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Sarcopenia in IBD patients and the role of nutritional and physical activity interventions in its management – a systematic review

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ABSTRACT

Inflammatory Bowel Diseases (IBD), namely Ulcerative Colitis and Crohn's Disease, are chronic, relapsing, inflammatory conditions of the gastrointestinal tract, with multifactorial pathophysiology. They are often complicated by sarcopenia, which is defined as a condition of skeletal muscle system characterized by a generalized loss of skeletal muscle mass and muscle function. Sarcopenia and pre-sarcopenic conditions are important to be diagnosed and maintained in the course of IBD, as they exert detrimental impact on the therapy outcomes. There is increased probability of therapy failure such as change of pharmacotherapy, hospitalization or

surgical intervention, in individuals with sarcopenia. There are multiple mechanisms underlying this complication in IBD: e.g. malnutrition, disrupted gut microbiota, pharmacotherapy, and elevated inflammatory cytokines. Nevertheless, there are some possible interventions that can be undertaken to counteract this complication. Fundamental interventions in IBD-related sarcopenia are: accurate nutrition, micronutrient supplementation and properly adjusted physical activity. IBD patients should do 3-5 moderate-intensity trainings per week. Exercise programs should combine aerobic, resistance and flexibility exercises. Resistance training is the first-line therapy in management of sarcopenia. This kind of exercises was proven to improve muscle mass, strength and physical performance. Aerobic activity is also important as it enhances metabolic capacity of the muscles.
However, further research is required to define specific recommendations for nutritional and exercise interventions validated for the group of patients with IBD-related sarcopenia.

Keywords

IBD, sarcopenia, Crohn's disease, colitis ulcerosa, inflammatory bowel disease

1. INTRODUCTION

Inflammatory Bowel Disease (IBD) is a term comprising two main disease entities: Ulcerative Colitis (UC) and Crohn's Disease (CD). The incidence and prevalence of these diseases is gradually increasing in most of the countries[1]. The pathophysiology of IBD is multifactorial. In individuals with susceptibility genes, the chain of dysfunctional interactions between environmental factors and the host's immune system leads to the breakdown of the intestinal homeostasis[2–4]. UC and CD share some characteristics, but there are some major differentiating features in terms of symptomatology and pathophysiology of these diseases. UC is characterized by ulcerations limited to the mucosal layer which stretch continuously from rectum upward occupying large bowel. On the other hand, in CD inflammation spreads deeper than mucosa, and can involve the whole intestinal wall thickness. Lesions are present in every part of gastrointestinal tract – from mouth to colon – and are not continuous, divided by sections of healthy intestine. What is more, in CD there is a tendency to form fistulas, perianal lesions and strictures, which are uncommon in UC[5].

IBD is often complicated by sarcopenia. There are plenty of factors contributing to this state in IBD patients, such as: chronic inflammation, malnutrition[6], decreased physical activity, gut microbiota dysbiosis and pharmacotherapy[1].

According to the consensus on sarcopenia, first formulated by the European Working Group on Sarcopenia in Older People (EWGSOP) in 2010, sarcopenia is defined as a condition of skeletal muscle system characterized by a generalized loss of skeletal muscle mass and muscle function (strength or performance)[7]. In compliance with this consensus, both criteria must be fulfilled and confirmed by the patient's documentation to diagnose sarcopenia. Updated EWGSOP2 guidelines for sarcopenia from 2018 reflect a better understanding of this condition[8,9]. While the definition of sarcopenia remained similar, the diagnostic focus has been shifted from the reduction in muscle mass to the decrease in muscle strength as a key characteristic. According to the diagnostic algorithm presented in current guidelines: the first step is assessment of muscle strength in a functional test. What is more, sarcopenia was primarily perceived as an age-related condition. Nowadays it is agreed that there are numerous circumstances that lead to development of sarcopenia such as: ageing, poor nutrition, physical inactivity, inflammatory diseases, neurological disorders, etc[10,11].

Although term sarcopenia was first used in the study by Rosenburg[12] in 1989, it was first included in the International Classification of Diseases (ICD) under the code M62.84 only in September 2016[13]. Before that it was not considered as a separate disease entity. This was a significant step in the recognition of this condition because it led to greater awareness of this problem among physicians.

In compliance with EWGSOP2, the severity of sarcopenia can be graded into three stages: probable sarcopenia, confirmed sarcopenia and severe sarcopenia[14]. In pre-sarcopenia there is reduced muscle strength only. To confirm the diagnosis of sarcopenia there has to be low muscle quantity or quality present. Severe sarcopenia is diagnosed when, in the course of confirmed sarcopenia, there is impairment of physical performance.

According to EWGSOP2 Guidelines[8,9] on sarcopenia, muscle strength can be easily assessed by handgrip strength measured by a dynamometer. It is an available, non-invasive method that can be used as a primary tool for targeting patients with probable sarcopenia. Muscle mass can be measured by DXA (dual-energy X-ray absorptiometry) or bioelectrical impedance. Whereas physical performance can be assessed using functional tests such as rising from chair unassisted, gait speed or the Short-Physical Performance Battery[15,16].

2. SARCOPENIA IN IBD

According to the systematic review concerning the epidemiology of sarcopenia in IBD patients[17], this condition was much more prevalent in the study population than in the general population without any defined diseases. Sarcopenia was diagnosed in 17% of 393 IBD patients compared with 10% of the individuals from general population[18]. What is more, myopenia (reduced muscle mass) and pre-sarcopenia (reduced muscle strength) were reported to be much more prevalent in IBD patients. Myopenia was confirmed to appear in 40% of patients and pre-sarcopenia was present in over 30% of patients[17]. The before mentioned conditions were much more prevalent in CD patients than in UC patients (35% and 45% vs. 32% and 43%, consecutively). The major factor correlated with sarcopenia in IBD was disease activity. The MRI assessment of body composition in patients with CD showed that in active disease sarcopenia was more common and SMI (skeletal muscle index) was lower[19,20].

The discussed complications of IBD: pre-sarcopenia, sarcopenia and myopenia exert significant effect on IBD outcomes. Results of numerous studies prove the risk of therapy failure resulting in change of pharmacotherapy, hospitalization or surgical intervention in patients with complications on the spectrum of sarcopenia[21–23]. In the study by *Grillot et al.*[24] researchers used CT imaging to measure body composition and defined sarcopenia using SMI (skeletal muscle index). The results showed sarcopenia in 58% of CD patients. Individuals with sarcopenia had much more adverse outcomes comprising: hospitalizations (61.2% vs 36.1%), digestive surgery (63.3% vs 27.8%) and abscesses (51% vs 16.7%) than non-sarcopenic patients during the follow-up[24]. Myopenia was proven to be an independent risk factor of pharmacotherapy failure and loss of response to anti-TNF-α drugs in CD and to corticosteroids in active severe UC[25,26]. Another publication by *Ge et al.*[27] investigated the relationship between sarcopenia imaged by CT and outcomes in acute severe UC (ASUC). The study showed that a significantly greater proportion of sarcopenic patients with ASUC required colectomy and rescue therapy in comparison with patients without sarcopenia[27].

These studies confirm the salience of body composition analysis and diagnosis of sarcopenia in IBD patients for better prognosis and treatment of these patients. The prevalence of this complication as well as its influence on the therapy outcomes highlights the importance of assessment of muscle loss and weakening in this group of patients.

3. MECHANISMS OF SARCOPENIA IN IBD PATIENTS

3a. MALNUTRITION

There are several mechanisms that contribute to pathogenesis of sarcopenia in IBD patients, including: malnutrition, physical inactivity, inflammation, pharmacotherapy, and microbiome dysbiosis. Among the above mentioned, the major factor inducing muscle loss in IBD is malnutrition[28,29].

CD and UC are chronic, relapsing and remitting, inflammatory diseases of the gastrointestinal tract. Approximately 20-85% of patients with IBD are diagnosed with malnutrition of diverse intensity[30]. There are some fundamental differences in the pathophysiology of these two disease entities and, as a result, there tend to be different patterns of malnutrition in these groups of patients. Protein-energy malnutrition as well as specific micronutrient deficiencies are more common in CD[30]. In CD inflammatory process involves the whole gastrointestinal tract – from mouth to the rectum, in contrast to UC which is limited to the large bowel. Malnutrition in CD is more common compared to UC due to significant malabsorption which is an effect of the loss of intestinal surface area as a result of ongoing inflammation, fistulae formation or surgical resections. Secondly, individuals with CD tend to develop malnutrition over a long period of time. In contrary, UC patients tend to maintain healthy nourishment in remission with rapid development of malnutrition in acute relapses[30,31].

Malnutrition is one of the main causes of sarcopenia in IBD patients. The main determinant of malnutrition in individuals with IBD is decreased oral intake[32]. Patients often have lower appetite because of various symptoms from gastrointestinal tract, such as: nausea, vomiting, diarrhea, abdominal pain which result from the disease itself. Another common cause of nausea and loss of appetite is pharmacotherapy[33].

Malabsorption is strictly related to the pathophysiology of IBD: primarily to the impaired mucosal function due to inflammation. Defective epithelial transport and damaged epithelial barrier lead to decreased ability to digest and absorb micro- and macronutrients. Particularly detrimental, in terms of nutrient absorption, can be the ileal localization of CD[34]. Persistent inflammation can even cause protein-losing enteropathy and chronic blood loss leading to microcytic anemia[35,36].

A very prevalent complication of IBD is small intestinal bacterial overgrowth (SIBO), which is especially common in CD patients with ileal involvement and after surgical excision of

ileocecal valve. In such conditions, translocation of colonic bacteria to small bowel occurs, leading to numerous gastrointestinal symptoms. Bacteria produce osmotically active substances which cause diarrhea, bloating and abdominal pain. Intensified intestinal motility and shortened gastrointestinal transit time leads to reduced digestion and absorption of micoro- and macronutrients[32,37]. Additionally, SIBO is proven to be associated with increased intestinal wall permeability[38].

Despite the advances in the pharmacological treatment of IBD, surgical interventions are still indispensable in some situations. It is estimated that 25%-35% of UC patients and 70% up to 90% of CD patients will need surgery at some point of their disease management[39,40]. This is why surgical interventions need to be taken into consideration in the discussion over malnutrition in IBD patients. Resection of a big segment of small intestine can lead to impaired digestion and absorption resulting in watery stools. Excision of big portion of ileum can be followed by bile salt diarrhea because of the decreased bile acids uptake in the intestine[41]. What is more, hospitalization itself is often associated with reduced food intake and immobilization[42]. As mentioned in the following paragraph, chronic inflammation and persistent advantage of inflammatory cytokines (e.g. TNF-α, Il-1 β, Il-6, Il-12) in the organism, lead to increased catabolism, which also contributes to malnutrition. They also have anorexiogenous effect and further decrease food intake[43].

Patients with IBD are extremely endangered with protein-energy malnutrition, which is a key driver of sarcopenia. Adequate protein supply and absorption is necessary to muscle protein synthesis. Muscle regeneration is also not possible in chronic malnutrition, which results in muscle wasting [42,44].

3b. MICRONUTRIENT AND VITAMIN DEFFICIENCIES

The most common micronutrient deficiencies are iron, folic acid, vitamin B12 and vitamin D[45]. Folic acid can be significantly decreased due to use of certain drugs, which are fundamental in IBD treatment, including mesalazine, sulphasalazine or methotrexate. It is due to decreased absorption and competitive inhibition by the above-mentioned folate antagonists used in pharmacotherapy. Folic acid deficiency is similarly frequent in patients with IBD independently of the differential diagnosis. In contrary, studies show that prevalence of vitamin B12 deficiency is significantly higher in patients with CD compared to patients with UC[46]. There are numerous mechanisms leading to insufficient levels of vitamin B12 in patients with CD, including: inflammation of the distal ileum, SIBO, fistulae. Especially patients after ileal or ileocolonic

resection are at increased risk of vitamin B12 deficiency[47].

Vitamin B12 and folate levels are significantly correlated with sarcopenia. Studies show that in patients with deficiency of these vitamins muscle strength and mass is declined[48–50]. Vitamin B12 and folate are necessary as cofactors in the transition pathway of homocysteine into methionine. Therefore, reduced levels of these vitamins contribute to elevation of homocysteine levels. Hyperhomocysteinemia is an important cardiovascular risk factor which is connected with higher incidence of thromboembolic events in IBD[32,42,51]. What is more, homocysteine can impair muscle function leading to muscle protein hydrolysis and impairment of muscle regeneration, through multiple mechanisms. Homocysteine takes part in inactivation of nitric oxide synthase (NOS) pathway, increases oxidative stress in endoplasmic reticulum, and interferes with signaling pathways of TGF-β. All these processes predispose to development of sarcopenia[52,53].

Patients with lower levels of folate tend to have lower muscle strength. The possible mechanism of this dependency is the influence of folate on DNA synthesis, protein synthesis, neurotransmitter formation and epigenetic changes such as methylation of DNA[49].

Prevalence of vitamin D deficiency in IBD patients oscillates from 16% up to 95% depending on the study reviewed.[45,54] Low levels of vitamin D have a well-documented association with lower muscle mass, strength and performance and are predictive of further muscle loss[55]. Vitamin D deficiency was proven to be associated with increased fall risk due to reduction of appendicular muscle mass (ASMM) and muscle strength[56,57]. Severe vitamin D insufficiency can lead to muscle wasting which can cause muscle pain and waddling gait[58].

Another consequence of malnutrition in IBD is mineral deficiencies including iron, zinc and selenium. Iron depletion in IBD patients is multifactorial, dependent on chronic inflammation in the organism, blood loss, etc. Iron deficiency correlates well with the activity of the disease, being more prevalent in relapses than remissions[59,60]. Low levels of iron can cause muscle dysfunction, as iron ions are important in cellular metabolic pathways, mitochondrial function and insulin signaling[61].

Zinc was found to be deficient in approximately 15% of individuals with IBD[62]. Zinc functions as an anti-oxidant, as it is a co-factor of superoxide dismutase (SOD), which is a crucial enzyme in cellular defense against oxidative stress[63]. Another deficient mineral: selenium, is a co-factor of another anti-oxidative enzyme: glutathione peroxidase, which participates in degradation of reactive oxygen and nitrogen species[64,65]. Deficiency of these microelements can lead to increased formation of reactive oxygen species which contribute to muscle degeneration and development of sarcopenia[66,67].

Malnutrition, both energy-protein malnutrition and micronutrient deficiencies, is a serious, prevalent complication of IBD, especially CD. This is a crucial factor in development of IBD-related sarcopenia.

3c. INFLAMMATION

Chronic inflammation is another crucial factor that affects muscle strength and functionality in patients with IBD. The plasma levels of pro-inflammatory cytokines, including: TNF-α, Il-1β, Il-6, Il-12, Il-21, Il-23 are elevated causing the promotion of inflammation in tissues, immune cell recruitment and disruption of intestinal barrier[68–72]. Complex cytokine signaling pathways mediate processes of protein catabolism and decrease synthesis of muscles.

TNF-α activates the NF-κB pathway, therefore promoting the expression of muscle-specific ubiquitin ligases: MuRF-1 and atrogin-1, which are a part of the ubiquitin-proteasome system involved in degradation of muscle proteins[73,74].

Interleukin 6 (Il-6) is another crucial agent in the pathogenesis of muscle atrophy in IBD. Il-6 can exert both positive and negative effect on skeletal muscles depending on its concentration, clinical context and time of action. During physical exercise, acute and moderate increase of Il-6 levels supports muscles metabolism and regeneration. Chronic elevation of Il-6 levels, present in inflammatory diseases, activates the JAK/STAT and NF-κB pathways causing an increase in expression of proteolytic enzymes and catabolism of muscle proteins. Raised levels of Il-6 and TNF-α also lead to suppression of insulin-like growth factor 1 (IGF-1), a pivotal anabolic hormone which stimulates muscle growth and regeneration[73,75]. Reduced levels of IGF-1 result in decreased PI3K pathway activation and therefore decreased mTORC1 signaling, which results in decline of protein synthesis[75,76].

IL-1β is one of the major inflammatory cytokines in the innate and adaptive immune system. It is also involved in the regulation of Il-17 production which is an important cytokine overexpressed in IBD patients. IL-1β contributes to the pathogenesis of sarcopenia by promoting inflammation and formation of reactive oxygen species (ROS)[44]. The oxidative stress leads to damage of the muscle cells and also interferes with intracellular signaling pathways involved in skeletal muscle catabolism[77,78].

Understanding the complex mechanisms underlying the pathophysiology of IBD has allowed the development of effective biological therapies targeting specific cytokines[3]. Biological treatment is a commonly used advanced treatment option in patients with IBD. According to British Guidelines on IBD management[79], currently in the UK approximately 30% of CD and

15% of UC patients are treated with biologics. Biologics used in CD therapy comprise: anti-TNF-α, anti-integrin, anti-Il12/23 and anti-Il23, while biologics used in UC therapy comprise: anti-TNF-α, anti-integrin, anti-Il12/23, anti-Il23, oral JAK inhibitors, and S1P-inhibitors[80]. There are very few studies raising the issue of the influence of biological treatment on the prevalence of sarcopenia in IBD. *Subramaniam et al.* observed improvement in muscle mass and strength, in patients with acute CD flare, who were treated with anti-TNF-α agent[81]. Similar results were obtained by *Csontos et al.* who confirmed an alleviation of muscle parameters after 12 weeks of treatment with anti-TNF-α biologic in IBD patients[82].

3d. GUT-MUSCLE AXIS

Healthy intestinal microbiota lies at the basis of well-functioning gut-muscle axis and is fundamental in skeletal muscle homeostasis[83]. Gut microbiota, in the process of fermentation of fibers, produces short chain fatty acids (SCFA), which have multidirectional effects. SCFA, such as butyrate, propionate regulate immune and metabolic homeostasis as well as gene expression. SCFA have anti-inflammatory effect as they promote production of anti-inflammatory cytokines, e.g. Il-10 and suppress production of inflammatory cytokines, e.g. TNF-α**,** IL-6**,** and IL-12. Additionally, butyrate enhances the integrity of epithelial barrier of the mucosa, therefore preventing translocation of bacteria and reducing inflammation[84]**.** SCFA, especially acetate and butyrate have antioxidant properties due to upregulation of superoxide dismutase (SOD) enzyme which reduces the production of reactive oxygen species[85]. Butyrate was also proven to stimulate muscle stem cells (satellite cells) proliferation and differentiation, supporting muscle hyperplasia and regeneration[86]. The study by *Liu et al.* on animal model showed that SCFA activate mTOR signaling pathway therefore stimulating protein synthesis. They proved that SCFA produced by intestinal bacteria counteract the development of age-related muscle dysfunction and sarcopenia[87].

This is why, preserving a heathy gut-muscle axis is significant in muscle homeostasis and prevention of sarcopenia. Intestinal microbiome composition is dependent on multiple factors, including: accurate nutrition and supply of macro- and micronutrients, e.g. folate, vitamin B12; pharmacotherapy, etc. In IBD patients, there are various nutritional deficiencies which can impair function of gut microbiota[88].

4. NUTRITIONAL INTERVENTIONS IN SARCOPENIA IN IBD

IBD patients are at increased risk of malnutrition, therefore should be regularly screened for this complication. They should have regular check-ups for micronutrient deficiencies which can be adjusted by appropriate supplementation of vitamins and minerals[89]. Energy-protein and micronutrient deficiencies further lead to development of sarcopenia which exerts detrimental effect on the clinical outcomes in IBD patients. Relevant nutritional interventions should be considered fundamental in holistic management of IBD patients.

According to ESPEN Guidelines on Clinical Nutrition in IBD[89], there is no universal diet that can be recommended in the general population of IBD patients. Diet should be adjusted to the individual needs, activity of the disease and clinical symptoms of the patient.
If oral food intake is constricted or insufficient, patient nutrition can by supported with the use of oral nutritional supplements (ONS), enteral nutrition (EN) or eventually parenteral nutrition (PN)[90]. ONS help patients increase the intake of calories and macronutrients and are first-line choice in nutritional support. Patients who cannot satisfy energetic and nutritional needs of their organism by oral intake, benefit from EN. PN is recommended in individuals with malabsorption or shortened small intestine (in CD, after resections), whose intestines cannot absorb necessary nutrients, however if possible, the use of EN has advantage over PN use[91,92]. Exclusive EN is proven to be effective in induction of remission only in mild active CD in children and adolescents[93]. Serum levels of particular vitamins and minerals, including: iron, folate, vitamin B12, vitamin D, calcium, magnesium, potassium, etc. should be regularly checked and supplementation of these microelements should be adjusted to individual needs[89].

Considering age-related sarcopenia, appropriate diet together with physical activity, is an established primary factor in mitigation of this condition. Likewise, supplementation of deficiencies and adequate nutrition can serve as a key tool in prevention of sarcopenia related with IBD. Albeit, studies on this topic are lacking and there are still no specific nutritional recommendations for prevention and treatment of IBD-related sarcopenia.
According to the article by *Morley et al.*, the fundamental aspects of the diet in sarcopenia comprise sufficient protein and caloric intake and prevention of micronutrient deficiencies[94]. Total protein intake should count from 1 g/kg to 1,5 g/kg daily, in patients with no kidney dysfunction. Additionally, supplementation of β-hydroxy β-methylbutyrate (HMB) and creatine

may be of some benefit in patients with sarcopenia, but further research in IBD patients is warranted to establish the validity of such intervention[14,94].

5. PHYSICAL EXERCISE IN SARCOPENIA IN IBD

It is well-established that appropriate physical activity is recommended in supportive management of IBD[95]. However, there are scarce clinical guidelines concerning the topic of physical activity in IBD patients. Individual approach is highly recommended, with exercise programs suited to patients' clinical state and needs. Prevailing guidelines from the American Heart Association and the American Academy of Sports Medicine recommend regular physical activity consisting of moderate intensity aerobic training 5 times per week or high intensity training 3 times a week[96]. These are universal recommendations for everyone aged 18-65. The only guidelines on the topic of physical activity, concerning the population of individuals with IBD, were published in 1998 by *Ball et al.*[97]. However, they were formulated on the basis of data from healthy individuals. There are no guidelines concerning physical activity, which are based on validated data for IBD patients[95]. According to report by *Ball et al.* IBD patients should engage in moderate-intensity training, 3-5 times a week. Exercise programs should combine aerobic, resistance and flexibility (stretching) exercises. Patients should adjust their trainings to the activity of the disease, limiting their physical activity during acute relapses[97]. Low, moderate and high intensity exercises are proven to improve quality of life, body composition, cardiorespiratory fitness, bone mineral density (BMD), maintain gut microbiota and reduce inflammatory markers in patients with IBD[98].

The vital approach in improvement of muscle mass, strength and functionality in patients with sarcopenia is physical activity[14]. It is recommended for patients with sarcopenia to do two full-body trainings per week[99]. Resistance training it the first-line therapy in management of sarcopenia.[100] Resistance training is defined as any physical exercises with use of external resistance such as free weights, elastic bands, body weight, etc. which yield skeletal muscle contractions. This kind of exercises has been proven in numerous studies to improve muscle mass, strength and physical performance[101]. Study by *Chang et al.*[44] examined patients with sarcopenia before and after 12-week program of regular resistance training and supplementation with branched-chain amino acids, calcium, and vitamin D3. They observed a significant decrease of plasma levels of inflammatory cytokines (TNF-α, IL-1β, and IL-6) in the study group. What is more, after 12 weeks of regular resistance training and nutritional supplementation, patients exhibited improvement in muscle mass and strength[44]. Resistance

training leads to activation of mTOR signaling pathway thus mediates muscle hypertrophy through increased protein synthesis[102].

It is proven that aerobic training ameliorates metabolic capacity of muscles through enhanced mitochondrial biogenesis in muscle cells[103]. Aerobic activity was also proven to induce muscle hypertrophy, in contrary to the common belief that muscle mass is only increased due to strength exercises[104].

Physical activity, both aerobic and resistance exercises, improve immune function and exert a positive effect in chronic inflammation by reducing inflammatory markers[105].

Interleukin-6 displays pleiotropic action in human organism[106]. It is primarily associated with acute phase response and chronic inflammatory conditions, such as autoimmune diseases. What is less known, is that Il-6 is an important signaling agent in skeletal muscles – myokine, engaged in physiological response to physical activity[73]. It is produced in the contracting muscle during prolonged activity[106]. Muscle-derived Il-6 binds to membrane receptors on satellite cells and activates the JAK/STAT3 signaling pathway, leading to activation of transcription of specific genes resulting in proliferation and differentiation of the muscle stem cells, thus inducing myogenesis and skeletal muscle hypertrophy[107]. Additionally, Il-6 released during physical activity increases secretion of GLP-1 (glucagon–like peptide 1) which is engaged in the repair processes in damaged intestinal mucosa[108].

What is more, studies show that serum level of Il-6 is inversely related to physical activity[109]. Il-6 is released from different tissues in diverse clinical conditions. Apart from the above mentioned activity in skeletal muscles, Il-6 is released from adipocytes and leukocytes in chronic inflammatory conditions. It was proven that aerobic physical activity tended to reduce levels of Il-6, CRP and TNF-alpha, exerting and anti-inflammatory effect in patients with chronic low-grade inflammation[110,111].

Study by *Saxena et al.*[112] in animal model of chemically induced colitis revealed reduction of inflammatory cytokines, including TNF-α, IL-1β and increase in Il-6 and anti-inflammatory Il-10, in exercise-trained mice. This proves that exercise exerts anti-inflammatory effect in colitis and may alleviate colitic symptoms[112].

According to the article by *Gulick et al.*[113] individuals who have regular physical activity, particularly resistance training and moderate intensity aerobic training, have significantly higher levels of serum IGF-1which is an anabolic agent participating in muscle growth and regeneration.

6. CONCLUSION

IBD is a chronic inflammatory disease of the gastrointestinal tract. Sarcopenia, defined as decreased muscle mass, strength and functionality, is a common complication of this disease entity. There are multiple factors underlying this condition in IBD patients, mainly: chronic inflammation, pharmacotherapy, macro- and micronutrient deficiencies, low physical activity and defective microbiome. The importance of sarcopenia, as an IBD complication, should be emphasized, as it is substantially prevalent and detrimental for the clinical outcomes in IBD patients. Sarcopenia can be perceived as a strong predictor of treatment outcomes, including: hospitalization, clinical course and need for surgery. In this article, we focused on the nutritional and physical exercise interventions, which are undeniably important in counteracting and therapy of IBD-related sarcopenia. There are available data from studies based on the populations of individuals with age-related sarcopenia but specific recommendations for patients with IBD-related sarcopenia are still lacking. Further research is warranted in the field of nutritional and exercise interventions in patients with IBD-related sarcopenia. It is crucial to obtain data validated for this specific group of patients in order to determine individualized recommendations and assess the efficacy of these interventions.

REFERENCES

1. Mendes J, Simões CD, Martins JO, Sousa AS. INFLAMMATORY BOWEL DISEASE AND SARCOPENIA: A FOCUS ON MUSCLE STRENGTH - NARRATIVE REVIEW. *Arq Gastroenterol*. 2023;60:373-382. doi:https://doi.org/10.1590/S0004-2803.230302023-45

2. Wallace KL, Zheng LB, Kanazawa Y, Shih DQ. Immunopathology of inflammatory bowel disease. *World J Gastroenterol*. 2014;20(1):6-21. doi:10.3748/wjg.v20.i1.6

3. Friedrich M, Pohin M, Powrie F. Cytokine Networks in the Pathophysiology of Inflammatory Bowel Disease. *Immunity*. 2019;50(4):992-1006. doi:10.1016/j.immuni.2019.03.017

4. Intestinal homeostasis and its breakdown in inflammatory bowel disease - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/21677746/

5. (PDF) Endoscopic Diagnosis and Differentiation of Inflammatory Bowel Disease. Accessed December 25, 2024. https://www.researchgate.net/publication/305721789_Endoscopic_Diagnosis_and_Differentiation_of_Inflammatory_Bowel_Disease

6. Scaldaferri F, Pizzoferrato M, Lopetuso LR, et al. Nutrition and IBD: Malnutrition and/or Sarcopenia? A Practical Guide. *Gastroenterol Res Pract*. 2017;2017:8646495. doi:10.1155/2017/8646495

7. Fielding RA, Vellas B, Evans WJ, et al. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc*. 2011;12(4):249-256. doi:10.1016/j.jamda.2011.01.003

8. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(1):16-31. doi:10.1093/ageing/afy169

9. Cruz-Jentoft AJ, Bahat G, Bauer J, et al. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing*. 2019;48(4):601. doi:10.1093/ageing/afz046

10. Mijnarends DM, Koster A, Schols JMGA, et al. Physical activity and incidence of sarcopenia: the population-based AGES-Reykjavik Study. *Age Ageing*. 2016;45(5):614-620. doi:10.1093/ageing/afw090

11. Muscaritoli M, Anker SD, Argilés J, et al. Consensus definition of sarcopenia, cachexia and pre-cachexia: joint document elaborated by Special Interest Groups (SIG) "cachexia-anorexia in chronic wasting diseases" and "nutrition in geriatrics." *Clin Nutr*. 2010;29(2):154-159. doi:10.1016/j.clnu.2009.12.004

12. Summary comments - ScienceDirect. Accessed December 14, 2024. https://www.sciencedirect.com/science/article/abs/pii/S0002916523436945

13. Anker SD, Morley JE, von Haehling S. Welcome to the ICD-10 code for sarcopenia. *J Cachexia Sarcopenia Muscle*. 2016;7(5):512-514. doi:10.1002/jcsm.12147

14. Marzetti E, Calvani R, Tosato M, et al. Sarcopenia: an overview. *Aging Clin Exp Res*. 2017;29(1):11-17. doi:10.1007/s40520-016-0704-5

15. Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/21527165/

16. Exter SH, Koenders N, Wees P, Berg MGA. A systematic review of the psychometric properties of physical performance tests for sarcopenia in community-dwelling older adults. *Age Ageing*. 2024;53(6):afae113. doi:10.1093/ageing/afae113

17. Fatani H, Olaru A, Stevenson R, et al. Systematic review of sarcopenia in inflammatory bowel disease. *Clin Nutr*. 2023;42(8):1276-1291. doi:10.1016/j.clnu.2023.05.002

18. Prevalence of sarcopenia in the world: a systematic review and meta- analysis of general population studies - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/28523252/

19. Labarthe G, Dolores M, Verdalle-Cazes M, et al. Magnetic resonance imaging assessment of body composition parameters in Crohn's disease. *Dig Liver Dis*. 2020;52(8):878-884. doi:10.1016/j.dld.2020.06.024

20. Magnetic resonance imaging assessment of body composition parameters in Crohn's disease - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/32622612/

21. Combination of sarcopenia and high visceral fat predict poor outcomes in patients with Crohn's disease - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/33531636/

22. Holt DQ, Varma P, Strauss BJG, Rajadurai AS, Moore GT. Low muscle mass at initiation of anti-TNF therapy for inflammatory bowel disease is associated with early treatment failure: a retrospective analysis. *Eur J Clin Nutr*. 2017;71(6):773-777. doi:10.1038/ejcn.2017.10

23. Pedersen M, Cromwell J, Nau P. Sarcopenia is a Predictor of Surgical Morbidity in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2017;23(10):1867-1872. doi:10.1097/MIB.0000000000001166

24. Grillot J, D'Engremont C, Parmentier AL, et al. Sarcopenia and visceral obesity assessed by computed tomography are associated with adverse outcomes in patients with Crohn's disease. *Clin Nutr*. 2020;39(10):3024-3030. doi:10.1016/j.clnu.2020.01.001

25. Holt DQ, Varma P, Strauss BJG, Rajadurai AS, Moore GT. Low muscle mass at initiation of anti-TNF therapy for inflammatory bowel disease is associated with early treatment failure: a retrospective analysis. *Eur J Clin Nutr*. 2017;71(6):773-777. doi:10.1038/ejcn.2017.10

26. Ge X, Xia J, Wu Y, et al. Sarcopenia assessed by computed tomography is associated with colectomy in patients with acute severe ulcerative colitis. *Eur J Clin Nutr*. 2022;76(3):410-418. doi:10.1038/s41430-021-00953-y

27. Sarcopenia assessed by computed tomography is associated with colectomy in patients with acute severe ulcerative colitis - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/34131303/

28. Cederholm T, Barazzoni R, Austin P, et al. ESPEN guidelines on definitions and terminology of clinical nutrition. *Clin Nutr*. 2017;36(1):49-64. doi:10.1016/j.clnu.2016.09.004

29. Nishikawa H, Nakamura S, Miyazaki T, et al. Inflammatory Bowel Disease and Sarcopenia: Its Mechanism and Clinical Importance. *J Clin Med*. 2021;10(18):4214. doi:10.3390/jcm10184214

30. Goh J, O'Morain CA. Review article: nutrition and adult inflammatory bowel disease. *Aliment Pharmacol Ther*. 2003;17(3):307-320. doi:10.1046/j.1365-2036.2003.01482.x

31. Han PD, Burke A, Baldassano RN, Rombeau JL, Lichtenstein GR. Nutrition and inflammatory bowel disease. *Gastroenterol Clin North Am*. 1999;28(2):423-443, ix. doi:10.1016/s0889-8553(05)70063-7

32. Balestrieri P, Ribolsi M, Guarino MPL, Emerenziani S, Altomare A, Cicala M. Nutritional Aspects in Inflammatory Bowel Diseases. *Nutrients*. 2020;12(2):372. doi:10.3390/nu12020372

33. Hanauer SB, Stathopoulos G. Risk-benefit assessment of drugs used in the treatment of inflammatory bowel disease. *Drug Saf*. 1991;6(3):192-219. doi:10.2165/00002018-199106030-00005

34. Capristo E, Addolorato G, Mingrone G, Greco AV, Gasbarrini G. Effect of disease localization on the anthropometric and metabolic features of Crohn's disease. *Am J Gastroenterol*. 1998;93(12):2411-2419. doi:10.1111/j.1572-0241.1998.00696.x

35. Hébuterne X, Filippi J, Al-Jaouni R, Schneider S. Nutritional consequences and nutrition therapy in Crohn's disease. *Gastroenterol Clin Biol*. 2009;33 Suppl 3:S235-244. doi:10.1016/S0399-8320(09)73159-8

36. Kaitha S, Bashir M, Ali T. Iron deficiency anemia in inflammatory bowel disease. *World J Gastrointest Pathophysiol*. 2015;6(3):62-72. doi:10.4291/wjgp.v6.i3.62

37. Saltzman JR, Russell RM. Nutritional consequences of intestinal bacterial overgrowth. *Compr Ther*. 1994;20(9):523-530.

38. Rutgers HC, Batt RM, Proud FJ, et al. Intestinal permeability and function in dogs with small intestinal bacterial overgrowth. *J Small Anim Pract*. 1996;37(9):428-434. doi:10.1111/j.1748-5827.1996.tb02443.x

39. Wexner SD, Rosen L, Lowry A, et al. Practice parameters for the treatment of mucosal ulcerative colitis--supporting documentation. The Standards Practice Task Force. The American Society of Colon and Rectal Surgeons. *Dis Colon Rectum*. 1997;40(11):1277-1285. doi:10.1007/BF02050809

40. Gardiner KR, Dasari BVM. Operative management of small bowel Crohn's disease. *Surg Clin North Am*. 2007;87(3):587-610. doi:10.1016/j.suc.2007.03.011

41. Role of bile acid malabsorption in pathogenesis of diarrhea and steatorrhea in patients with ileal resection. I. Response to cholestyramine or replacement of dietary long chain triglyceride by medium chain triglyceride - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/5029077/

42. Lucendo AJ, De Rezende LC. Importance of nutrition in inflammatory bowel disease. *World J Gastroenterol*. 2009;15(17):2081-2088. doi:10.3748/wjg.15.2081

43. Cabré E, Gassull MA. Nutrition in inflammatory bowel disease: impact on disease and therapy. *Curr Opin Gastroenterol*. 2001;17(4):342-349. doi:10.1097/00001574-200107000-00008

44. Chang KV, Wu WT, Chen YH, et al. Enhanced serum levels of tumor necrosis factor-α, interleukin-1β, and -6 in sarcopenia: alleviation through exercise and nutrition intervention. *Aging (Albany NY)*. 2023;15(22):13471-13485. doi:10.18632/aging.205254

45. Weisshof R, Chermesh I. Micronutrient deficiencies in inflammatory bowel disease. *Curr Opin Clin Nutr Metab Care*. 2015;18(6):576-581. doi:10.1097/MCO.0000000000000226

46. Huang S, Ma J, Zhu M, Ran Z. Status of serum vitamin B12 and folate in patients with inflammatory bowel disease in China. *Intest Res*. 2017;15(1):103-108. doi:10.5217/ir.2017.15.1.103

47. Headstrom PD, Rulyak SJ, Lee SD. Prevalence of and risk factors for vitamin B(12) deficiency in patients with Crohn's disease. *Inflamm Bowel Dis*. 2008;14(2):217-223. doi:10.1002/ibd.20282

48. (PDF) Association between folic acid levels and sarcopenia in American adults: evidence from NHANES. Accessed December 15, 2024. https://www.researchgate.net/publication/380204116_Association_between_folic_acid_levels_and_sarcopenia_in_American_adults_evidence_from_NHANES

49. Serum folate predicts muscle strength: a pilot cross-sectional study of the association between serum vitamin levels and muscle strength and gait measures in patients >65 years old with diabetes mellitus in a primary care setting - PMC. Accessed December 15, 2024. https://pmc.ncbi.nlm.nih.gov/articles/PMC5070191/

50. Ates Bulut E, Soysal P, Aydin AE, Dokuzlar O, Kocyigit SE, Isik AT. Vitamin B12 deficiency might be related to sarcopenia in older adults. *Exp Gerontol*. 2017;95:136-140. doi:10.1016/j.exger.2017.05.017

51. Vascular complications of inflammatory bowel disease - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/3080643/

52. Veeranki S, Tyagi SC. Defective homocysteine metabolism: potential implications for skeletal muscle malfunction. *Int J Mol Sci*. 2013;14(7):15074-15091. doi:10.3390/ijms140715074

53. Lu B, Shen L, Zhu H, Xi L, Wang W, Ouyang X. Association between serum homocysteine and sarcopenia among hospitalized older Chinese adults: a cross-sectional study. *BMC Geriatr*. 2022;22:896. doi:10.1186/s12877-022-03632-0

54. Mouli VP, Ananthakrishnan AN. Review article: vitamin D and inflammatory bowel diseases. *Aliment Pharmacol Ther*. 2014;39(2):125-136. doi:10.1111/apt.12553

55. Low vitamin D status is associated with reduced muscle mass and impaired physical performance in frail elderly people - PubMed. Accessed December 11, 2024. https://pubmed.ncbi.nlm.nih.gov/23942175/

56. Visser M, Deeg DJH, Lips P, Longitudinal Aging Study Amsterdam. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. *J Clin Endocrinol Metab*. 2003;88(12):5766-5772. doi:10.1210/jc.2003-030604

57. Vitamin D treatment for the prevention of falls in older adults: systematic review and meta-analysis - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/20579169/

58. Vitamin D and Sarcopenia/Falls - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/26059567/

59. Antunes CV de A, Hallack Neto AE, Nascimento CR de A, et al. Anemia in inflammatory bowel disease outpatients: prevalence, risk factors, and etiology. *Biomed Res Int*. 2015;2015:728925. doi:10.1155/2015/728925

60. Alves RA, Miszputen SJ, Figueiredo MS. Anemia in inflammatory bowel disease: prevalence, differential diagnosis and association with clinical and laboratory variables. *Sao Paulo Med J*. 2014;132(3):140-146. doi:10.1590/1516-3180.2014.1323568

61. Serum iron level is independently associated with sarcopenia: a retrospective study | Scientific Reports. Accessed December 25, 2024. https://www.nature.com/articles/s41598-024-61429-0

62. Vagianos K, Bector S, McConnell J, Bernstein CN. Nutrition assessment of patients with inflammatory bowel disease. *JPEN J Parenter Enteral Nutr*. 2007;31(4):311-319. doi:10.1177/0148607107031004311

63. Zinc is an Antioxidant and Anti-Inflammatory Agent: Its Role in Human Health - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/25988117/

64. Rederstorff M, Krol A, Lescure A. Understanding the importance of selenium and selenoproteins in muscle function. *Cell Mol Life Sci*. 2006;63(1):52-59. doi:10.1007/s00018-005-5313-y

65. Li J, Jiang C, Wu L, Tian J, Zhang B. Dietary selenium intake and sarcopenia in American adults. *Front Nutr*. 2024;11:1449980. doi:10.3389/fnut.2024.1449980

66. Rando TA. Oxidative stress and the pathogenesis of muscular dystrophies. *Am J Phys Med Rehabil*. 2002;81(11 Suppl):S175-186. doi:10.1097/00002060-200211001-00018

67. Baumann CW, Kwak D, Liu HM, Thompson LV. Age-induced oxidative stress: how does it influence skeletal muscle quantity and quality? *J Appl Physiol (1985)*. 2016;121(5):1047-1052. doi:10.1152/japplphysiol.00321.2016

68. Liu Z, Yadav PK, Xu X, et al. The increased expression of IL-23 in inflammatory bowel disease promotes intraepithelial and lamina propria lymphocyte inflammatory responses and cytotoxicity. *J Leukoc Biol*. 2011;89(4):597-606. doi:10.1189/jlb.0810456

69. Yen D, Cheung J, Scheerens H, et al. IL-23 is essential for T cell-mediated colitis and promotes inflammation via IL-17 and IL-6. *J Clin Invest*. 2006;116(5):1310-1316. doi:10.1172/JCI21404

70. Interleukin-6 trans-signaling in inflammatory bowel disease - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/17045835/

71. Mucosal imbalance of IL-1 and IL-1 receptor antagonist in inflammatory bowel disease. A novel mechanism of chronic intestinal inflammation - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/7868909/

72. Sands BE, Kaplan GG. The role of TNFalpha in ulcerative colitis. *J Clin Pharmacol*. 2007;47(8):930-941. doi:10.1177/0091270007301623

73. Muñoz-Cánoves P, Scheele C, Pedersen BK, Serrano AL. Interleukin-6 myokine signaling in skeletal muscle: a double-edged sword? *FEBS J*. 2013;280(17):4131-4148. doi:10.1111/febs.12338

74. Skeletal muscle atrophy and the E3 ubiquitin ligases MuRF1 and MAFbx/atrogin-1 - PMC. Accessed December 15, 2024. https://pmc.ncbi.nlm.nih.gov/articles/PMC4166716/

75. Tumor necrosis factor alpha blockade restores growth hormone signaling in murine colitis - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/15887111/

76. Lucia Casadonte CJ, Brown J, Strople J, Neighbors K, Fei L, Alonso EM. Low Insulin-like Growth Factor-1 Influences Fatigue and Quality of Life in Children With Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2018;67(5):616-621. doi:10.1097/MPG.0000000000002057

77. Dual Role of Reactive Oxygen Species in Muscle Function: Can Antioxidant Dietary Supplements Counteract Age-Related Sarcopenia? - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/31387214/

78. Reactive oxygen species in sarcopenia: Should we focus on excess oxidative damage or defective redox signalling? - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/27161871/

79. Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut*. 2019;68(Suppl 3):s1-s106. doi:10.1136/gutjnl-2019-318484

80. Selinger CP, Rosiou K, Lenti MV. Biological therapy for inflammatory bowel disease: cyclical rather than lifelong treatment? *BMJ Open Gastroenterology*. 2024;11(1):e001225. doi:10.1136/bmjgast-2023-001225

81. Subramaniam K, Fallon K, Ruut T, et al. Infliximab reverses inflammatory muscle wasting (sarcopenia) in Crohn's disease. *Aliment Pharmacol Ther*. 2015;41(5):419-428. doi:10.1111/apt.13058

82. Csontos ÁA, Molnár A, Piri Z, et al. The Effect of anti-TNFα Induction Therapy on the Nutritional Status and Dietary Intake in Inflammatory Bowel Disease. *J Gastrointestin Liver Dis*. 2016;25(1):49-56. doi:10.15403/jgld.2014.1121.251.tnf

83. Dhaliwal A, Quinlan JI, Overthrow K, et al. Sarcopenia in Inflammatory Bowel Disease: A Narrative Overview. *Nutrients*. 2021;13(2):656. doi:10.3390/nu13020656

84. Schroeder BO, Bäckhed F. Signals from the gut microbiota to distant organs in physiology and disease. *Nat Med*. 2016;22(10):1079-1089. doi:10.1038/nm.4185

85. Huang W, Guo HL, Deng X, et al. Short-Chain Fatty Acids Inhibit Oxidative Stress and Inflammation in Mesangial Cells Induced by High Glucose and Lipopolysaccharide. *Exp Clin Endocrinol Diabetes*. 2017;125(2):98-105. doi:10.1055/s-0042-121493

86. Murray RL, Zhang W, Liu J, et al. Tributyrin, a Butyrate Pro-Drug, Primes Satellite Cells for Differentiation by Altering the Epigenetic Landscape. *Cells*. 2021;10(12):3475. doi:10.3390/cells10123475

87. Liu C, Wong PY, Wang Q, et al. Short-chain fatty acids enhance muscle mass and function through the activation of mTOR signalling pathways in sarcopenic mice. *Journal of Cachexia, Sarcopenia and Muscle*. 2024;15(6):2387-2401. doi:10.1002/jcsm.13573

88. Shanahan F, van Sinderen D, O'Toole PW, Stanton C. Feeding the microbiota: transducer of nutrient signals for the host. *Gut*. 2017;66(9):1709-1717. doi:10.1136/gutjnl-2017-313872

89. Bischoff SC, Bager P, Escher J, et al. ESPEN guideline on Clinical Nutrition in inflammatory bowel disease. *Clinical Nutrition*. 2023;42(3):352-379. doi:10.1016/j.clnu.2022.12.004

90. Santarpia L, Alfonsi L, Castiglione F, et al. Nutritional Rehabilitation in Patients with Malnutrition Due to Crohn's Disease. *Nutrients*. 2019;11(12):2947. doi:10.3390/nu11122947

91. Parenteral Nutrition in Patients with Inflammatory Bowel Disease Systematic Review, Meta-Analysis and Meta-Regression - PubMed. Accessed December 17, 2024. https://pubmed.ncbi.nlm.nih.gov/31766687/

92. Peripheral parenteral nutrition is no better than enteral nutrition in acute exacerbation of Crohn's disease: a prospective trial - PubMed. Accessed December 17, 2024. https://pubmed.ncbi.nlm.nih.gov/2118925/

93. The Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update - PubMed. Accessed December 15, 2024. https://pubmed.ncbi.nlm.nih.gov/33026087/

94. Morley JE, Argiles JM, Evans WJ, et al. Nutritional Recommendations for the Management of Sarcopenia. *J Am Med Dir Assoc*. 2010;11(6):391-396. doi:10.1016/j.jamda.2010.04.014

95. Engels M, Cross RK, Long MD. Exercise in patients with inflammatory bowel diseases: current perspectives. *Clin Exp Gastroenterol*. 2017;11:1-11. doi:10.2147/CEG.S120816

96. Wl H, Im L, Rr P, et al. Physical activity and public health: updated recommendation for adults from the American College of Sports Medicine and the American Heart Association. *Medicine and science in sports and exercise*. 2007;39(8). doi:10.1249/mss.0b013e3180616b27

97. Ball E. Exercise guidelines for patients with inflammatory bowel disease. *Gastroenterol Nurs*. 1998;21(3):108-111. doi:10.1097/00001610-199805000-00002

98. Ordille AJ, Phadtare S. Intensity-specific considerations for exercise for patients with inflammatory bowel disease. *Gastroenterology Report*. 2023;11:goad004. doi:10.1093/gastro/goad004

99. Hurst C, Robinson SM, Witham MD, et al. Resistance exercise as a treatment for sarcopenia: prescription and delivery. *Age Ageing*. 2022;51(2):afac003. doi:10.1093/ageing/afac003

100. Dent E, Morley JE, Cruz-Jentoft AJ, et al. International Clinical Practice Guidelines for Sarcopenia (ICFSR): Screening, Diagnosis and Management. *The Journal of nutrition, health and aging*. 2018;22(10):1148-1161. doi:10.1007/s12603-018-1139-9

101. Dose–Response Relationships of Resistance Training in Healthy Old Adults: A Systematic Review and Meta-Analysis | Sports Medicine. Accessed December 14, 2024. https://link.springer.com/article/10.1007/s40279-015-0385-9?utm_source=getftr&utm_medium=getftr&utm_campaign=getftr_pilot&getft_integrator=sciencedirect_contenthosting

102. mTOR signaling and the molecular adaptation to resistance exercise - PubMed. Accessed December 14, 2024. https://pubmed.ncbi.nlm.nih.gov/17095929/

103. Erlich AT, Tryon LD, Crilly MJ, et al. Function of specialized regulatory proteins and signaling pathways in exercise-induced muscle mitochondrial biogenesis. *Integr Med Res*. 2016;5(3):187-197. doi:10.1016/j.imr.2016.05.003

104. Konopka AR, Harber MP. Skeletal muscle hypertrophy after aerobic exercise training. *Exerc Sport Sci Rev*. 2014;42(2):53-61. doi:10.1249/JES.0000000000000007

105. Beavers KM, Brinkley TE, Nicklas BJ. Effect of exercise training on chronic inflammation. *Clin Chim Acta*. 2010;411(11-12):785-793. doi:10.1016/j.cca.2010.02.069

106. Nash D, Hughes MG, Butcher L, et al. IL-6 signaling in acute exercise and chronic training: Potential consequences for health and athletic performance. *Scand J Med Sci Sports*. 2023;33(1):4-19. doi:10.1111/sms.14241

107. Serrano AL, Baeza-Raja B, Perdiguero E, Jardí M, Muñoz-Cánoves P. Interleukin-6 is an essential regulator of satellite cell-mediated skeletal muscle hypertrophy. *Cell Metab*. 2008;7(1):33-44. doi:10.1016/j.cmet.2007.11.011

108. Ellingsgaard H, Hauselmann I, Schuler B, et al. Interleukin-6 enhances insulin secretion by increasing glucagon-like peptide-1 secretion from L cells and alpha cells. *Nat Med*. 2011;17(11):1481-1489. doi:10.1038/nm.2513

109. Hamer M, Sabia S, Batty GD, et al. Physical activity and inflammatory markers over 10 years: follow-up in men and women from the Whitehall II cohort study. *Circulation*. 2012;126(8):928-933. doi:10.1161/CIRCULATIONAHA.112.103879

110. Abd El-Kader SM, Al-Shreef FM. Inflammatory cytokines and immune system modulation by aerobic versus resisted exercise training for elderly. *Afr Health Sci*. 2018;18(1):120-131. doi:10.4314/ahs.v18i1.16

111. Zheng G, Qiu P, Xia R, et al. Effect of Aerobic Exercise on Inflammatory Markers in Healthy Middle-Aged and Older Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Front Aging Neurosci*. 2019;11:98. doi:10.3389/fnagi.2019.00098

112. Saxena A, Fletcher E, Larsen B, Baliga MS, Durstine JL, Fayad R. Effect of exercise on chemically-induced colitis in adiponectin deficient mice. *J Inflamm (Lond)*. 2012;9(1):30. doi:10.1186/1476-9255-9-30

113. Gulick CN, Peddie MC, Cameron C, Bradbury K, Rehrer NJ. Physical activity, dietary protein and insulin-like growth factor 1: Cross-sectional analysis utilising UK Biobank. *Growth Hormone & IGF Research*. 2020;55:101353. doi:10.1016/j.ghir.2020.101353