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High-Intensity Interval Training (HIIT), Anti-Inflammatory Nutritional Intake, and Aging in Obese Patients: Literature Review

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ABSTRACT

Obesity has become a global epidemic affecting 650 million people worldwide. The burden of obesity is reflected in healthcare costs and disability. Aging and systemic inflammation play important roles. Training is essential to reduce metabolic risk factors. High-intensity interval training (HIIT) has been shown in many studies to reduce obesity as well as inflammation and improve adipose tissue. Another approach to obesity management is nutritional control. Manipulation of dietary composition, elimination or restriction of certain food groups, and scheduling adjustments are strategies used. Importantly, the aging process is also accelerated by obesity and disrupts the immune response. Physical training can improve health in elderly individuals with obesity by reducing body fat and systemic inflammation.

Keywords: aging; anti-inflammatory; high-intensity interval training (HIIT); nutritional intake; obesity.

INTRODUCTION

In recent decades, the prevalence of obesity has increased and become a global epidemic. Data show that more than 1.9 billion (39%) adults worldwide are overweight, and around 650 million (13%) are obese [1]. There is a relationship between a body mass index (BMI) >24.9 kg/m^2 and mortality, with a higher hazard ratio in men compared to women [2]. A study of 3.6 million adults in the UK demonstrated that life expectancy from age 40 was 4.2 years shorter in obese men and 3.5 years shorter in obese women (BMI 30.0 kg/m^2) compared to individuals with a healthy weight (BMI 18.5–24.9 kg/m^2) [3]. Overweight and obesity contribute to 2.4 million deaths and 70.7 million disability-adjusted life years (DALYs) in women, and 2.3 million deaths and 77.0 million DALYs in men, based on data from 195 countries [4]. In addition to the above burden, obesity also contributes significantly to both direct and indirect healthcare costs [3].

Most obese individuals do not reach the recommended amount of weekly physical activity, at least 150 minutes of moderate aerobic activity or 75 minutes of vigorous aerobic activity per week, plus 2–3 strength training sessions weekly. Inadequate time is cited as the main barrier to achieving this target [5].

Modalities such as high-intensity interval training (HIIT) have become increasingly popular in recent years. HIIT is a specific form of cardiovascular exercise consisting of alternating periods of exercise and recovery with varying durations [6]. HIIT protocols can improve cardiometabolic risk indices in obese patients with metabolic syndrome [7]. HIIT reduces inflammatory markers by significantly improving visceral adipose tissue and body composition [8].

Besides exercise, increasing research shows the potential benefits of anti-inflammatory nutritional supplementation in obesity. Ashtary et al. (2021) found that nanocurcumin supplementation improved glycemic and lipid profiles, inflammation, and systolic blood pressure [9]. Dietary modification, especially caloric restriction with anti-inflammatory nutrient intake combined with exercise, is essential in obesity management [10].

Obesity is also closely related to chronic inflammation and has many negative effects [10]. Aging is a natural event associated with progressive changes in vital organs [11]. There is a relationship between aging with decreased lean body mass, increased fat mass, and chronic inflammatory status that increases proinflammatory mediators [12]. Reducing inflammation is an important treatment target [10].

Given the potential positive effects of HIIT and anti-inflammatory nutrition, as well as the link between aging and inflammation in obese patients based on the above, the authors are interested in reviewing HIIT, anti-inflammatory nutrient intake, and aging in obese patients.

Obesity

The World Health Organization (WHO) classifies obesity based on Body Mass Index (BMI). Adipose tissue is mainly composed of lipid-rich cells called adipocytes. The primary function of adipose tissue is to store energy in the form of triglycerides (TG) when there is an energy surplus, which can later be broken down into free fatty acids and glycerol during periods of starvation or fasting. A long-term imbalance between energy intake and expenditure causes a substantial increase in the amount of stored triacylglycerol in adipocytes, leading to obesity [2]. BMI measurement for obesity is a simple technique that has been widely used to estimate body fat mass and is accurate in most adult populations except bodybuilders and pregnant women [13].

High-Intensity Interval Training (HIIT) in Obese Patients

Exercise is an essential component that helps prevent obesity by increasing energy expenditure to reduce body weight, lower metabolic risk factors, and enhance adipose tissue health [14]. Recommended physical activity for obesity control ranges from 150 to 250 minutes per week or up to 60 minutes per day. HIIT is characterized by short periods performed above the lactate threshold, nearing maximal oxygen consumption (VO2max), interspersed with light exercise or rest, allowing performance of extra high intensity. HIIT protocols are based on the Wingate test, which consists of supra-maximal power output. The common type of HIIT is sprint interval training (SIT), where individuals perform several all-out efforts (100% maximal work capacity) with recovery periods on a cycle ergometer [15]. Low-volume HIIT protocols (75% - <100% of maximal work capacity) are increasingly used, as they tend to be more applicable for obese individuals compared to Wingate-based HIIT [2,15].

Evidence shows that HIIT can reduce adiposity and abdominal visceral fat despite variations across studies regarding exercise protocols used. One study comparing 12 weeks (3 - 4 sessions/week) of moderate intensity continuous training (MICT at 60% VO2max) versus HIIT (90% VO2max, repeated 4-minute intervals with 3-minute recovery) on abdominal adipose tissue in obese young women found similar reductions in subcutaneous and visceral abdominal fat in both groups. A 10-week combined continuous and HIIT regimen improved insulin sensitivity in adipose tissue [2]. An 8-week-long HIIT intervention (3 sessions/week, 32 minutes/session) better enhanced anaerobic power, adipokine levels, and blood pressure in elderly overweight populations due to physiological responses [16].

The impact of HIIT (10 x 4 min at 90% HRmax, 2 min recovery) in overweight women showed significant increases in whole-body fat oxidation, but ß-adrenergic and insulin signaling in subcutaneous abdominal adipose tissue remained unchanged, indicating HIIT did not alter intracellular signaling pathways controlling fat mobilization or storage in subcutaneous abdominal fat [17]. HIIT also effectively reduces ß-amyloid deposition by regulating NLRP3 inflammasome activity [18]. Another study revealed that two weeks of Wingate-based SIT (3 sessions/week) produced similar reductions in body fat percentage, subcutaneous, and visceral abdominal fat as MICT (40–60 minutes at 60% VO2max) in healthy subjects with insulin resistance [19].

Earlier studies comparing various HIIT protocols in overweight and obese subjects generally agree that HIIT plays a positive role in combating obesity through fat reduction, improving adipose tissue, and fighting inflammation [19]. Further research may open new potential in developing prevention and treatment strategies for obesity.

Anti-Inflammatory Nutritional Intake in Obese Patients

The main approach in obesity management is the implementation of a diet combined with increased physical activity. Manipulation of diet composition, elimination/restriction of specific food groups (such as plant-based diets and Mediterranean diets), and time manipulation (intermittent fasting) can be applied. There remains debate regarding the optimal macronutrient composition of food [2]. Some nutritional compositions have potential anti-inflammatory effects, such as foods containing medium-chain fatty acids (caprylic acid (8:0), capric acid (10:0), and lauric acid (12:0)), short-chain fatty acids (SCFAs) (butyric acid (4:0), valeric acid (5:0), and caproic acid (6:0)), and branched-chain fatty acids (BCFAs) [20].

The intake of various polyphenols (monomeric flavonoids) together with carbohydrates (neutral sugars in cereal grain walls or ionic polysaccharides in legumes) has been hypothesized to modulate the immune system by downregulating NF-kB activation pathways and reducing cytokine production. SCFAs are produced by certain gut microbes in response to fiber-rich diets [21]. Besides being substrates for energy production in colonocyte mitochondria (butyrate) and hepatocytes (propionate), SCFAs modulate the immune system by being converted to acetyl-CoA to increase acetylation and activate signaling pathways through G protein-coupled receptors (GPCR) such as free fatty acid receptors 2 and 3 (FFA2 and FFA3), and within the nucleus, enhance gene transcription by inhibiting histone deacetylase (HDAC). Activation of peroxisome proliferator-activated receptor gamma (PPAR-gamma) and inhibition of NF-kB activity further contribute to anti-inflammatory activity by suppressing inflammatory cytokines such as tumor necrosis factor-α (TNF-α), MCP-1, and IL-6 through GPR41 activation in macrophages [20].

Other nutrient sources play a role in anti-inflammatory actions, including monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA). One of the most common MUFAs, omega-9 oleic acid (18:1n-9), is present in high amounts in vegetable oils (especially olive oil) and certain nuts. Preclinical studies show MUFAs act anti-inflammatory by counteracting the effects of saturated long-chain fatty acids on hepatocytes, including limiting saturated fatty acid-induced lipotoxicity, reducing endoplasmic reticulum stress, lowering reactive oxygen species production, and inhibiting transcription factors NF-kB and NLRP3 (nucleotide-binding oligomerization domain-like receptor pyrin domain-containing-3) by binding to PPAR-gamma and GPR120, plus activation of AMPK phosphorylation [22]. MUFAs may also induce anti-inflammatory gene expression, such as adiponectin, via PPAR-gamma activation, thereby reducing IL-6 and TNF-α production. Another anti-inflammatory mechanism is MUFA-induced polarization of macrophages from M1 to M2 phenotype, promoting secretion of several anti-inflammatory factors such as MGL2, IL-10, TGFβ1, and MRC1[20].

Regarding PUFAs, in vitro and in vivo studies support the hypothesis that n-3 and n-6 PUFAs have opposing immune system effects: anti-inflammatory for n-3 and pro-inflammatory for n-6. Concerns about n-6 PUFAs such as linoleic acid (LA, 18:2n-6), found in vegetable oils, nuts, grains, meat, and eggs, are based on mechanisms that increase arachidonic acid (AA; 20:4n-6) conversion, subsequent pro-inflammatory eicosanoids production (PGE2, leukotriene B4), and reduced conversion of alpha-linolenic acid (ALA, 18:3n-3) to eicosapentaenoic acid (EPA, 20:5n-3) and/or docosahexaenoic acid (DHA, 22:6n-3) due to competition for elongase and desaturase enzymes, resulting in lower anti-inflammatory lipid mediators (resolvins, docosatrienes, protectins). However, human studies provide weak evidence for pro-inflammatory effects of dietary LA. Instead, high LA intake affects immune stimuli minimally and may even have anti-inflammatory potential through nitrosylated LA and 13-hydroxyoctadecadienoic acid. Conversely, ALA from plant sources (seeds and certain nuts) is essential and a precursor for anti-inflammatory eicosanoid production. ALA itself has weak direct anti-inflammatory effects but is a substrate for DHA and EPA synthesis, which inhibit NF-kB by binding PPAR-gamma and specific GPCRs in adipocytes and macrophages, reducing inflammatory cytokine production [20].

Plant-based diets (PBD), consisting of plant-derived foods, have shown beneficial effects on blood lipids and adiposity. PBDs are associated with a reduced risk of chronic diseases and a body mass index reduction of 4.4 kg/m^2 after six months without energy restriction in overweight or obese people. The mechanisms may involve changes in satiety and inflammation pathways [23]. Various analyses report that PBDs improve inflammatory profiles in obese patients. Many plant foods contain bioactive compounds with anti-obesity and anti-inflammatory effects [2].

Bioactive compounds are substances with biological activities that improve health. Fruits, vegetables, nuts, grains, and spices are rich in bioactive compounds. There is a strong link between the health benefits of foods with bioactive compounds and their ability to regulate gene expression in adipose tissue [2]. As mentioned, BCFA-containing compounds have anti-inflammatory effects by inhibiting lipopolysaccharide (LPS)-induced classical pro-inflammatory transcription pathways (NF-kB and TLR-4). In humans, serum BCFA levels inversely correlate with C-reactive protein (CRP) levels [20]. Therefore, dietary interventions that limit side effects and include more bioactive food compounds can be effective strategies for preventing obesity. Compared with animal product-rich diets, PBDs contain less total fat, saturated fat, cholesterol, and total energy, while being rich in unsaturated fatty acids and fiber [2].

Some food sources containing active peptides can also act as anti-inflammatory agents. Dairy products are the richest source of bioactive peptides, which can also be obtained from other foods including fish (such as tuna, sardines, anchovies, herring, and salmon), eggs, and meat products (e.g., beef muscle and blood), as well as plant sources like wheat, corn, soy, rice, spinach, sorghum, and mushrooms. Bioactive peptides exhibit better anti-inflammatory properties when they have short chains, as they are more likely to pass through the intestinal barrier intact and be absorbed more quickly. The main pathways influenced by bioactive peptides are the NF-kB pathway, MAPK, Janus kinase signal transducer and activator of transcription (JAK-STAT), and peptide transporter 1 (PepT1) [24].

Mechanisms involved include: (i) the presence of positively charged amino acid residues (arginine, lysine, and histidine), especially at the N- and/or C-terminal positions, which have anti-inflammatory activity against lipopolysaccharide (LPS)-stimulated inflammatory responses and chemokine receptor activation; (ii) the presence of hydrophobic amino acid residues (phenylalanine, leucine, tyrosine, glycine, and tryptophan) at the N-terminal position, which have been shown to interact with cell membranes and potentially disrupt inflammatory signaling cascades by binding Ca2+ and interfering with NF-kB signaling and cytokine production; (iii) the presence of electron-donor radical scavenger amino acids (glutamate, aspartate, and proline) that provide antioxidant activity and protect against inflammation caused by reactive oxygen species (ROS) [25].

Additional potential effects of some bioactive peptides that indirectly influence inflammation include antioxidant activity (inhibiting lipid oxidation, metal chelation, and reducing activity), antihypertensive activity (inhibiting angiotensin-1 converting enzyme), antimicrobial activity (direct action against Gram-positive or Gram-negative pathogenic bacteria), and regulatory activity on gut microbiota imbalance (normalizing populations of Bacteroidetes and Firmicutes in the colon) [20]

Besides nutritional composition, caloric regulation and timing have also been discussed as important. A negative energy balance required to reduce body weight is achieved by daily calorie restriction of 20–40%. A strategy of periodic and repeated energy restriction, called intermittent fasting (IF), involves abstaining from caloric foods and drinks for specific periods interspersed with normal eating. The main goal of fasting is to promote changes in metabolic pathways, cellular processes, and hormones.

Common physiological changes observed in response to IF include increased insulin sensitivity and decreased blood pressure, body fat, fasting glucose, and inflammation. IF leads to a 3–8% body weight reduction after 3 to 24 weeks and a 4–14% reduction after 6 to 24 weeks when compared to energy restriction. In young overweight women, intermittent energy restriction is an effective intervention for weight loss. However, IF might have harmful effects on children and the elderly [2].

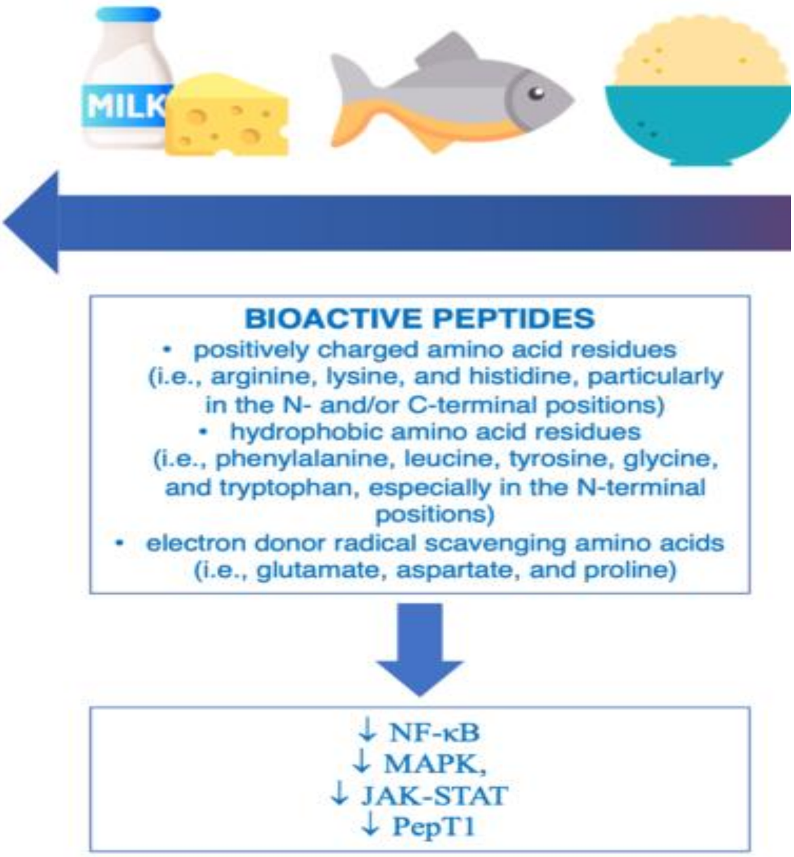

FIGURE 1: Inflammatory Pathways Affected by Nutrient Sources Rich in Bioactive Peptides.

Exercise Effects and Inflammation in Elderly Obese Patients

Pro-inflammatory cytokines related to obesity and aging include TNF-α, IL-6, and CRP, which cause peripheral blood mononuclear cells to remain in a pro-inflammatory state. This pro-inflammatory profile shifts macrophage polarization from the M2 (anti-inflammatory) phenotype to M1 (pro-inflammatory). Additionally, the CD8+ to CD4+ T cell ratio increases with obesity, limiting the secretion of anti-inflammatory cytokines that inhibit macrophage migration from CD4+ regulatory T cells. In fact, obesity can accelerate aging, and older adults with obesity have impaired immune responses [26]. Obesity and increased age-related inflammatory cytokines cause worsening damage-associated molecular patterns and immunosenescence, increasing morbidity and mortality [27].

Exercise is a modifiable factor to combat age-related obesity by counteracting positive energy balance and modulating immune cells, adipokines, and inflammatory cytokines. Young adults with obesity have IL-6 levels comparable to normal individuals when they exercise. Furthermore, young obese adults who exercise show positive correlations with BMI, waist-to-hip ratio, and fasting insulin levels [28]. Previous discussions also indicate various benefits of high-intensity interval training (HIIT) for obese patients. These effects are achieved through anti-inflammatory activity and improved endothelial function. Physical exercise improves general health in elderly obese individuals by reducing body fat and systemic inflammation. Increased physical activity improves body composition and insulin-like growth factor 1 (IGF-1) in elderly adults with sarcopenic obesity [24].

Increased IGF-1 levels inhibit astrocyte responses to inflammatory insults, thus modulating neuroinflammation. Physical exercise weakens obesity-related meta-inflammation and modifies metabolic hormones that can combat chronic inflammation and obesity-related conditions. Aerobic exercise for 10 months significantly reduces CRP, IL-6, and IL-18 in overweight elderly adults. In elderly adults with obesity and diabetes, 6 months of exercise decreases CRP and IL-18. Exercise interventions also reduce inflammation (IL-6, CRP, and TNF-α) in middle-aged and older adults with type 2 diabetes [29]. Collectively, these findings indicate that exercise interventions are effective methods to reduce systemic inflammation in elderly adults with obesity. Older overweight adults with higher physical activity levels express lower IL-6 inflammatory cytokine concentrations regardless of weight loss. This supports the use of exercise to improve systemic inflammation in elderly obese adults with the added benefit of reducing sarcopenia [27].

Combining diet and exercise is most effective for improving visceral adipose tissue, systemic inflammation, blood pressure, lipid profiles, and insulin sensitivity in elderly obesity, as repeatedly emphasized in this review. A one-year diet and exercise intervention improves insulin sensitivity more than diet or exercise alone in elderly obese adults. Reductions in CRP, TNF-α, and increases in adiponectin were observed after combined diet and exercise interventions in this population. Reduction of hormonally active visceral adipose tissue in obese adults is mediated by IL-6 released from skeletal muscle during exercise, which also acts as an anti-inflammatory agent to reduce chronic systemic inflammation. Calorie restriction and exercise over 15 weeks significantly reduce systemic inflammation (reductions in CRP, IL-6, TNF-α, IL-8, monocyte chemoattractant protein-1 [MCP-1]), subcutaneous adipose tissue inflammation, increase adiponectin, and improve insulin sensitivity in severely obese participants [27,30].

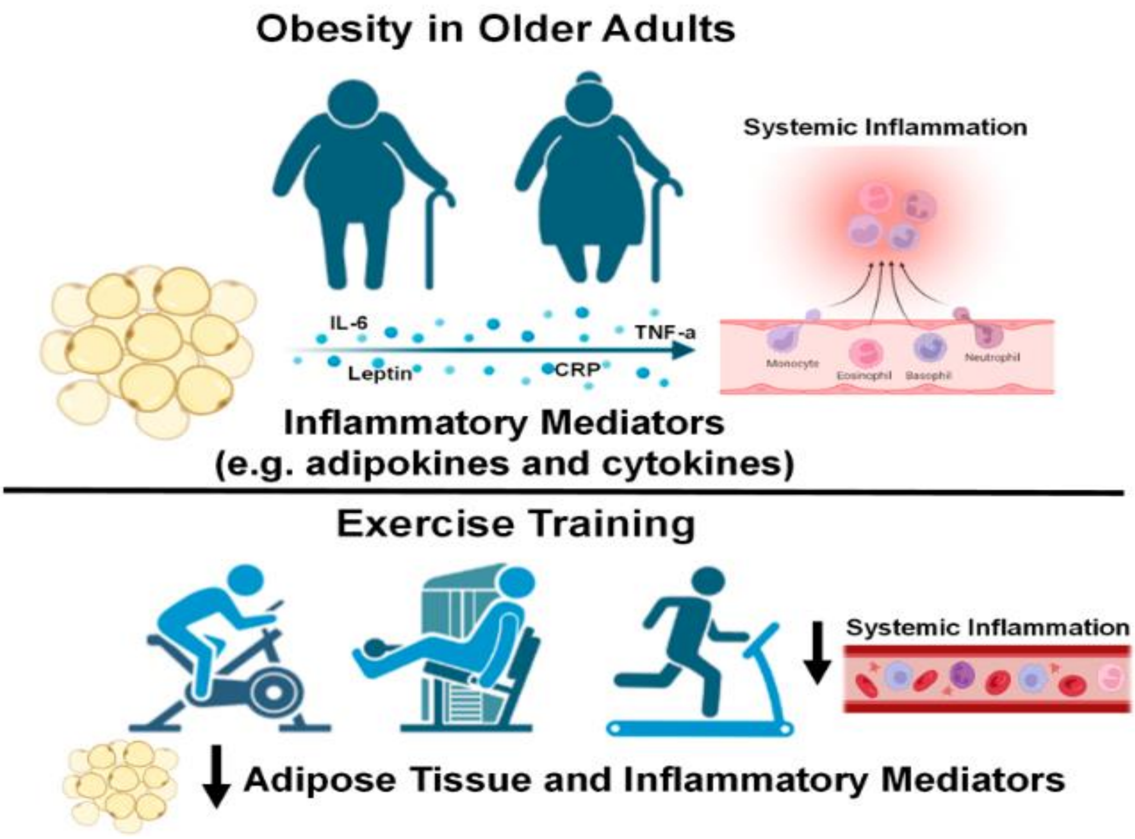

FIGURE 2: Effects of exercise and systemic inflammation in elderly obese patients [27].

CONCLUSION

The incidence of obesity continues to rise, becoming a global epidemic. Exercise plays an important role in preventing obesity by increasing energy expenditure to reduce body weight, lowering metabolic risk factors, and improving adipose tissue health. High-Intensity Interval Training (HIIT) involves short periods of exercise performed above lactate threshold, near VO2max, interspersed with light exercise or rest, allowing high-intensity training to be sustainable. Various studies have found links between HIIT and reductions in obesity and related morbidities. Another approach to obesity management is diet. Manipulating diet composition, eliminating/restricting certain food groups, and timing strategies can be used as management tools. Obesity can also accelerate aging processes and impair immune responses. Physical exercise can improve health in elderly individuals with obesity by reducing body fat and systemic inflammation.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest related to the publication of this research article.

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