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The Impact of Physical Activity on the Clinical Course of Crohn's Disease

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Abstract

Introduction and Aim: Crohn's Disease (CD) is a chronic inflammatory bowel disease (IBD) characterized by periods of remission and relapse. The influence of lifestyle, particularly physical activity, on the course of IBD is increasingly recognized. This study aims to examine the impact of physical activity on the clinical course of Crohn's disease and the development of associated complications.

Methods and Materials: This research will involve a systematic review of the literature published between 2010 and 2025. Relevant studies will be identified by searching electronic databases including PubMed and Google Scholar databases. The search strategy will utilize a combination of keywords related to Crohn's disease, physical activity, exercise, and osteopenia. Studies published in English and Polish that examine the effect of exercise interventions on adult CD patients will be included. Studies evaluating the impact of exercise on disease activity, quality of life, bone mineral density, and other relevant outcomes will be considered. The methodological quality of the included studies will be assessed using appropriate tools. Data extraction and synthesis will be performed following established guidelines for systematic reviews.

Results and Conclusion: A comprehensive studies review suggests that physical activity can be a valuable tool in managing Crohn's Disease and preventing complications such as osteopenia. Exercise appears to offer benefits for bone health, mental well-being and overall quality of life of patients with CD. It’s important to note that further research is needed to determine the optimal type, intensity, and duration of exercise for individuals with CD, as well as to identify strategies to promote adherence to exercise programs.

Keywords

Crohn's disease, physical activity, exercise, osteopenia

Introduction

Crohn's disease is a global health concern, with increasing incidence in newly industrialized countries **(1)**. While incidence rates have stabilized in Western Europe, they remain lower in Eastern Europe **(2)**. A global map shows that regions of New Zealand, Canada, Scotland, France, the Netherlands, and Scandinavia have the highest incidence **(3)**. Some studies show the global prevalence of IBD increased by 31% from 1990 to 2017, reaching 89.6 cases per 100,000 people **(4)**. The condition exhibits a bimodal pattern, with the majority of cases occurring between the ages of 15-30 and 40-60. Crohn's disease is more prevalent in urban rather than rural settings. The condition is highly common among Northern Europeans and individuals of Jewish ancestry. Conversely, the prevalence is low among Asians, Africans, and South Americans **(5)**. Crohn's disease and ulcerative colitis are distinct pathological conditions that are collectively categorized as "inflammatory bowel diseases" **(5)**. CD commonly affects the terminal ileum and proximal colon, with inflammation often being discontinuous, patchy, segmental, and transmural in nature **(6)**. Patients may initially present with nonspecific symptoms, and some may lack a clear family history of the condition **(5)**. CD can present with a wide range of gastrointestinal symptoms, including abdominal pain, diarrhea, rectal bleeding, weight loss, and malnutrition **(7,8)**. These symptoms arise from chronic inflammation of the intestinal wall, which can lead to ulcerations, strictures, fistulas, and abscesses **(9)**. Crohn's disease can also present with extraintestinal manifestations, frequently affecting the eyes, skin, liver, and joints **(5)**. Patients with CD are at increased risk of developing osteopenia and bone loss due to a combination of factors, including chronic inflammation, malnutrition, malabsorption of vitamin D and calcium, and the use of corticosteroids **(10)**. The early onset of Crohn's disease in the majority of cases underscores the need for timely but sustained treatment to mitigate disease exacerbations and progression with associated intestinal complications **(11)**. The disease course is characterized by periods of active inflammation interspersed with periods of remission, with the frequency and severity of relapses varying considerably between individuals **(12)**. The unpredictable and often debilitating nature of CD significantly impacts a patient's physical and emotional well-being, affecting their ability to perform daily activities, work, and engage in social interactions **(10,13)**. The etiology of CD is multifactorial, involving a complex interplay of genetic susceptibility, environmental triggers, and immune dysregulation **(14)**. While the precise mechanisms remain unclear, current understanding points towards a combination of genetic predisposition, environmental factors, and an aberrant immune response directed against the gut microbiota **(15)**. Contemporary treatment approaches for individuals with

Crohn's disease have evolved beyond solely aiming for clinical remission. While the identification of characteristic findings through ileocolonoscopy and histology remains the gold standard for diagnosis, a comprehensive assessment also involves evaluating laboratory abnormalities, including micronutrient deficiencies, utilizing cross-sectional imaging to ascertain the extent, severity, and complications of transmural disease, and conducting a psychosocial assessment **(6)**. The introduction of potent advanced therapies and the development of treatments targeting alternative novel pathways with enhanced safety profiles have ushered in a new era of healing in the management of Crohn's disease **(6)**. The importance of lifestyle modifications, including dietary changes, stress management, and physical activity, in the management of chronic inflammatory diseases like CD is increasingly emphasized **(10,16)**.

This study aims to systematically review the literature on the effects of physical activity on the clinical course of Crohn's Disease and the development of associated complications. By synthesizing the existing evidence, this review seeks to provide a comprehensive overview of the benefits and potential risks of exercise in patients with CD and offer practical recommendations for incorporating physical activity into their management.

Materials and Method of Research

This research will involve a systematic review of the literature published between 2010 and 2025. Relevant studies will be identified by searching electronic databases including PubMed and Google Scholar databases. The search strategy will utilize a combination of keywords related to Crohn's disease, physical activity, exercise, and osteopenia. Studies published in English and Polish that examine the effect of exercise interventions on adult CD patients will be included. Studies evaluating the impact of exercise on disease activity, quality of life, bone mineral density, and other relevant outcomes will be considered. The methodological quality of the included studies will be assessed using appropriate tools. Data extraction and synthesis will be performed following established guidelines for systematic reviews.

Epidemiology of Osteopenia in Crohn's Patients

Reduced bone mineral density is one of the more common complications in patients with Crohn's disease. It is estimated that the prevalence of osteoporosis among individuals suffering from inflammatory bowel diseases ranges from 26% to 42% **(17)**. This risk increases with the duration of the disease, the number of exacerbations and the use of glucocorticoids in treatment

(18,19). Population-based studies also indicate a significantly higher incidence of osteoporotic fractures in this group of patients compared to the general population **(20)**.

Pathophysiology of Bone Mass Loss in Crohn's Disease

Bone mass loss in the course of Crohn's disease is a consequence of multifactorial pathophysiological mechanisms, involving both inflammatory factors and metabolic disturbances. The chronic inflammatory state, which is a characteristic feature of this disease entity, leads to an increased concentration of proinflammatory cytokines, such as tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6), which enhance the activity of osteoclasts and simultaneously inhibit osteoblastogenesis, contributing to increased bone resorption **(20,18)**. Furthermore, hormonal abnormalities, such as decreased levels of insulin-like growth factor 1 (IGF-1), oxidative stress, and changes in the composition and function of the intestinal microbiota, which can modulate calcium-phosphate metabolism and pathways regulating bone remodeling, also play a significant role in the pathogenesis of bone mineralization disorders **(21)**. In children and young adults with early-onset disease, deficits in muscle mass and strength are often observed, leading to impaired mechanical stimulation of the skeletal system and potentially exacerbating its mineralization disturbances **(22,23)**.

The Impact of Medications (particularly Glucocorticoids) on The Skeletal System

Glucocorticoids, commonly used in the treatment of exacerbations of Crohn's disease, have a significant impact on bone tissue metabolism. While in physiological conditions, cortisol plays a key role in regulating bone homeostasis - stimulating osteoblasts to synthesize collagen and modulating the maturation and activity of osteoclasts, which results in an increase in bone mineral density **(22)** - their chronic use is associated with adverse consequences for the skeletal system. Although the mechanism of the rapid loss of bone mass after the introduction of glucocorticoid treatment has not yet been clearly elucidated, the available data indicate that these drugs inhibit the synthesis of collagen, osteocalcin, and alkaline phosphatase. This leads to impaired osteoblast function, increased bone resorption through the activation of osteoclasts, and disruption of the bone matrix mineralization process **(24)**. Additionally, glucocorticoids reduce the expression of osteoprotegerin and stimulate the production of RANKL (receptor activator of nuclear factor κB ligand), as well as type III collagenase - factors playing a key role in the regulation of bone remodeling. These changes translate into a morphometric image of the bone structure, in which a reduction in the thickness of bone trabeculae is observed. In patients with Crohn's disease, due to intestinal absorption disorders and abnormal liver metabolism,

changes characteristic of osteomalacia are often found **(25)**. Long-term glucocorticoid therapy is associated with a significant increase in the risk of developing osteopenia and osteoporosis. Furthermore, these drugs can lead to hypocalcemia by impairing calcium absorption in the gastrointestinal tract and increasing its excretion by the kidneys **(24,26)**.

Significance of Nutritional Deficiencies (Calcium, Vitamin D)

Vitamin D plays a crucial role in the process of proper bone tissue mineralization. It belongs to the group of hormones that directly modulate the activity of bone-forming and bone-resorbing cells, as well as indirectly influence calcium-phosphate homeostasis. Vitamin D stimulates the differentiation of osteoblasts, participates in the process of formation and maturation of osteoclasts, and conditions the proper mineralization of osteoid. Furthermore, by inhibiting the secretion of parathormone (PTH), it limits bone resorption, and by increasing calcium absorption in the gastrointestinal tract, it prevents bone mass loss, significantly reducing the risk of osteoporosis and fractures **(27)**. In patients with Crohn's disease, vitamin D deficiency is a common phenomenon, especially during disease flare-ups and after intestinal resections. The main causes are disorders of absorption of fat-soluble vitamins (A, D, E, K), which result from damage to the intestinal mucosa and chronic inflammation **(25,27)**. Additionally, limited exposure to sunlight, the use of elimination diets, and chronic inflammatory processes further decrease the already low level of vitamin D **(21,24,28)**. Deficiencies of vitamin D and calcium lead to disturbances in calcium-phosphate balance, secondary hyperparathyroidism, increased bone resorption, and, consequently, to a decrease in bone mineral density.

The Health Consequences and Quality of Life of People with Bone Loss

Bone loss in Crohn's disease carries serious health consequences, such as an increased risk of fractures, spinal deformities, chronic pain, and impaired physical function. In young adults, it may mean failing to reach peak bone mass, which increases the risk of osteoporosis later in life **(22,23)**. Reduced quality of life, fear of injury, and limitations in daily physical activity are important aspects that impact patient well-being **(28)**. Therefore, early identification of risk and preventive interventions are crucial.

3.2 The Impact of Exercise on The Functioning of The Immune and Inflammatory Systems

Patients with inflammatory bowel diseases (IBD) experience a systemic increase in the concentration of proinflammatory cytokines, such as TNF-α, IFN-γ, IL-1, IL-6, IL-12, and IL-

18, which intensify catabolic processes and lead to muscle mass loss. These cytokines have a direct impact on muscle metabolic pathways, including inhibition of the anabolic mTORC1 pathway and activation of degradation pathways, such as NF-κB or ubiquitin-proteasome. Physical activity, by inducing acute, physiological stress, can act as a modulator of the immune response, helping to suppress chronic inflammation. Additionally, exercise promotes the activation of receptors such as PPAR-γ, whose expression is typically reduced in IBD and which have the ability to inhibit NF-κB and limit its pro-inflammatory action. In this way, regular physical activity can counteract the chronic activation of the immune system, reducing the severity of symptoms **(29)**. Regular physical activity, particularly resistance training (resistance exercise, RE), has a modulating effect on the functioning of the immune system through the regulation of the inflammatory response. The muscle hypertrophy induced by resistance exercise is the result of mechanisms such as an increase in mechanical tension, metabolic stress, and microtrauma to muscle fibers. This process stimulates an inflammatory response, characterized by the release of pro-inflammatory (IL-1β, TNF-α) and anti-inflammatory cytokines (IL-1RA, IL-10, IL-6). The use of concentric and isometric training, in contrast to eccentric training, leads to a beneficial strengthening of the body's defense mechanisms against oxidative stress, while simultaneously limiting the increased inflammatory response **(30)**. Regular physical activity, especially when conducted in a controlled and patient-tailored manner, can significantly modulate the immune response and inflammatory processes in the course of inflammatory bowel diseases. In a 12-week physical intervention study in IBD patients, a significant decrease in fecal calprotectin was observed, as well as an increase in the number of patients in clinical remission, confirming the anti-inflammatory potential of exercise **(31)**. Importantly, studies have confirmed that moderate physical activity does not lead to disease exacerbations and is safe even in its active stage **(31,10)**. It is worth noting that pharmacological treatment remained stable in most participants, emphasizing that the observed changes were the result of a non-pharmacological intervention. Integrated programs (e.g. COBMINDEX) have also shown an impact on the gut microbiome, a decrease in IFN levels, and an improvement in inflammatory parameters, suggesting that physical activity may interact with the brain-gut-immune axis **(32)**. Studies indicate that moderate exercise improves the immune response, while very high-intensity exercise may have the opposite effect - weakening the body's defense mechanisms. In the context of IBD, regular physical activity can support natural immune mechanisms and contribute to the reduction of systemic inflammation, making it a potentially valuable complement to pharmacological treatment **(33)**.

Recent evidence suggests that physical activity can counteract dysbiosis and modify the intestinal microenvironment. Studies in animal models and in obese populations have shown that regular physical exercise changes the composition of the microbiome, increases the production of short-chain fatty acids, and reduces endotoxemia by limiting the circulation of lipopolysaccharide complexes. The potential mechanisms by which physical activity can influence the immune system and the intestinal microbiome include: the secretion of anti-inflammatory myokines such as irisin, IL-15, myostatin, BDNF, decorin, and SPARC (secreted protein acidic and rich in cysteine), as well as a reduction in inflammasome activity through the downregulation of caspase-1 and NLRP3, and muscle-microbiome interactions that activate the AMPK pathways and transcription factors related to lipid metabolism (e.g. PPAR), and changes in gastrointestinal function such as shortened intestinal transit time, increased intestinal IgA levels, decreased bile acid concentrations, and modulation of the HPA axis. Furthermore, individuals who lead a sedentary lifestyle have a higher risk of IBD, while physical activity in childhood may have a protective effect.

3.3 The Role of Physical Activity in Reducing Stress and Improving Mental Well-being

Physical activity plays a key role in shaping psychological well-being, which is particularly important for patients with chronic diseases such as inflammatory bowel diseases (IBD). In the case of children and adolescents participating in exercise programs, improvements were observed not only in physical condition, but also in quality of life and reduced fatigue - which was also confirmed by the patients' parents **(31)**. Regular physical exertion has a positive effect on the nervous system by increasing the release of endorphins and neurotrophic growth factors, contributing to mood improvement, reduction of depressive symptoms, and increased motivation **(31,32,33)**. The studies also emphasized the psychosocial effects of exercise - participants reported improved sleep, increased self-confidence, a sense of agency, and control over their own body. The physical activity program was an impulse for many to make positive lifestyle changes and a source of pride and satisfaction **(13,34)**. Data indicate that even moderate activity can significantly improve the well-being of IBD patients. Most of the study participants reported improved mood and overall mental state after exercising **(34)**. The COBMINDEX program, which combined elements of cognitive-behavioral therapy, mindfulness, and physical activity, also showed a reduction in symptoms of psychological distress, which correlated with a decrease in inflammation and a more balanced gut microbiota composition **(32)**.

It is important to note, however, that not all patients react the same way - some respondents

reported worsening of well-being after exercising, most often due to fatigue, abdominal pain, increased need to use the bathroom, and joint pain **(10)**. Such reactions indicate the need to individualize training and conduct them under the supervision of trained personnel, taking into account the patient's clinical condition. Mood disorders such as depression and anxiety are much more common in the IBD population than in the general population - as many as 25% of patients have a formal diagnosis of one of these conditions. They are more common in women, in people with longer disease duration, and in patients with fistulas and strictures **(34)**. Importantly, individuals with higher scores on the HADS scales are more likely to lead a sedentary lifestyle, which can further exacerbate mental symptoms and worsen quality of life **(34,35)**.

In summary, physical activity is an effective, non-pharmacological psychological support in the treatment of IBD - it improves mood, reduces stress, has a beneficial effect on sleep and self-esteem, and also helps patients regain a sense of normalcy and empowerment. Its therapeutic potential should be fully utilized as an element of comprehensive care for patients with a chronic disease.

3.4 Preventing Sarcopenia and Muscle Weakness

Sarcopenia, defined as the loss of muscle mass and strength, is a common complication among patients with inflammatory bowel diseases, particularly Crohn's disease. This phenomenon is particularly significant in the context of chronic inflammation, malnutrition, absorption disorders, and a sedentary lifestyle **(29,33,34)**. Regular physical activity, especially resistance training (resistance exercise, RE), plays a key role in preventing sarcopenia. RE training activates PI3K-Akt/mTOR, MAPK, and calcium-dependent signaling pathways, which stimulate muscle protein synthesis and support muscle mass gain. Additionally, this activity promotes the action of anabolic factors, such as hepatocyte growth factor, and myokines with anti-inflammatory and regenerative effects (IL-5, IL-6, IL-10) **(30,31)**. In IBD patients, chronic release of proinflammatory cytokines, such as TNF-α, leads to a predominance of catabolic over anabolic processes, resulting in muscle protein degradation. TNF-α inhibits the mTORC1 pathway and activates genes responsible for muscle atrophy (MAFBx, MURF-1), while decreased IGF-1 levels further disrupt protein synthesis processes **(29)**. Increased local activity of 11β-HSD1 and the associated rise in cortisol levels amplify the catabolic effects. Vitamin D supplementation, essential for proper muscle function, can also support the prevention of sarcopenia **(29)**. In an interventional study, a 12-week exercise program led to improved physical fitness in IBD patients, which can be associated with improved muscle mass and

function, despite the lack of detailed numerical data on strength **(31)**. Additionally, many participants reported improved daily functioning - longer walks, improved posture, easier return to daily responsibilities - confirming the effectiveness of exercise in counteracting muscle weakness **(13)**. Observational studies have shown a clear relationship between the level of physical activity and muscle mass and musculoskeletal fitness. Patients with higher activity levels exhibited better functioning, higher quality of life, and greater work productivity **(33,34)**. However, despite the known benefits, many patients face real barriers to engaging in physical activity. The most commonly reported are chronic fatigue, as well as pain and other health problems **(10)**. These limitations indicate the need to individualize training programs and adapt them to the patient's capabilities and clinical condition, taking into account psychosocial aspects.

In summary, regular physical activity - especially resistance training - supported by an appropriate diet and supplementation, should be an integral part of the prevention and treatment of sarcopenia in IBD patients, regardless of the disease phase.

3.5 Physical Activity as a Way to Prevent Bone Degradation - The Impact of Weight-Bearing Exercises on Bone Density

Physical activity, especially resistance and weight-bearing exercises, is an essential element in the prevention of bone mineralization disorders such as osteopenia and osteoporosis. It has been shown that regular physical training mechanically stimulates osteoblasts, limits bone resorption and has a beneficial effect on bone mineral density (BMD) **(30)**. Patients with inflammatory bowel diseases, especially young people and children with Crohn's disease (CD), belong to the high-risk group for the development of osteopenia and osteoporosis. These disorders are the result of chronic inflammation, nutritional deficiencies (including calcium and vitamin D), the use of glucocorticoids and limited physical activity **(33,34)**. It is estimated that even 50% of CD patients develop osteopenia and 13% develop osteoporosis **(33,34)**. Clinical studies have confirmed that physical exercises, even of moderate intensity, lead to an improvement in BMD, especially in the hip and spine regions. In one study, a 12-month training program resulted in a significant increase in bone density in active patients compared to the control group. This effect was maintained only in those who continued their activity after the program ended, emphasizing the importance of consistency and long-term intervention **(34)**. Physical activity also indirectly affects bone health by supporting muscle mass and strength, thereby improving the biomechanics of the skeletal system. Maintaining an appropriate fat-free body mass (LBM) through exercise positively influences bone loading and their adaptation to mechanical stress

(36). Despite the proven benefits, as many as 80% of IBD patients admitted that they had periods during the course of the disease when they were unable to exercise regularly. The reasons were relapses of symptoms, fatigue, and pain **(10)**. Therefore, effective training programs should be individually tailored to the patient's clinical condition, taking into account the phase of the disease and in cooperation with a physiotherapist and a therapeutic team **(10)**. In summary, physical activity - as a safe, available and effective method - should be a standard element in the strategy for preventing osteopenia and osteoporosis in IBD patients, regardless of age. Particular attention should be paid to its implementation in the pediatric and adolescent population, where the intensive development of the skeletal system is taking place **(30,33,34,36)**.

Recommendations on The Amount, Intensity, and Types of Physical Exercises for Individuals with Crohn's Disease

Despite the lack of standardized, universally endorsed guidelines for physical activity in individuals with Crohn's disease, current evidence suggests that exercise is both safe and beneficial as a complementary therapy for patients across all age groups. However, physical activity should be considered a complementary approach rather than a substitute for pharmacological treatment **(37)**. Exercise recommendations for individuals with CD should be tailored to individual needs, taking into account factors such as disease severity, current pharmacological regimen, physical limitations, and patient age **(10)**. In general, low- to moderate-intensity physical activity appears to be well-tolerated, particularly during periods of remission or mild disease activity **(15)**. It is crucial that patients remain attentive to their bodily responses, adjusting exercise intensity and duration accordingly. For adult patients, some studies recommend engaging in a minimum of 150 minutes of moderate-intensity aerobic activity per week, ideally distributed over several days **(10)**. Resistance training targeting major muscle groups may also be beneficial and is typically suggested 2–3 times weekly **(10)**. Additional literature proposes physical activity guidelines for individuals with inflammatory bowel disease more broadly, advocating for aerobic sessions lasting 20–60 minutes on 2–5 days per week, along with resistance training on at least two occasions weekly. However, these guidelines were developed prior to the availability of disease-specific evidence and are primarily based on studies conducted in healthy populations. In pediatric populations, a 12-week intervention combining thrice-weekly exercise sessions with dietary counseling demonstrated improvements in gastrointestinal symptoms, fatigue, and quality of life among children diagnosed with IBD **(31)**. Current physical activity recommendations for children and adolescents aged 5–17 years include a minimum of 60 minutes of moderate to vigorous activity

daily, encompassing activities such as running, swimming, or team sports. Furthermore, exercises that promote muscle and bone strength should be incorporated at least three times per week **(38)**. Ultimately, physical activity prescriptions for CD patients should be individualized. While the majority of available data highlight the safety and efficacy of incorporating exercise into disease management, it is prudent to initiate activity gradually and to seek guidance from healthcare professionals with expertise in managing inflammatory bowel diseases.

Conclusion

In summary, an increasing number of scientific studies indicate the beneficial impact of regular physical activity on the clinical course of Crohn's disease and the reduction of the risk of its complications. A properly planned training program, tailored to the individual patient's capabilities, taking into account the degree of disease advancement and current symptoms, can serve as a valuable adjunct to pharmacological therapy. The introduction of moderate physical activity can contribute to: strengthening the immune response, reducing systemic inflammation, improving the composition of the gut microbiota and gastrointestinal function, as well as to beneficial psychological effects, such as stress reduction and mood improvement. Furthermore, exercise can help counteract the loss of muscle mass and reduce the risk of osteopenia and osteoporosis, which are common complications in patients with inflammatory bowel diseases. Despite these positive indications, there is a significant research gap regarding the influence of specific forms of physical activity on various aspects of the course of Crohn's disease. There is still a lack of clear guidelines on the optimal intensity, frequency, and duration of training that would be safe and effective for this group of patients. Available studies are often limited by small sample sizes, short observation periods, and significant variability in intervention design. Therefore, further well-designed randomized studies involving larger groups of patients are necessary to develop standardized recommendations for physical activity in the context of Crohn's disease.

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Authors do not report any disclosures.

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