MEDICAL NUTRITION THERAPY APPROACHES IN THE MANAGEMENT OF LYMPHEDEMA

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ABSTRACT

Lymphedema is a condition caused by the accumulation of protein-rich fluid in the interstitial space due to inadequate lymph drainage. The most important factors for treatment are preventing the development of lymphedema in the early stages and preventing and slowing down its progression if it has developed. Successful treatment of lymphedema requires a long and challenging process and requires a multidisciplinary approach. Nutrition is one of the main components in the therapeutic management of vascular diseases. It is thought that dietary therapies that provide ideal body weight control, support intestinal health, prevent the development of edema, prevent overload increase in the lymphatic system, and support the immune system can be considered one of the treatment components of disease management. This review aims to examine the results of the studies in the literature on the nutritional treatment of lymphedema.

Key words: Lymphedema, vascular disease, edema, nutritional treatment

LENFÖDEM YÖNETİMİNDE TIBBİ BESLENME TEDAVİSİ YAKLAŞIMLARI

ÖZ

Lenfödem; lenf drenajındaki yetersizlik sonucunda proteinden zengin sıvının interstisyel alanda birikimi ile oluşan bir durumdur. Lenfödemin ilk evrelerde gelişiminin önlenmesi, gelişmiş ise ilerlemesinin engellenmesi ve yavaşlatılması tedavi için en önemli unsurlardandır. Uzun ve zor bir süreç gerektiren lenfödem tedavisinin başarılı olabilmesi multidisipliner bir yaklaşım gerektirmektedir. Beslenme, damar hastalıklarının terapötik yönetiminde temel bileşenlerden biridir. İdeal vücut ağırlığı kontrolü sağlayan, bağırsak sağlığını destekleyen, ödem gelişimini önleyici, lenfatik sistemdeki aşırı yük artışını engelleyici ve immün sistemi destekleyici diyet tedavilerinin hastalık yönetiminin tedavi bileşenlerinden biri olarak kabul edilebileceği düşünülmektedir. Bu derlemede lenfödemin beslenme tedavisine yönelik literatürde yer alan çalışma sonuçlarını incelemek amaçlanmıştır.

Anahtar kelimeler: Lenfödem, damar hastalığı, ödem, beslenme tedavisi

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INTRODUCTION

Lymphedema is defined as a chronic and progressive condition characterized by permanent swelling of the extremities because of abnormal accumulation of protein-rich fluid, which develops due to malformation in the lymphatic circulatory system, developmental retardation, or acquired disorders in the anatomical structure that forms the lymphatic system (1, 2). Although it is usually characterized by edema in the extremities, it may also develop in the face, neck, trunk, and genital organs (3).

The most common signs and symptoms are recurrent cellulitis, deterioration of skin texture, the feeling of heaviness and tension in the affected area, tingling, pain, discomfort, edema, noticing that jewelry such as rings, watches, bracelets are tight, tight clothing and underwear, fibrosis, induration, Peau d'orange skin changes, papillomatosis, hyperkeratosis, Positive Stemmer sign (4).

Although the incidence of lymphedema in Turkey is not known exactly, it shows a wide range of distribution due to the difference in diagnostic and classification criteria and the diversity of patient criteria (5, 6). In the literature, primary lymphedema is reported to occur at a rate of 1 in 100,000 (7). The probability of secondary lymphedema is 99% compared to primary lymphedema. The prevalence of secondary lymphedema is 1 in 1000 and the mean age at the time of diagnosis varies between 50 and 58 years (8).

In a study conducted in Turkey, 68 (28%) of 240 patients developed lymphedema after breast cancer treatment (9). The risk of developing lymphedema after cancer treatment is lifelong and the total incidence increases as the follow-up period increases (10). In one study, the average lymphedema occurred at 17 months, and it was found that it developed at the earliest at 1 month and the latest at 109 months (11). It is estimated that there are approximately 200 million cases of lymphedema worldwide (5, 7). However, considering the presence of patients who are undiagnosed, delayed, or never reached treatment, the estimates are thought to be below the prevalence (7).

Surgical and non-surgical (conservative) treatment methods are used in the management of lymphedema. While surgical treatment is applied as a treatment option in advanced cases of lymphedema, "Complex Decongestive Therapy", which does not involve surgical intervention, is accepted as the gold standard for the treatment of lymphedema. This treatment, also known as complex decongestive physiotherapy, consists of four basic components: manual lymph drainage, compression therapy, skincare, and therapeutic exercise methods (12). Manual lymph drainage aims to support lymph drainage; compression aims to maintain the integrity of the extremity; skin care aims to maintain skin integrity and minimize the risk of infection; and exercise aims to regulate joint mobility and lymph drainage (13). In addition, alternative treatment methods such as kinesiological taping, aqua therapy methods, pilates, and yoga applications can be used to the conditions and needs of the individual. One of the most important steps of a successful treatment is "patient education" (14).

METHOD

In this review, PubMed, Science Direct, and Google Scholar databases were searched using the keywords "lymphedema and nutrition or diet or body weight control or obesity", and studies published between 2007 and 2022 in Turkish and English

were included. As a result of the literature search, 13 articles were analyzed within the scope of the study. The author and publication year, study aim, sample size, characteristics of the study group, research design, and results of the included studies are summarised in Table 1.

Nutrition Therapy Approaches in Lymphedema

Prevention of the development of lymphedema in the early stages and stopping or slowing down its progression if it has developed are the most important factors for treatment. Successful treatment of lymphedema, which requires a long and challenging process, requires a multidisciplinary approach (15). Therefore, recommendations for adequate and balanced nutrition are always associated with healthy lymphatic drainage (16).

In a study, it was determined that there was a significant relationship between the stage of lymphedema and inadequate nutrient intake of individuals (17). Therefore, it is recommended to target an adequate and balanced diet that will reduce the risk factors associated with obesity in patients with lymphedema and enable them to reach their ideal body weight (18). It is important to increase hydration and limit sodium intake while maintaining an ideal body weight (19). It is also stated that a balanced and healthy diet, including whole grains, fish, fruit, and vegetables, and avoiding foods high in fat and cholesterol, will greatly reduce the risk factors associated with lymphedema (20).

There is no specific dietary plan for the treatment of lymphedema. The accepted approach in the treatment of lymphedema is to follow a diet low in fat and salt, which contributes to maintaining an ideal body weight (20). It would be appropriate to evaluate individuals with lymphedema individually and plan nutritional therapy according to their needs (21). In the following, the accepted nutritional therapy approaches for individuals with lymphedema are summarised in the literature. In this direction, the aims of nutrition therapy in individuals with lymphedema according to the literature are summarised in Figure 1.

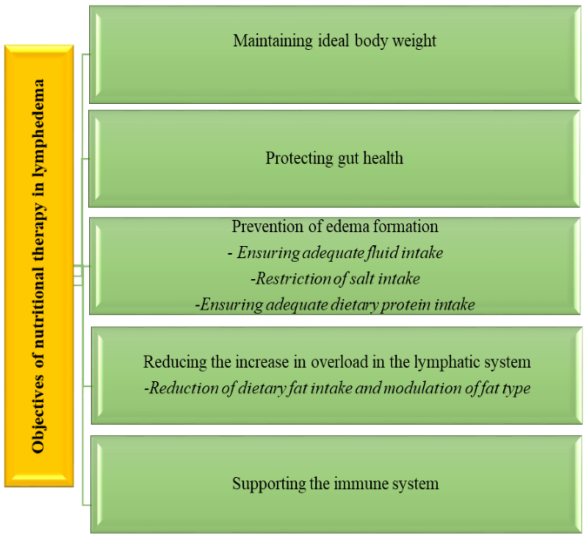

Figure 1. Aims of nutritional therapy in lymphedema.

Maintaining ideal body weight

Obesity is an important risk factor for the development of lymphedema. Patients who developed lymphedema after breast cancer treatment and had a higher Body Mass Index (BMI) had a higher incidence of lymphedema (22); It is known that patients with a BMI >30 are three times more at risk than patients with a BMI <25 (23).

Obesity worsens lymphedema and this may be related to an exaggerated chronic inflammatory response (24). In experimental studies, it has been reported that lymphatic dysfunction can develop because of obesity, chronic high-fat diet-induced obesity leads to increased dendritic cell migration in lymph nodes as well as collecting lymphatic vessel function, while diet-induced visceral fat

Table 1. Findings related to study characteristics.

Reference	Objective	Sample	Research design	Conclusion
Tenkorang et al (2021) (17)	To determine the nutritional status of lymphedema patients	86 female individuals	Cross-sectional study Nutrient intakes of the individuals were evaluated by taking 24-hour retrospective food consumption records.	There were widespread inadequate nutrient intakes associated with the lymphedema stage.
Shaw et al (2007) (32)	To compare the effect of different dietary interventions on arm volume	64 women with lymphedema after breast cancer	Randomised into 3 groups. Group 1: dietary energy intake restricted (1000-1200 kcal/day) Group 2: low-fat diet (20% of energy) with no change in energy intake (isoenergetic) 3rd group: The control group was followed up for 24 weeks.	Body weight, BMI, and skinfold thickness decreased significantly in the intervention groups compared to the control group. Reductions were more pronounced in the group with reduced energy intake. No significant relationship was found between the groups in edema volume, but a significant correlation (r: 0.423; p=0.002) was shown between the decrease in body weight and the decrease in edema volume.
Shaw et al (2007) (33)	To evaluate body weight control in individuals with lymphedema due to breast cancer	20 female individuals	Individuals were randomized into 2 groups; the intervention group was given a weight loss diet with 1000 -1200 kcal energy and the control group was given a booklet containing healthy nutrition information. They were followed up for 12 weeks.	It was determined that there was a significant decrease in edema volumes, body weight, and BMI values of the individuals in the group applying diet after the intervention.
Keith et al. (2020) (34)	To determine the effect of a ketogenic diet on body weight loss, edema volume, and quality of life in individuals with lymphedema	10 individuals with lymphedema with BMI >30 kg/m ^{2}	Intervention group n= 6 Control group n= 4 Intervention group The ketogenic diet (carbohydrate restriction of less than 20 g/day, moderate protein intake of 50 to 75 g/day, and unrestricted fat consumption) was applied. Both groups were followed up for 18 weeks at two-week intervals.	Average body weight decreased by 8% after the intervention. There were also significant decreases in body fat and BMI values. Reduction in body weight was positively correlated with a reduction in edema volume and a reduction in the impact of lymphedema (r = 0.8; P = 0.005; r = 0.76; p = 0.01, respectively). Reduction in limb volume is positively correlated with Lymphedema Life Scale Scores (r = 0.65; p < 0.05).
Navaei et al. (2020) (36)	To evaluate the effects of symbiotic supplementation* on edema volume	88 obese and overweight women with lymphedema after breast	In a randomized, double-blind, controlled clinical trial.	In the group receiving symbiotic supplementation, there was a

	and some oxidative markers in obese and overweight patients with lymphedema after breast cancer. ** 10^9 CFU/g *of Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum, Streptococcus thermophiles* and 38.5 mg FOS	cancer	Individuals were randomized to either symbiotic supplement (n=44) or placebo (n=44) groups and followed for 10 weeks.	significant decrease in serum MDA levels and an increase in serum SOD concentration compared to placebo. No significant changes were observed in serum GPx, TAC, and edema volume between the groups.
Vafa et al. (2020) (37)	The effect of energy restriction and symbiotic supplementation on quality of life and edema volume	135 overweight and obese individuals with lymphedema	A randomized, double-blind, controlled clinical trial. Intervention group: 10 days on energy-restricted diet with symbiotic supplementation of 10^9 CFU	There is a significant decrease in quality-of-life score, edema volume (29.72%), and BMI (3.01%) in the intervention group compared to the control group.
Wang et al (2022) (44)	Effect of a high-fat diet on the development of lymphedema	1476 individuals with a history of breast cancer	Retrospective study	Patients on a high-fat diet were 2.47 times more likely to have lymphedema than those on a low-fat diet.
Ryu et al (2016) (45)	Determination of the relationship between the risk of secondary lymphedema and changes in serum phospholipid fatty acid composition in breast cancer survivors	A total of 60 women with unilateral breast cancer and lymph node dissection	BMI, serum lipid profiles, bioimpedance data by single frequency bioimpedance analysis, and serum phospholipid compositions were analyzed.	The risk of secondary lymphedema after breast cancer is associated with changes in serum phospholipid fatty acid composition.
Oliveira and César (2007) (46)	To investigate the effect of complex decongestive physical therapy (CDP) combined with the use of medium chain triglycerides (MCT) as a dietary intervention in individuals with upper limb lymphedema	10 women who underwent mastectomy and showed homolateral upper extremity lymphedema with surgery	The control group (n= 5), which underwent physical therapy treatment consisting of CDP (three times a week for four weeks); and the MCT group (n= 5), which underwent the same physical therapy protocol for four weeks and utilized MCT oil for approximately 50-60% of total lipid consumption, were compared.	There was a greater reduction in circumference and volume measurements in the MCT group and the difference between the groups was significant. There was no significant difference between the groups in skinfold thickness or whole-body water measurement. The feeling of heaviness in the arms after the intervention was significantly less in the MCT group compared to before the intervention.
Totmaj et al (2022) (49)	To evaluate the effect of symbiotic supplementation* in combination with a low-calorie diet on IL-10, TGF-β, VEGF, adiponectin, and	88 obese and overweight women with lymphedema after breast cancer	A randomized, double-blind, controlled clinical trial. Individuals were randomized to either symbiotic supplement	Body weight, BMI, body fat percentage and waist circumference showed a more significant decrease in the symbiotic group after 10 weeks

	edema volume in obese individuals with lymphedema (* 10^9 CFU/g *of Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum, Streptococcus thermophiles* and 38.5 mg FOS)		(n=44) or placebo (n=44) groups and followed for 10 weeks. The diet of the individuals was planned as 55-65% carbohydrate, 20-35% fat, and 10-15% protein of the total energy with an energy restriction of 500-1000 kcal per day (minimum predicted energy intake 1200 kcal).	of intervention. IL-10, VEGF, adiponectin, and TGF-β concentrations did not differ significantly between the two groups. Symbiotic supplementation for 10 weeks had beneficial effects on VEGF and IL-10 levels in women with lymphedema. Symbiotic use also reduced the volume of arm lymphedema.
Schmitz et al (2019) (50)	To evaluate the effect of home exercise, diet, and combined treatment in obese individuals with lymphedema after breast cancer	351 obese individuals with lymphedema	In the randomized controlled study, individuals were divided into 4 groups and followed up for 52 weeks. Group 1: 52-week home-based exercise program consisting of strength/resistance training twice a week and 180 minutes of walking per week. Group 2: A meal replacement program including 7 portions of fruit and vegetables per day for the first 20 weeks and 52 weeks of lifestyle change counselling. Group 3: Both exercise and nutrition counselling Group 4: Control group.	All three interventions did not result in a significant change in edema volume, clinical course, and findings of lymphedema. A home-based exercise program including walking and slow progressive resistance exercise is considered safe, while supervised, facility-based programs may provide more lymphedema-specific benefits.

accumulation leads to atrophy of mesenteric lymph nodes in obese mice. Furthermore, high-fat diet-induced obesity exacerbated inflammation and fibrotic tissue accumulation in a murine model of lymphedema (25-28). In a study conducted to determine the effect of Western diet-induced obesity on the occurrence of lymphatic valve dysfunction, it was reported that lymphatic valve dysfunction may be a critical component of obesity-induced lymphedema in mice fed a Western diet for 14 weeks in association with Western diet-induced metabolic changes (29).

Obesity can impair lymphatic function by impairing the function of lymphatic vessels and/or suppressing normally functioning lymphatics with increased lymph fluid (30). Obesity increases the risk of lymphedema because of increased production of lymph in an enlarged limb that exceeds the capacity of the lymphatic system, external compression of the lymphatics by adipose tissues, and direct injury to the lymphatic system by changes in body weight or diet. Lymphatic injury initiates a cycle of lymphatic dysfunction leading to the accumulation of interstitial fluid. Impaired lymphatic clearance causes inflammation and promotes fibro adipose deposition. In turn, fibrosis and fat accumulation further impair lymphatic function, causing a feed-forward cycle. So, lymphatic function is reciprocally related to the expansion of adipose tissue. Structural lymphatic abnormality is seen in obese adults, and in some cases, lymphatic damage may be irreversible (31).

In a study conducted to compare the effect of different dietary interventions on edematous arm volume, 64 women with lymphedema after breast cancer were randomized into 3 groups. Group 1: dietary energy intake was restricted (100-1200 kcal/day), group 2: low-fat diet (20% of energy) with no change in energy intake (isoenergetic), and group 3: control group was followed up for 24 weeks. It was determined that there was a statistically significant decrease in body weight, BMI, and skinfold thickness in both intervention groups compared to the control group, more pronounced in the group with reduced energy intake. It was also shown that there was a significant correlation (r: 0.423; p=0.002) between the decrease in body weight and the decrease in edema volume (32). In another study by Shaw et al (2007), it was determined that energy-reduced dietary intervention for 12 weeks provided a significant reduction in edema volumes, body weight, and BMI values in individuals who developed lymphedema due to breast cancer (33). In another study, the effect of the ketogenic diet on body weight loss, edema volume, and quality of life in individuals with lymphedema was evaluated and 10 individuals with lymphedema with BMI >30 kg/m^2 were included in the study. The patients were randomized as an intervention group (n= 6) and the control group (n= 4) was followed up for 18 weeks at two-week intervals. The ketogenic diet (carbohydrate restriction of less than 20 g/day, moderate protein intake of 50-75 g/day, and unlimited fat consumption) was applied to the intervention group. The mean body weight decreased by 8% after the intervention. Reduction in body weight was positively correlated with reduction in edema volume and lymphedema symptoms ($r = 0.8$; $p = 0.005$; $r = 0.76$; $p = 0.01$, respectively). In addition, reduction in limb volume was positively correlated with Lymphedema Life Scale Scores ($r = 0.65$; $p < 0.05$) (34).

Obesity-induced lymphedema is the only type of lymphedema that is reversible. Following body weight loss through diet or a bariatric procedure, lymphatic clearance can improve due to decreased lymph production and/or restore function of the lymphatic vessels (30).

Protection of intestinal health

Although it is known that some probiotics, especially Lactobacilli, reduce the risk of ROS accumulation due to their antioxidant activities (35), there are a limited number of studies in the literature evaluating synbiotic supplementation in patients with lymphedema (36, 37). In a study conducted to evaluate the effects of symbiotic supplementation on edema volume and some oxidative markers in obese and overweight patients with lymphedema after breast cancer, it was determined that there was a significant decrease in serum malondialdehyde (MDA) levels and an increase in serum superoxide dismutase (SOD) concentration in the group receiving symbiotic supplementation compared to placebo. No significant changes were observed in serum glutathione peroxidase (GPx), total antioxidant capacity (TAC), and edema volume between the groups (36). In another study evaluating the effects of energy restriction and symbiotic supplementation on quality of life and edema volume in patients with lymphedema, 135 overweight and obese individuals were administered an energy-restricted diet with symbiotic supplementation (10^9 Colony Forming Unit (CFU) /day probiotic bacteria and 38.5 mg fructooligosaccharide) for 10 days and a significant decrease in total quality of life score, edema volume and BMI was determined compared to the control group. With all these properties, symbiotics may alleviate symptoms related to lymphedema, contribute to the improvement of physical and functional disorders, and improve the quality of life of individuals with lymphedema (37).

Prevention of edema formation

-Ensuring adequate fluid intake

Hydration balance in lymphedema is considered essential to maintain tissue fluid homeostasis (38). Lymp fluid is a dense protein-containing fluid that accumulates in the extracellular space. Fluid restriction causes more protein to accumulate in the extracellular space (where the lymph fluid accumulates). The negatively charged protein causes an increase in osmotic pressure, which will draw more fluid into the extracellular space creating more lymphedema, and the body releases fluid from the intracellular space to the extracellular space. Thus, fluid restriction is a trigger for lymphedema (39, 40).

Approximately 2500 mL of water is lost daily, including 1500 mL from the kidneys, 500 mL from the skin, 300 mL from the intestines, and 300 mL from respiration. This loss should be replaced with water taken with food and drinks. The total recommended daily fluid intake is 2500 mL for men and 2000 mL for women. Fluid requirement should be met primarily with water and an average daily water consumption of 1500 mL is recommended. Tea, coffee, and alcohol consumption may cause urinary water loss, which may lead to an increase in protein concentration in the extracellular space and trigger edema (38). Therefore, it is important to provide the fluid requirement with water (41).

-Restriction of salt intake

High salt intake causes salt to be stored in the skin as sodium and chloride ions. Immune cells regulate this storage, along

with blood pressure and other lymphatic functions. Over time, a high-salt diet causes abnormal lymphatic capillary growth (hyperplasia) in the skin and reduces lymphatic pumping activity. A high-salt diet also increases the number of Th17 cells (CD17+ helper T cells that produce Interleukin-17), which are highly pathogenic and proinflammatory. Keeping salt intake below 500-1500 mg/day and increasing the consumption of potassium-containing vegetables are known to have a positive effect on lymph and blood circulation. It is stated that Himalayan salt may be a good option as it has a naturally balanced sodium and potassium content (41, 42).

-Ensuring adequate dietary protein intake

There is a misconception among individuals with lymphedema that restricting protein intake will prevent the development of edema. These individuals think that by consuming less protein-containing foods, there will be less protein in tissue fluids and the risk of lymphedema will decrease. In lymphedema, less protein intake does not affect the protein in the tissue fluid. On the contrary, not consuming enough protein or, more commonly, not digesting proteins can cause edema caused by protein deficiency malnutrition (38).

Dietary protein intake does not correlate with protein excess in the interstitial matrix; therefore, appropriate protein intake is recommended to synthesize essential amino acids in patients with lymphedema. Although high-quality organic protein is generally preferred, it is recommended that approximately 10-15% of the daily energy intake should come from proteins (21).

Reducing the increase in overload in the lymphatic system

-Reduction of dietary fat intake and modulation of fat type

Lymphatic vessels play an important role in intestinal lipid absorption; impaired lymphatic vessel function leads to increased adipose tissue accumulation in patients with lymphedema (43). A high-fat diet is an independent risk factor for lymphedema. In a retrospective study in which the dietary habits of 1476 patients with a history of breast cancer were evaluated, it was determined that 122 of the individuals developed lymphedema and the likelihood of lymphedema in patients who followed a high-fat diet before hospitalization was 2.47 times higher than those who followed a low-fat diet (HR = 0.558; 95%CI = 0.345 0.902; p = 0.017) (44). In another study involving a total of 60 women with unilateral breast cancer who had undergone lymph node dissection, total polyunsaturated fatty acids (PUFAs), fatty acid desaturase activity indices, and Arachidonic acid (AA)/ Eicosapentaenoic Acid (EPA) ratios were found to be increased in serum phospholipids of breast cancer survivors with lymphedema. It is suggested that evaluation of AA/EPA ratios to predict the risk of inflammatory disorders and modification of dietary fat intake in individuals with a history of breast cancer may be useful (45).

Medium-chain fatty acids reach the portal circulation after passing through enterocytes and are transported to the liver with albumin without passing through the lymphatic system. It is thought that differentiating the type of dietary fat intake may be useful in individuals with lymphedema to reduce the overload increase in the lymphatic system. In a study conducted to compare the effect of complex decongestive physical therapy (CDP) with the use of medium chain

triglyceride (MCT) as a dietary intervention in individuals with upper extremity lymphedema, 10 female individuals were divided into 2 groups; physical therapy consisting of CDP three times a week (Control group n= 5); and physical therapy consisting of CDP three times a week (Control group n= 5); and the same physical therapy protocol with approximately 50-60% of the total lipid consumption using MCT oil (MCT Group n= 5) were followed for four weeks. The MCT group showed a greater reduction in circumference and volume measurements, but no significant difference in skinfold thickness or whole-body water measurements. The feeling of heaviness in the arms after the intervention was significantly less in the MCT group compared to before the intervention. This is the only study evaluating the use of MCT in individuals with lymphedema and further studies are recommended to fully characterize its effects (46).

Supporting the immune system

The lymphatic system also functions as an important immune organ closely linked to the adipose tissue and metabolic system, which is affected by inflammatory processes caused by intestinal dysbiosis and visceral obesity (16).

Macrophages in adipose tissue secrete signaling factors, including vascular endothelial growth factor (VEGF), which triggers the formation of leaky lymphatic vessels leading to more edema, inflammation, and obesity (4). In the literature, it is reported that individuals with lymphedema have various sources of VEGF signaling (47, 48). Deficient lymphatic vessels, smaller than normal lymphatic vessels, insufficient lymphatic vessels, and overgrowth of lymphatic vessels appear to be the result of genetic polymorphisms in primary lymphedema. Fibrous tissue formation is due to excessive signaling of fibroblast growth factor 2 (FGF2). The consumption of the following VEGF and FGF2 inhibiting nutrients, which may play a major role in the reduction of inflammation and remission of lymphedema, may be beneficial (42). The negative effects of oxidative stress, which is another important aspect of the pathophysiology of lymphedema, can be reduced by including antioxidant nutrients in the diet (49).

These foods and nutrients;

- ✓ Green tea catechins
- ✓ Genistein in soya beans
- ✓ Lycopene in tomatoes, watermelon, and other bright red fruits
- ✓ Omega 3 fatty acids
- ✓ Flavonoids in spinach, onion, parsley, beetroot, and thyme
- ✓ Polyphenolic flavonoids in lettuce, chicory, rocket, and red lettuce
- ✓ Proanthocyanidins in cocoa, cinnamon, cranberries, apples, grapes, black currant, dates
- ✓ Anthocyanidins in blackberries, grapes, and red wine.
- ✓ Curcumin is contained in turmeric.
- ✓ Vitamin K2 and fermented foods, prebiotics
- ✓ Beta-cryptoxanthin in bright orange, red, or yellow foods.
- ✓ Pomegranate, all kinds of berries, walnuts, and red grapes are indicated as (42).

Symbiotic supplementation may have a positive effect on lymphedema not only by protecting the gut microbiota but also by its anti-inflammatory effect. It is stated that symbiotic supplementation may have beneficial effects on arm lymph volume in individuals with lymphedema by increasing the levels of anti-inflammatory

markers. In a randomized, double-blind, controlled clinical trial conducted by Totmaj et al (2022) to evaluate the effect of symbiotic supplementation with a low-calorie diet on IL-10, TGF-β, VEGF, adiponectin, and edema volume in obese individuals with lymphedema, 88 obese and overweight women with lymphedema after breast cancer were randomized to symbiotic supplementation (n=44) or placebo (n=44) groups and followed for 10 weeks. The symbiotic supplement contained 10^9 CFU/g of *Lactobacillus casei, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Bifidobacterium breve, Bifidobacterium longum, Streptococcus thermophiles* and 38.5 mg FOS. In addition, an energy restriction of 500-1000 kcal/day was applied to the individuals (minimum energy intake was 1200 kcal/day), and their diets were planned so that 55-65% of the total energy was carbohydrate, 20-35% was fat and 10-15% was protein. Body weight, BMI, body fat percentage and waist circumference showed a more significant decrease in the symbiotic group after 10 weeks of intervention. IL-10, VEGF, adiponectin, and TGF-β concentrations did not differ significantly between the two groups. Symbiotic supplementation for 10 weeks had beneficial effects on VEGF and IL-10 levels in women with lymphedema. Symbiotic use also reduced the volume of arm lymphedema (49).

CONCLUSION AND RECOMMENDATIONS

Assessing the nutritional status of individuals with lymphedema will help to identify treatment principles that will improve the overall health and quality of life of this population. Therefore, it is necessary to determine the need for appropriate nutritional intervention in addition to current disease management strategies. Since obesity is a condition that damages lymphatic vessels, worsens lymphedema, and causes inflammation, patients are advised to maintain an ideal body weight. Meeting all nutrient requirements with an adequate and balanced diet will both support the protection of general health and provide the nutritional treatment goals needed by an individual with lymphedema.

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