Lymphology 58 (2025) 108-118

A CASE SERIES ON COMBINING MODIFIED MEDITERRANEAN DIET AND KETOGENIC DIET IN A "SANDWICH" APPROACH FOR PATIENTS WITH LIPEDEMA AND COMORBIDITIES

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ABSTRACT

The Ketogenic Diet (KD) is currently the most widely studied nutritional approach for patients with lipedema, although its use may cause important drawbacks especially in case of comorbidities. A Modified Mediterranean Diet (MMed) is more easily adaptable, better tolerated, and can be temporarily replaced by a ketogenic diet for a short period of time if necessary using a sort of "sandwich" approach. We report 10 clinical cases with lipedema and comorbidities subjected to a hypocaloric MMed for 6 months. All patients were properly assessed by anthropometric measurements and body composition before and at the end of nutritional treatment. Only 2 patients needed a short period of KD due to poor response to MMed. At the end of 6-month follow-up, patients showed weight loss with reduction in body circumferences and improvement in body composition. In the two cases where it was necessary to resort to a period of KD, good results were achieved allowing a return to the MMed for the maintenance. In patients suffering from lipedema with associated comorbidities and concomitant pharmacological treatments, the use of MMed as first line treatment allows achievement of better metabolic balance, greater compliance, and improved body composition.

Keywords: Lipedema; Comorbidities; Ketogenic diet; Modified Mediterranean diet; Nutritional approach.

INTRODUCTION

Lipedema: clinical aspects

Lipedema is a chronic disease, classified among subcutaneous adipose tissue (SAT) disorders characterized by a symmetrical, bilateral disproportional expansion of the SAT in the extremities (typically sparing hands and feet), compared to that in the torso. This condition is accompanied by increased physical sensitivity, pain, discomfort, swelling and heaviness in the body areas with lipedema-related volume increase. Patients with lipedema often experience easy bruising in affected areas. The estimated prevalence of lipedema is 1:72,000, most of whom are females (men with lipedema are extremely rare) (1). According to studies conducted by Child et al. (2), lipedema is likely a genetic condition with X-linked dominant inheritance, but this is far from determined.

Patients with lipedema frequently suffer from other comorbidities such as insulin-resistance (46%), Hashimoto's thyroiditis (27%), hypovitaminosis D (50%), hypermobility (15-20%), endometriosis (11%), menstrual cycle alterations (21%), poly-cystic

ovary syndrome (PCOS), systemic nickel allergic syndrome (SNAS), osteoporosis, anaemia, hepatic insufficiency, etc.

Lipedema adipose tissue is characterized by a hyperplasia and hypertrophy of adipocytes, which leads to chronic tissue hypoxia and release of macrophages and cytokines, with a resulting low-grade systemic inflammation. Lipedema fat is resistant to standard hypocaloric dietetic and exercise approaches, and therefore only 5% of patients succeed in losing weight and fat mass (3-7).

The chronic inflammation status causes oxidative stress and also insulin-resistance, which operates at two levels: in the adipose tissue increasing lipogenesis and decreasing lipolysis, and in the muscles reducing glucose uptake and protein synthesis, with a consequent reduction in muscular glycogen storage and sarcopenia.

Lipedema is also characterised by a reduction in release of adiponectin and leptin, which normally counter inflammation and regulate glucose metabolism, so when their levels are lower glucose metabolism is dysregulated resulting in a higher production of advanced glycation end products (AGEs) and insulin-resistance.

Another factor which seems to contribute to the maintenance of the inflammatory status, is the alteration of intestinal permeability ("leaky gut") and microbiota composition (dysbiosis). These conditions frequently lead to colitis, irritable bowel syndrome (IBS), food allergies and intolerances that tend to maintain the inflammation if not considered in the nutritional treatment (8).

Dietetic and nutritional approach to lipedema

Only recently has dietary intervention been included in conservative non-pharmacological treatment of lipedema. Although there are still no standardized protocols for the dietary treatment of lipedema, the main approaches studied in literature mainly focus on a low-carb diet. This is due to its effect of reducing inflammation and pain perception (9-13), support of the lymphatic system, and its ability to counter typical insulin-resistance of lipedema adipose tissue by lowering blood insulin and glucose, leading to suppression of the hyperinsulinemia effects (1,10,14-16).

Among the low-carb diet approaches the main studied ones have been KD, MMed and the diet for Rare Adipose Disorders (RAD). Although there is a lack of clinical trials concerning KD in treatment of lipedema, it is considered the most effective approach at the moment for its efficacy in terms of weight loss, regulation of inflammation and oxidative stress, reduction of edema, and of sensitivity to mechanical, thermal and neuropathic pain, increase in sense of satiety, and reduction of depression (17-22).

However, KD is not easily adapted to every patient, since some problems can occur: 1) lack of adherence to the diet in patients who are not able to manage the strictness of the KD, or those not achieving expected results, or even those undoing achieved results after ceasing the diet resulting in an even worse initial point; 2) even considering KD could be based on the Mediterranean approach, including unsaturated fats such as olive oil, nuts and avocado, it can never be compared to the Mediterranean diet (MD) in terms of the adequate amount of fruit and vegetables, and therefore it can never have the same positive healthy effects as the MD; 3) KD is not suitable for every kind of patients due to its high level of fats (70-80%), which can be poorly tolerated in cases of pathological conditions and concomitant pharmacological treatment like hepatic dysfunctions or insufficiency, cancer treatment, diabetes, hypertension, dyslipidaemias, previous cholecystectomy, malabsorption syndrome etc.; 4) the KD should not be followed for a long period (usually recommended no longer than 12 weeks), so it is not the best option when it comes to educate the patient to a dietetic lifestyle to be maintained for life.

On the contrary, a dietetic approach characterized by an higher amount of carbohydrates (35-40% of the total energy amount) and a lower amount of fats (35-45%) compared to the ketogenic distribution of macronutrients, can be more easily accepted and therefore followed by patients. This diet also provides a

TABLE 1
Clinical cases with Type and Stage of lipedema and comorbidities

Patients	Diagnosis of lipedema	Comorbidities
1	Lipedema type 3, stage 3	Hypercholesterolemia
2	Lipedema types 3 and 4, stage 2	History of non-Hodgkin's lymphoma
3	Lipedema type 3, stage 2	Crohn's disease,
4	Lipedema type 3, stage 2	IBS (Irritable Bowel Syndrome),
5	Lipedema type 3, stage 2	Insulin-dependent diabetes
6	Lipedema type 2 and 4, stage 2	Hypercholesterolemia
7	Lipedema type 3, stage 2	Liver dysfunction,
8	Lipedema types 3 and 4, stage 3	Liver dysfunction,
9	Lipedema type 3, stage 2	IBS
10	Lipedema type 3, stage 2	Hypercholesterolemia

higher amount of antioxidant, anti-inflammatory and immunomodulatory micronutrients such as polyphenols, tocopherols, resveratrol, vitamin C, vitamin A, which have been demonstrated to operate also at the epigenetic level by modulating the expression of genes related to inflammation and oxidative stress.

Di Renzo et al. (1) examined the effects of a hypocaloric MMed on patients suffering from lipedema compared to a control group, focusing on the fat mass (FM) loss in upper and lower limbs and the improvements on general health status, perception of pain, fatigue and other typical problems arising in this category of patients. Results showed a significant loss of FM and a general improvement in quality of life, with a reduction in asthenia, pain and anxiety thanks to the improvement of body condition.

Di Renzo et al. also conducted a different study (3), based on a diet inspired by the MD in terms of food choice but very low in carbohydrates (< 10% of the total energy expenditure) and therefore ketogenic, which they classified as Modified Mediterranean Keto-Diet (MMKD). They concluded that a ketogenic or ketogenic-like diet could never reach the same anti-inflammatory effect of the typical MD or similar. After 1-year on MMKD, patients showed a significant loss of BW, FM, waist and hip circumferences, with a maintained lean mass throughout the entire duration of the study, contrary to the results of very low-calorie ketogenic diets (VLCKD) observed in other studies (10,19,22).

Among the low-carb approaches, Herbst (23) introduced the Rare Adipose Disorders diet (RAD), which is based on: 1) a low intake of lacteals, animal-derived protein and fats, simple sugars, carbohydrates with a high glycemic index, salt, wheat, products with a high content of preservatives and sweeteners, processed food, junk food, alcohol, soy; and 2) a high intake of fruit, vegetables, cereals, plant-based proteins and fats, grass-fed meat, wild-caught fish, free-range eggs, carbohydrates

with a low glycemic index (generally anti-inflammatory foods). There is no indication about the macronutrient distribution concerning the RAD diet, but it is rather a guide to food quality.

MATERIALS AND METHODS

Study design and subjects

Inclusion criteria were adults with lipedema with or without functional lymphatic and venous insufficiency. Exclusion criteria were subjects with eating disorders (ED) and inability to follow the nutritional plan for a proper period of time. Subjects were enrolled between October 2024 and May 2025. A total of 10 women diagnosed with lipedema type 2, 3, or 4 and stage 2 or 3, with comorbidities (*Table 1*), aged 34 to 55 years old, with BMI between 27.0 and 44.5 kg/m^2, underwent a specific nutritional approach together with the treatment of associated disorders. All patients received detailed information about the study and provided written informed consent prior to enrollment.

Clinical evaluation and diagnosis of lipedema, as well as determination of lipedema type and stage, were performed at baseline (T0) by a physician with expertise in lymphology and adipose disorders.

Anthropometric evaluation

Body weight and height were measured using a weight scale with altimeter (SECA, Hamburg, Germany), and used to calculate BMI (Body Mass Index) as body weight (kg)/ height (m^2). Subjects were classified as normal weight, overweight or obese, based on the classification of the World Health Organization (WHO) (24-25).

Hip and waist measurements were obtained. Hip (= the largest part of the buttocks), waist (= the midway between the lower rib and the iliac crest) and thigh circumference were measured at baseline and at every check-up using a flexible and extensible metric tape. All the anthropometric measurements were taken while the subject was only wearing underwear.

We evaluated body composition at baseline and at every check-up by a bioelectrical impedance analysis using a bioimpedance analyser (BIA 101 BIVA® Pro, Akern, Florence, Italy), that measured resistance (Rz), reactance (Xc) and phase angle (PhA) through an alternating current at a frequency of 50 kHz, applied by means of 2 electrodes placed on the right hand and 2 on the right foot after cleansing the skin with alcohol. Before analysis, patients were asked to fast for at least 8 hours and to avoid coffee and physical exercise for at least 12 hours, in order not to get an overestimated result of basal metabolic rate (BMR). Measurements were made on an electrically isolated medical bed, while the subjects were only wearing underwear and were laying in supine position with legs at 45° compared to the median line on the body and the arms at 30° from the trunk, in such a way that every limb was separated from the others.

Obtained results were processed by Bodygram software, resulting in a complete evaluation of body composition for total body water (TBW), extracellular body water (ECW), intracellular body water (ICW), fat mass (FM), fat free mass (FFM), body cell mass (BCM), musculoskeletal mass Janssen (SMM), appendicular skeletal muscle mass (ASMM), basal metabolic rate (BMR), and total daily energy expenditure (TDEE).

Nutritional Anamnesis and Dietary Assessments

An accurate anamnesis was performed for each patient in order to assess physiological status (digestion, bowel function, sleep, menstrual function), pathological status, allergies, intolerances, pharmacological therapy, weight history, dietetic history, lifestyle (daily physical activity level, smoke, alcohol consumption etc.). Dietary habits were also examined.

Pain Level Assessment

Level of pain perceived by patients before and after the nutritional intervention was assessed utilizing a visual analogue scale (VAS)

TABLE 2
Total Daily Energy Expenditure (TDEE), energy restriction percentage compared to the TDEE, dietary energy intake and macronutrient distribution (% of proteins, carbohydrates and fats of the total energy intake) in all enrolled patients

Patients	TDEE (kcal/die)	Energy deficit (%)	Dietary energy intake (kcal/day)	Proteins (%)	Carbo-hydrates (%)	Fats (%)
1	2250	-35	1450	30	5	65
2	1750	-28	1250	25	35	40
3	1950	-25	1450	25	35	40
4	2000	-30	1400	25	40	35
5	1800	-27	1300	25	40	35
6	2000	-35	1300	30	5	65
7	2000	-30	1400	25	40	35
8	2200	-27	1600	25	40	35
9	2000	-30	1400	20	40	40
10	2350	-32	1600	25	40	35

where patients rated their pain from 0 ("no pain at all") to 10 ("worst possible pain").

Nutritional intervention

Diets were either MMed or a combined nutritional intervention, that we called "sandwich" approach, which consists in an initial MMed regimen, a subsequent short period of KD if necessary, and finally a return to the MMed.

A total of 10 patients underwent 6 months of a moderate-carbohydrate diet. Of the 10 patients, 8 followed the MMed for the whole period of 6 months. In 2 cases KD was necessary for 2 months in between the MMed in the sequence of 2 initial months of MMed, followed by 2 months of KD, and then 2 months of MMed for maintenance. This combined nutritional approach had become necessary due to a response block to the first phase of MMed dietary regimen.

The MMed consisted in a daily caloric intake varying between 1250 and 1600 kcal, with an average caloric restriction of 500-800 kcal/day compared to the daily energy requirements. The distribution of macronutrients was set as follows: 35-40% of the total energy expenditure of carbohydrates, 35-45% of fats and 20-25% of proteins. The caloric distribution of the meals depended on the patients' needs according to habits and work shifts.

The energy intake of dietary plans was elaborated according to individual energy need (calculated as basal metabolic rate (BMR) x physical activity level (PAL)), aiming to lose baseline weight. Dietary plans were tailored based on eating habits and preferences, but

also on comorbidities.

The MMed is based on the consumption of typical Mediterranean food with a lower daily carbohydrate intake compared to the glucidic intake recommended by the typical Mediterranean diet (45-60%). The MMed's daily macronutrient intake is broken down as follows: 35-40% of the total energy expenditure of carbohydrates, 35-45% of fats and 20-25% of proteins (*Table 2*). From a qualitative point of view, MMed consists of lipid sources mainly of vegetable origin (extra-virgin olive oil, olives of good quality, avocado, nuts, oilseeds), complex carbohydrate sources (to promote effect of dietary fiber modulation of inflammation, immune response, and intestinal microbiota composition), seasonal fruits and vegetables, fermented foods (yogurt, kefir), and protein sources mainly of plant origin. It was recommended to consume legumes with a frequency of 3-5 times/week) and/or protein sources rich in anti-inflammatory substances including omega-3, vitamins and antioxidants and consumption of fish 3-4 times/week preferring the blue fish and wild salmon, and consumption of eggs from hens raised on land with a frequency of 2-3 times/ week. It was also recommended to limit the consumption of saturated fats, added sugars, processed foods, salt (to be partly replaced with the use of anti-inflammatory spices and herbs, such as curry, turmeric, rosemary etc.) and soy (for its content in phytoestrogens, which are demonstrated to enhance the lipogenesis in lipedema).

The patients were advised to take supplements mainly based on bromelain, L-carnitine, diosmin, hesperidin, vitamin C, vitamin B, caffeine, melilot, guarana and birch, variously combined together. Moreover, patients were suggested to drink about 1.5 liters of water per day, avoiding alcohol.

For each of the 10 patients, anthropometric measurements and body composition were evaluated by bioimpedance, at the beginning and at the end of the nutritional treatment. For each patient the daily caloric requirement (TDEE) was estimated based on basal metabolism estimates (via BIA and Harris-Benedict formula) and reported daily physical activity level (LAF), from which the average daily caloric intake of the diet was established. The food plan was also formulated on the basis of other comorbidities and dietary habits and preferences. This also helped to ensure good adherence to the diet throughout the 6-month follow-up. The choice of macronutrient distribution was based on already existing eating habits and daily physical activity level, in order to ensure good adherence to the diet and avoid energy losses during the day.

Patients were also advised to perform low-impact physical activities such as walking, Pilates, yoga, exercise bikes, swimming, aqua gym, and light weight training.

RESULTS

Enrolled subjects presented with various stages and types. Lipedema at stage 2 was found in 80% of cases with stage 3 was found in 20% of cases. Lipedema of type 2 and 4 was found in 10% of patients, type 3 in 70%, and type 3 and 4 in 20% (*Table 1*).

At the end of the 6-months follow-up, all cases showed a significant weight loss with reduced body circumferences and a clear improvement in body composition in terms of reduction of FM and increase in fat free mass (FFM), but also an improvement in the distribution of body water between the extra- and intracellular compartment. An average reduction of weight loss of 10.8 kg was obtained, an improvement of BMI from 31.2 to 26.9 kg/m^2, a reduction of waist, hips, and thighs circumference respectively of 12.4 cm and 11.5 cm, a fat mass decrease of 9 kg and extracellular water decrease of about 2 L (*Table 3*).

Patients also reported an improvement in symptoms related to lipedema (mainly reduction in volume, pain and heaviness) and improvement of functional lymphatic insufficiency, which had been demonstrated mainly at the deep lymphatic circulation by lymphoscintigraphy. These changes were documented using the lymphatic transport index (LTI – normal value < 10) and improvement in functional lymphatic insufficiency was demonstrated by a decrease in LTI (average pre-treatment LTI value 15, and post-treatment 7) (*Fig. 1*) with a marked improvement in the

TABLE 3
Clinical outcome after dietary intervention with MMed or MMed + KD + MMeed

Patients	Weight loss (kg)	T0 BMI (kg/m²)	T1 BMI (kg/m²)	Waist loss (cm)	Hips loss (cm)	Fat Mass loss (kg)	Extra-Cellular Water loss (L)
1*	-7.7	35	31.8	-7.2	-4.8	-8.4	-0.8
2	-10.0	30.2	26.1	-15	-12	-6.6	-3.4
3	-12.4	29.6	23.2	-16	-8	-10.3	-2.1
4	-11.0	28.9	24.9	-19	-20	-10	-1.0
5	-8.8	27	22.8	-7	-12	-7.2	-1.6
6*	-11.1	32.6	28.7	-14.4	-16.5	-10.2	-0.9
7	-16.5	28	22	-9	-4	-12.7	-3.8
8	-12.3	44.5	39.4	-13.5	-16	-9.4	-2.9
9	-9.3	27	23.7	-6	-12	-8.1	-1.2
10	-9.4	29	26.8	-17	-10	-7.2	-2.2
Average	-10.8	31.2	26.9	-12.4	-11.5	-9.0	-2.0

*2 patients utilized the combined nutritional approach (MMed + KD + MMeed) (patients 1 and 6) and the other 8 patients utilized only MMed.

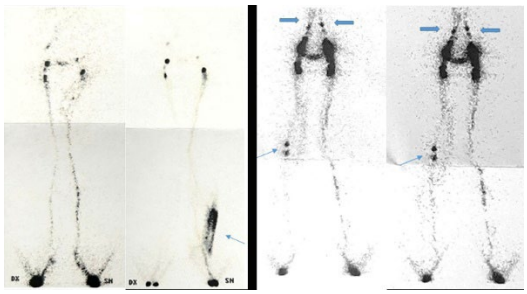

Fig. 1. *(Left Panels) Pre-treatment lymphoscintigraphy shows impairment of the deep lymphatic circulation (popliteal nodes are not visualized bilaterally), poor visualization of lumbar-aortic chains, and minimal dermal backflow in the left leg. Lymphatic transport index value is 16 for these images. (Right Panels) Post-treatment lymphoscintigraphy shows improved deep lymphatic circulation on the right (popliteal nodes visualized), visualization of iliac and lumbar-aortic chains, and disappearance of dermal backflow in the left leg. Lymphatic transport index value is improved to 9 for these images.*

quality of life and body perception. There was also a marked improvement in pain perception, with an average pain reduction of 48% (*Table 4*), and a consequent improvement in quality of life and body perception.

Eighty percent of subjects did not need a change in the diet because during the entire period of study since they showed positive results in terms of weight loss with good adherence to the diet. In two patients, a modification to the nutritional plan was needed (case 1 and case 6 in *Table 3*), because of a lack of response to the MMed (patient 1) and a block of efficacy of the MMed after 2 months (patient 6). In these 2 cases, a ketogenic diet was conducted for 2 months, with a good response in terms of weight loss, reduction in hips and waist circumference (*Table 5*), and distribution of body water. Afterwards, the 2 patients returned to the MMed for the maintenance of

TABLE 4
Pain level assessed by means of VAS, before (T0) and after (T1) the nutritional intervention

Patients	Level of pain (T0)	Level of pain (T1)	Pain reduction (%)
1	8	3	-62.5
2	3	2	-33.3
3	9	6	-33.3
4	10	5	-50
5	6	3	-50
6	7	3	-57
7	7	3	-57
8	10	6	-40
9	8	6	-25
10	7	2	-71.2
Average	7.5	3.9	-48

TABLE 5
Clinical waist, hip and thigh circumference results after dietary intervention for 8 patients with MMed and 2 patients with combined nutritional approach (MMed + KD + MMed sequence)

Patients	T0 waist (cm)	T1 waist (cm)	Waist loss (cm)	T0 hips (cm)	T1 hips (cm)	Hips loss (cm)	T0 thigh (cm)	T1 thigh (cm)	Thigh loss (cm)
1*	94	86.8	-7.2	126	121.2	-4.8	73	70	-3
2	93	78	-15	113	101	-12	65	60	-5
3	94	78	-16	114	106	-8	64	58	-6
4	108	89	-19	120	100	-20	71	57	-14
5	78.5	71.5	-7	107	95	-12	63.5	57	-6.5
6*	92.3	77.9	-14.4	120.5	104	-16.5	72	65	-7
7	94	85	-9	114	110	-4	67.5	64.5	-3
8	100.5	87	-13.5	136	120	-16	85	77	-8
9	94	88	-6	107	95	-12	65	61	-4
10	91	74	-17	119	109	-10	69	66	-3
Average	93.3	81.5	-12.4	117.6	106.1	-11.5	69.5	63.5	-5,9

*combined nutritional approach (MMed + KD + MMed sequence)

the dietary regimen (so called "sandwich" approach). At the moment, all patients are following the MMed with the aim of maintaining it with time and shift to KD for 1-3 months as needed.

DISCUSSION

Currently, the most examined dietary approach to patients with lipedema is the ketogenic diet. However, some cases require a different intervention which should have the main advantage to be easily conducted in the long run. Patients suffering from lipedema have to live with their pathology for their whole life, so they must be educated on how to manage it also from the nutritional point of view. To this regard we think that a Mediterranean-style moderate-carbohydrate diet could be a valid alternative to KD at least as a first approach. Our results, although just a preliminary experience and with a low number of patients, show that 80% of the cases had a good outcome with MMed and they did not need a KD. The KD should therefore not be considered the only possible option in the nutritional management of lipedema, but rather it can be a valid option either in not responsive cases to MMed or in cases in which MMed is no longer efficient. The KD can be performed as an in-between intervention within the Mediterranean nutritional path ("sandwich" approach), which can help MMed to get to a good response and/or boost its response, especially in those patients who suffer from comorbidities such as insulin-resistance, hormonal imbalances, hepatic insufficiency, hyperlipemia, etc.

Although other aspects need to be more deeply investigated, such as pain, sarcopenia and inflammatory status, we think that our preliminary results can be a good initial point to develop standardized nutritional guidelines for lipedema which can be more easily adapted to all kind of patients, with variable comorbidities, and easy to be conducted all lifelong.

Finally, dietary supplements with an anti-inflammatory, antioxidant, fat-burning, and pain-relieving action, like caffeine, bromelain, L-carnitine, vitamin C, vitamin B, melilot, guarana and birch can be effective in countering the typical symptoms of lipedema (26). Moreover, supplements which help control glucose levels and improve microcirculation and/or venous circulation, like diosmin and hesperidin, can be a valid support (23).

This research is limited primarily by the small number of participants and the relatively brief duration of the treatment. To better understand the true effectiveness of the interventions, future studies should involve larger cohorts and extend over longer timeframes. Moreover, the absence of a control group consisting of individuals without lipedema limits the ability to draw comparative conclusions about the treatment outcomes.

Our clinical experience has confirmed that lipedema can be effectively treated in the long term by an integrated anti-inflammatory nutritional approach in a multidisciplinary context and adapted to the comorbidities and eating habits of the patient using as a first line a dietary regime less restrictive (MMed) than other approaches such as KD. This dietetic intervention allows patients to maintain a good quality of life in the long term, avoiding the chronicling or maintenance of low-grade inflammatory status, onset of lymphatic complications and/or the progression of the disease to more advanced stages. Finally, our study shows that a nutritional intervention which combines MMed and KD (in a sort of "sandwich" approach) may allow better result, due to advantages obtained by the two approaches. This approach to nutritional intervention has the advantage to be followed by patients with more compliance, both in terms of quality of life and clinical outcome.

REFERENCES

1. Di Renzo, L, G Cinelli, L Romano, et al: Potential effects of a modified Mediterranean diet on body composition in lipoedema. Nutrients 13 (2021), 358. doi: 10.3390/nu13020358
2. Child, AH, KD Gordon, P Sharpe, et al: Lipedema: An inherited condition. Am. J. Med. Genet. A. 152A (2010), 970-976. doi: 10.1002/ajmg.a.33313
3. Vyas, A, G Adnan: Lipedema. In: StatPearls

[Internet]. Treasure Island (FL): StatPearls, Treasure Island, 2024.
4. Forner-Cordero, I, A Forner-Cordero, G Szolnoky: Update in the management of lipedema. Int. Angiol. 40 (2021), 345-357. doi: 10.23736/S0392-9590.21.04604-6
5. Poojari, A, K Dev, A Rabiee: Lipedema: Insights into morphology, pathophysiology, and challenges. Biomedicines 10 (2022), 3081. doi: 10.3390/biomedicines10123081
6. Annunziata, G, A Paoli, V Manzi, et al: The role of physical exercise as a therapeutic tool to improve lipedema: A consensus statement from the Italian Society of Motor and Sports Sciences (Società Italiana di Scienze Motorie e Sportive, SISMeS) and the Italian Society of Phlebology (Società Italiana di Flebologia, SIF). Curr. Obes. Rep. 13 (2024), 667-679. doi: 10.1007/s13679-024-00579-8
7. Lundanes, J, GE Storliløkken, MS Solem, et al: Gastrointestinal hormones and subjective ratings of appetite after low-carbohydrate vs low-fat low-energy diets in females with lipedema - A randomized controlled trial. Clin. Nutr. ESPEN 65 (2024), 16-24. doi: 10.1016/j.clnesp.2024.11.018
8. Ghods, M, I Georgiou, J Schmidt, et al: Disease progression and comorbidities in lipedema patients: A 10-year retrospective analysis. Dermatol. Ther. 33 (2020), e14534. doi: 10.1111/dth.14534
9. Lundanes, J, F Sandnes, KH Gjeilo, et al: Effect of a low-carbohydrate diet on pain and quality of life in female patients with lipedema: A randomized controlled trial. Obesity 32 (2024), 1071-1082. doi: 10.1002/oby.24026
10. Keith, L, CA Seo, C Rowsemitt, et al: Ketogenic diet as a potential intervention for lipedema. Med. Hypotheses 146 (2021), 110435. doi: 10.1016/j.mehy.2020.110435
11. Jeziorek, M, A Chachaj, M Sowicz, et al: The benefits of low-carbohydrate, high-fat (LCHF) diet on body composition, leg volume, and pain in women with lipedema. J. Obes. 18 (2023), 5826630. doi: 10.1155/2023/5826630
12. Jeziorek, M, A Szuba, K Kujawa, et al: The effect of a low-carbohydrate, high-fat diet versus moderate-carbohydrate and fat diet on body composition in patients with lipedema. Diabetes Metab. Syndr. Obes. 22 (2022), 2545-2561. doi: 10.2147/DMSO.S377720
13. Masino, SA, DN Ruskin: Ketogenic diets and pain. J. Child Neurol. 28 (2013), 993-1001. doi: 10.1177/0883073813487595
14. Cifarelli, V, GI Smith, S Gonzalez-Nieves, et al: Adipose tissue biology and effect of weight loss in women with lipedema. Diabetes. 9 (2024), db240890. doi: 10.2337/db24-0890
15. Lundanes, J, M Gårseth, S Taylor, et al: The effect of a low-carbohydrate diet on subcutaneous adipose tissue in females with lipedema. Front. Nutr. 7 (2024), 1484612. doi: 10.3389/fnut.2024.1484612
16. Jeziorek, M, A Szuba, M Sowicz, et al: The effect of a low-carbohydrate high-fat diet on laboratory parameters in women with lipedema in comparison to overweight/obese women. Nutrients 15 (2023), 2619. doi: 10.3390/nu15112619
17. Di, Renzo L, P Gualtieri, S Zomparelli, et al: Modified Mediterranean-ketogenic diet and carboxytherapy as personalized therapeutic strategies in lipedema: A pilot study. Nutrients 15 (2023), 3654. doi: 10.3390/nu15163654
18. Sørlie, V, AK De Soysa, ÅA Hyldmo, et al: Effect of a ketogenic diet on pain and quality of life in patients with lipedema: The LIPODIET pilot study. Obes. Sci. Pract. 8 (2022), 483-493. doi: 10.1002/osp4.580
19. Amato, ACM, JLS Amato, DA Benitti: The efficacy of ketogenic diets (low carbohydrate; high fat) as a potential nutritional intervention for lipedema: A systematic review and meta-analysis. Nutrients. 16 (2024), 3276. doi: 10.3390/nu16193276
20. Patton, L, L Ricolfi, M Bortolon, et al: Observational study on a large Italian population with lipedema: Biochemical and hormonal profile, anatomical and clinical evaluation, self-reported history. Int. J. Mol. Sci. 25 (2024), 1599. doi: 10.3390/ijms25031599.
21. Cannataro, R, S Michelini, L Ricolfi, et al: Management of lipedema with ketogenic diet: 22-month follow-up. Life 11 (2021), 1402. doi: 10.3390/life11121402
22. Verde, L, E Camajani, G Annunziata, et al: Ketogenic diet: A nutritional therapeutic tool for lipedema? Curr. Obes. Rep. 12 (2023), 529-543. doi: 10.1007/s13679-023-00536-x
23. Ehrlich, C, E Iker, KL Herbst, et al: Lymphedema and lipedema nutrition guide: Foods, vitamins, minerals and supplements. Lymph Notes. 2015.
24. Muscogiuri, G, L Verde, C Sulu, et al: Mediterranean diet and obesity-related disorders: What is the evidence? Curr. Obes.

Rep. 11 (2022), 287-304. doi: 10.1007/s13679-022-00481-1
25. Obesity: Preventing and managing the global epidemic. Report of a WHO Consultation. World Health Organ Tech. Rep. Ser. 894 (2000), 1-253.
26. Bonetti, G, KL Herbst, K Dhuli, et al: Dietary supplements for lipedema. J. Prev. Med. Hyg. 63 (2022), E169-E173. doi: 10.15167/2421-4248/jpmh2022.63.2S3.2758

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