suggesting a significant risk of bias, both between studies with small sample sizes (lower precision) shown at the bottom of the graph and in studies with large sample sizes shown at the top.

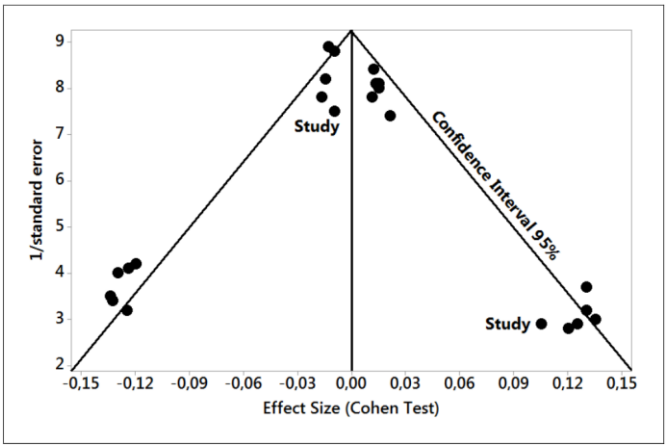

Figure 2. The symmetrical funnel-plot does not suggest a risk of bias among the small sample size studies shown at the bottom of the graph. Studies with high confidence and high recommendation are shown above the graph (n=23 studies). Source: Own authorship.

Main Outcomes – Lipedema, Dietary Therapy, and Plastic Surgery

In the context of preoperative lipedema nutritional treatment, dietary plans for people with lipedema should minimize postprandial insulin and glucose fluctuations and be sustainable in the long term. Healthy dietary patterns for lipedema may include whole foods, rich in enzymes, plant-based [13,14] or ketogenic diet (KD) [15]. Research favors low-carbohydrate plant-based diets, which correlate with decreased all-cause mortality compared to animal-based diets [16]. Furthermore, vitamin D levels should be monitored and normalized in people with lipedema [17].

Based on the literature findings selected by quality and risk of bias criteria, in recent years, the use of the KD as an appropriate nutritional treatment for lipedema has been raised in the literature. A clinical study conducted by Di Renzo et al. (2023) [18] evaluated the ketogenic diet and carboxytherapy in patients with lipedema. The modified Mediterranean ketogenic diet (MMKD) was used in combination with carboxytherapy. Since lipedema is characterized by microangiopathy, local hypoxia, and increased deposition of subcutaneous adipose tissue (SAT), carboxytherapy can improve painful symptoms and skin tone. Data analysis included 22 subjects, divided into three groups: 8 patients underwent MMKD combined with carboxytherapy sessions (KDCB group), 8 underwent only MMKD nutritional treatment (KD group), and 6 patients underwent only carboxytherapy sessions (CB group), totaling 10 weeks of treatment for all three groups. The ketogenic diet effectively induced weight and fat mass loss, including in the limbs, areas considered unresponsive to dietary therapy in patients with lipedema. However, the best results were obtained with the combination of the ketogenic diet and carboxytherapy, which showed improvements in body composition and skin texture and pain reduction, as well as improved sleep quality.

In this scenario, conservative therapeutic strategies in lipedema aim to reduce symptoms and prevent complications and disease progression. Thus, to improve the quality of life of patients with lipedema, it is essential to find a dietary strategy that aims at weight loss and reduction of fat mass in typical lipedema areas, such as the lower limbs, but that also aims at reducing pain caused by orthostatic edema and expansion of inflamed subcutaneous tissue. Regardless of BMI, early nutritional therapy is recommended at the time of

diagnosis to prevent the development of obesity and the progression of lipedema, as well as a preoperative measure [1,2].

The nutritional treatment, in this case, is a diet inspired by the Mediterranean (ketogenic) diet in terms of food choices, since it is low in carbohydrates, low in salt and simple sugars, does not include processed foods and is rich in antioxidant foods, such as foods with high concentrations of PUFA and MUFA (e.g., oily fish, nuts and extra virgin olive oil). These nutrients play an essential role in the inflammatory process, promoting an anti-inflammatory effect [3].

In this respect, it has already been found that a low-calorie diet based on foods rich in anti-inflammatory and antioxidant nutrients could contribute to the well-being of patients with lipedema, with improved quality of life, reduced asthenia, pain, and anxiety [3]. A clinical study conducted by the authors Di Renzo et al. (2021) [19] evaluated body composition and changes in general health status in a group of patients with lipedema (LIPPY) and a control group (CTRL) after four weeks of a modified Mediterranean diet (mMeD). 29 subjects were included in the data analysis, divided into two groups: 14 LIPPY and 15 CTRL. After the mMeD, both groups significantly reduced weight and body mass index. CTRL also showed a reduction in all circumferences and all fat mass compartments. LIPPY showed a decrease in fat mass in the upper and lower limbs. In LIPPY, an increase in patients' ability to perform various daily physical activities related to fat loss in the arms and legs was observed. According to the European Quality of Life scale, the possibility of LIPPY subjects performing simple daily activities with less fatigue, pain, and anxiety stands out.

Also, selenium is a trace element used by the human body in selenoproteins. Its main function is to reduce oxidative stress, which plays an important role in lipedema and lymphedema. In addition, selenium deficiency is associated with impaired immune function. In this sense, a retrospective cross-sectional study carried out by the authors Pfister et al. (2020) [20] determined the prevalence of selenium deficiency in these conditions and whether it is associated with disease severity and an associated medical condition, such as obesity. The data consisted of 791 patients during 2012-2019, in whom the selenium level was determined as part of the treatment. Selenium deficiency was found to be common in patients with lymphedema, lipedema, and lipolymphedema, affecting 47.5% of the studied population. Selenium levels were significantly lower in patients with obesity-related lymphedema compared to patients with cancer-related lymphedema.

Jeziorek et al. (2023) [21] analyzed changes in blood parameters after a low-carbohydrate, high-fat (LCHF) diet in women with lipedema compared to overweight or obese women. A total of 115 women were classified into two groups: a lipedema group and an overweight/obesity group. Both study groups followed the calorie-restricted LCHF diet for 7 months. A total of 48 women completed the study. A significant decrease in triglycerides and an increase in HDL-C concentrations were observed in both study groups. Despite the increase in LDL-C concentration observed in the lipedema group, the changes in LDL-C differed among individual patients. Improvements were observed in liver parameters, glucose tolerance, and a decrease in fasting insulin levels, although these were less pronounced in the lipedema group than in the overweight/obese group. Renal and thyroid functions were similar before and after the LCHF diet in both groups. The LCHF diet may be a valuable nutritional strategy for women with lipedema and those who are overweight/obese.

The authors Priglinger et al. (2020) [22] performed a complete comparative characterization of extracellular microRNAs (miRNAs) from the vascular stromal fraction (VSF) of healthy adipose tissue and lipedema. For this, we analyzed 187 extracellular miRNAs in concentrated conditioned medium (cCM) and specifically in small extracellular vesicles (sEVs) enriched by size exclusion chromatography. No significant difference in average particle size and concentration was observed between the sEV fractions in healthy individuals and those with lipedema. Most miRNAs were found to be predominantly located in the cCM compared to the sEV-enriched fraction. Surprisingly, hierarchical clustering of the most variant miRNAs showed that only the sEV miRNA profiles, but not the cCM miRNAs, were impacted by lipedema. Seven sEVmiRNAs (miR-16-5p, miR-29a-3p, miR-24-3p, miR-454-p, miR-144-5p, miR-130a-3p, let-7c-5p) were differentially regulated in lipedema compared to healthy individuals, while only one cCMmiRNA (miR-188-5p) was significantly downregulated in lipedema. These findings made it possible to identify the microRNAs produced by lipedema's VSF as important treatment targets.

Finally, precision nutrition is an emerging branch of nutritional science that aims to use modern omics technologies (genomics, proteomics, and metabolomics) to assess an individual's response to specific foods or dietary patterns and thus determine the most effective dietary or lifestyle interventions to prevent or treat specific problems, potentially targeting the nutritional treatment of lipedema more specifically. In fact, it can be used to comprehensively

characterize the thousands of chemicals in food, identify food byproducts in biofluids or human tissues, characterize nutrient deficiencies or excesses, monitor biochemical responses to dietary interventions, track long-term or short-term eating habits, and guide the development of nutritional therapies. Metabolomics can be combined with genomics and proteomics to study and advance the field of precision nutrition [23].

Conclusion

It was concluded that in the preoperative period of lipedema plastic surgery, the ketogenic diet effectively induced weight and fat mass loss, including in the limbs, areas considered unresponsive to dietary therapy in patients with lipedema. The best results were obtained with the combination of the ketogenic diet and carboxytherapy, which showed both improvement in body composition and reduction in pain, as well as improved sleep quality. Healthy dietary patterns for lipedema may include whole foods, enzyme-rich foods, plant-based foods, or ketogenic foods. Research favors low-carbohydrate, plant-based diets, which correlate with decreased all-cause mortality compared to animal-based diets. Furthermore, vitamin D levels should be monitored and normalized in people with lipedema. A hypocaloric diet based on foods rich in anti-inflammatory and antioxidant nutrients could contribute to the well-being of patients with lipedema, improving quality of life and reducing asthenia, pain, and anxiety. Selenium can reduce oxidative stress, which plays an important role in lipedema. MicroRNAs produced by the vascular stromal fraction of lipedema represent important therapeutic targets for the treatment of lipedema. Precision nutrition is an emerging branch of nutritional science that aims to use omics technologies (metabolomics) to better target the nutritional treatment of lipedema.

CRediT

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Informed Consent

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Conflict of Interest

The authors declare no conflict of interest.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

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It was performed.

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