Joana Patrícia Oliveira Martins da Silva

Sarcopenia and Inflammatory Bowel Disease: a literature review

Ciências da Nutrição
Faculdade de Ciências da Saúde
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Declaro para os devidos efeitos ter atuado com integridade na elaboração deste Trabalho de Projeto, atesto a originalidade do trabalho, confirmo que não incorri em plágio e que todas as frases que retirei de textos de outros autores foram devidamente citadas ou redigidas com outras palavras e devidamente referenciadas na bibliografia.

(Joana Patrícia Oliveira Martins da Silva)

Trabalho apresentado à Universidade Fernando Pessoa como parte dos requisitos para obtenção do grau de licenciado em Ciências da Nutrição

Orientadora:
Professora Doutora Ana Sofia Sousa

I. Dedicatória

À minha orientadora, Professora Ana Sofia Sousa. Aqui lhe exprimo a minha gratidão por toda a atenção, cuidado, disponibilidade e apoio que sempre demonstrou em todos os momentos, assim como, todos os conhecimentos e ensinamentos transmitidos ao longo deste percurso.

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O meu sincero, obrigada.

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IV. List of Abbreviations

BIA - Bioelectrical Impedance Analysis

BMI - Body Mass Index

BSG – British Society of Gastroenterology

CD - Crohn's Disease

CRP - C-Reactive Protein

CT - Computed Tomography

DEXA - Dual Energy X-ray Absorptiometry

ECCO - European Chron's and Colitis Organization

EEN - Exclusive Enteral Nutrition

EN - Enteric Nutrition

ESPEN - European Society for Clinical Nutrition and Metabolism

EWGSOP - European Working Group on Sarcopenia in Older People

FM - Fat Mass

HGS - Hand Grip Strength

IBD - Inflammatory Bowel Disease

ICU - Intensive care unit

IGF-1 - Insulin-like Growth factor-1

IL - Interleukin

MM - Muscle Mass

MRI - Magnetic Resonance Imaging

NF-κb - Nuclear Factor Kappa of the B Cells

PN - Parenteral Nutrition

SPPB - Short Physical Performance Battery

TLR - Toll-Like Receptor

TNF-α - Tumor Necrosis Factor Alpha

TPN - Total Parenteral Nutrition

TUG – Timed-Up and Go Test

UC - Ulcerative Colitis

VDR - Vitamin D Receptor

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VI. Abstract

Introduction: Sarcopenia is a disease characterized by the progressive loss of skeletal muscle strength and mass. This condition is a prognostic factor for several pathologies and can affect individuals at any age, with a significant incidence in chronic inflammatory states, such as Inflammatory Bowel Disease (IBD).

Aim: To present an overview on the current evidence regarding sarcopenia and nutritional management of this condition among IBD patients.

Results: IBD patients are at risk of developing sarcopenia and this must be taken considered in order to minimize the occurrence of further adverse clinical outcomes. Regarding strategies for the prevention and treatment of sarcopenia in IBD patients, the most commonly used strategies are oral nutritional supplements and enteral nutrition, supplementation with vitamin D and omega 3 fatty acids (associated with decreased inflammatory activity), combined with regular practice of physical activity, in order to maintain or increase muscle mass and function. Nevertheless, there are no specific guidelines concerning the prevention or treatment of sarcopenia in IBD patients.

Conclusion: The current evidence about sarcopenia in IBD patients is still scarce. Nevertheless, the early identification of sarcopenia in IBD patients if of utmost importance for an effective intervention. Further research is needed in order to establish specific guidelines for the identification and management of sarcopenia in IBD patients and also to reach a consensus in the most effective nutritional strategies.

Keywords: Sarcopenia, Inflammatory Bowel Disease, Malnutrition

VII. Resumo

Introdução: A sarcopenia é uma doença caracterizada pela perda progressiva da força e da massa muscular esquelética. Esta condição é um fator de prognóstico em diversas patologias, podendo afetar os indivíduos em qualquer idade, com incidência significativa em estados inflamatórios crônicos, como a Doença Inflamatória Intestinal (DII).

Objetivo: Apresentar uma visão geral das evidências atuais sobre a sarcopenia e prevenção e tratamento nutricional dessa condição nos pacientes com DII.

Resultados: Pacientes com DII apresentam risco de desenvolver sarcopenia, este é um ponto importante a ser levado em consideração para minimizar a ocorrência de resultados clínicos adversos. Em relação às estratégias de prevenção e tratamento da sarcopenia em pacientes com DII, as estratégias comumente utilizadas são o suporte nutricional, incluindo suplementos nutricionais orais e nutrição entérica, suplementação com vitamina D e ácidos gordos ômega 3 (associados à diminuição da atividade inflamatória), combinados com a prática de atividade física regular, a fim de manter / aumentar a massa muscular. Apesar disso, não há diretrizes específicas sobre a prevenção ou tratamento da sarcopenia em pacientes com DII.

Conclusão: As evidências atuais sobre a sarcopenia em pacientes com DII ainda são escassas. No entanto, a identificação precoce da sarcopenia em pacientes com DII é de extrema importância para uma intervenção eficaz. Mais pesquisas são necessárias para estabelecer diretrizes específicas para a identificação e tratamento da sarcopenia em pacientes com DII e também para chegar a um consenso sobre as estratégias nutricionais mais eficazes.

Palavras-chave: Sarcopenia, Doença Inflamatória Intestinal, Desnutrição

1. Introduction

Sarcopenia is a disorder marked by the progressive and generalized depletion of skeletal muscle mass associated with a decrease in strength and muscle function (1–8).

There is an increasing number of individuals presenting sarcopenia and it is estimated that this condition will affect more than 200 million people in the next 40 years (9).

In 2010, the European Working Group on Sarcopenia in Older People (EWGSOP) proposed that the diagnostic criteria of sarcopenia were based on at least two of the following: low muscle mass (MM), low muscle strength and low physical performance (9).

In 2018, the EWGSOP2 updated sarcopenia diagnostic criteria highlighting the importance of muscle strength and also introducing muscle quality as a possible diagnostic criteria (10).

Sarcopenia can be classified as acute (lasting less than 6 months) or chronic (lasting more than 6 months) (9,10). This condition increases the occurrence of adverse effects such as the risk of falls, fractures, physical disability, reduced quality of life (6,11), cognitive loss, decreased ability to perform activities of daily living (12), increased health care costs (increases the risk of hospitalization regardless of age) (13–15), morbidity and mortality (10,16).

Sarcopenia was considered a geriatric syndrome (7) as this condition is usually (16) associated with advanced age (1,6) due to the catabolism of the muscle tissue (17), i.e., primary sarcopenia (6). However, secondary sarcopenia can occur in younger adults (1). Secondary sarcopenia (6) can be a consequence of reduced oral intake (18), malabsorption (1), malnutrition (2), physical inactivity (3), decreased protein synthesis, increased proteolysis (2), insulin resistance (7), the progression of a neuro-degenerative disease, cachexia, inflammation (19) and chronic or severe infection (16,18). Among the diseases frequently associated with sarcopenia is Inflammatory Bowel Disease (IBD) (21).

IBD is a recurrent and chronic multifactorial disease that affects the digestive tract and it is usually developed in adolescence and early adulthood (5,18). This is an immune-mediated disease and can be caused by environmental factors (17), such as changes in dietary patterns (13), leading to the appearance of nutritional and metabolic disorders

(18), dysbiosis (imbalance in the intestinal flora), having a high impact on the patient's quality of life (3).

IBD has two main subtypes, Crohn's disease (CD) (18) and ulcerative colitis (UC) (22–25).

CD patients present a mortality risk 50% higher than general population (20). CD commonly affects the colon and ileum, but can affect the entire gastrointestinal tract from the mouth to the anus, being marked by complications in almost 50% of patients (5,8), in which the inflammation affects the entire thickness of the intestine, leading to the formation of abscesses, fistulas, stenosis and intestinal obstruction (3) often requiring surgery (26,27).

In UC, the inflammation is often restricted to the mucosa (3), except in the case of a fulminating disease. This does not involve the upper digestive tract or the small intestine, mostly it involves the rectum and sometimes the colon (3,13).

There are a consistent body of evidence about changes in body composition normally present in patients with CD, as well as the results of treatments already investigated (8). Notwithstanding this, little is known about the impact and inherent changes in patients with UC.(8) It is found that CD affects nutritional status and body composition more than UC, as the small intestine is the main site of nutrient absorption and this is the most affected intestinal organ/part in CD (13,28). This change in body composition may have consequences such as bone demineralization (osteoporosis and osteopenia); inadequate response to therapy; low quality of life; and also as the loss of lean mass but without alteration of the fat mass (FM) (14,21).

The decrease in MM and strength has been shown to be highly prevalent in CD (4), having a significant impact on patient's mobility (5) and quality of life (2) as well as becoming a predictive factor (17) for the increased need for surgery (5) and a higher rate of post-operative complications (29–32).

IBD patients, in addition to the chronic inflammation caused by the disease, also have a high risk of developing nutritional disorders (33). The development of these disorders, such as malnutrition and sarcopenia, are relevant factors that must be taken into account, as they occur in up to 60% of patients with CD (3), and can result in adverse clinical effects (21,34). Thus, a timely intervention for the prevention or treatment sarcopenia in IBD patients, particularly CD patients, should be performed to improve the well-being and physical functioning of these patients and minimize adverse effects (14,35).

The strong impact of IBD in patients nutrition status leads to a need to assess and exclude the presence of sarcopenia (11). The identification of sarcopenia can be performed through the assessment (7,34) of strength and MM using validated tools (37).

However, despite the association between IBD and the development of sarcopenia has been established, sarcopenia is not routinely assessed in clinical practice in IBD patients (14).

Therefore, the aim of this literature review is to present an overview on the current evidence regarding sarcopenia and the nutritional management of this condition among IBD patients (21).

2. Methods

For the development of this literature review, articles were collected that associate Sarcopenia with Inflammatory Bowel Disease. The articles were collected through different online search engines: PubMed and SciElo, using the following MeSH terms: "Sarcopenia AND (Inflammatory Bowel Disease OR Crohn Disease OR Ulcerative Colitis)".

Initially, 90 articles were found at PubMed and two articles were found in SciElo through database searching. After this search and the duplicate articles removed, the articles were selected based on the title and abstract, leading to the exclusion of those that did not meet the following inclusion criteria: articles in English or Portuguese; evaluation of the sarcopenic state; studies in humans only; through the last 11 years (since 2010); adult and elderly population. The articles excluded from the analysis were: written in other language than English or Portuguese; no assessment of sarcopenia; patients with sarcopenia but no IBD; animal studies; publication prior to 2010; studies in children and adolescents.

After a selection and a thorough analysis, a total of 41 articles were included.

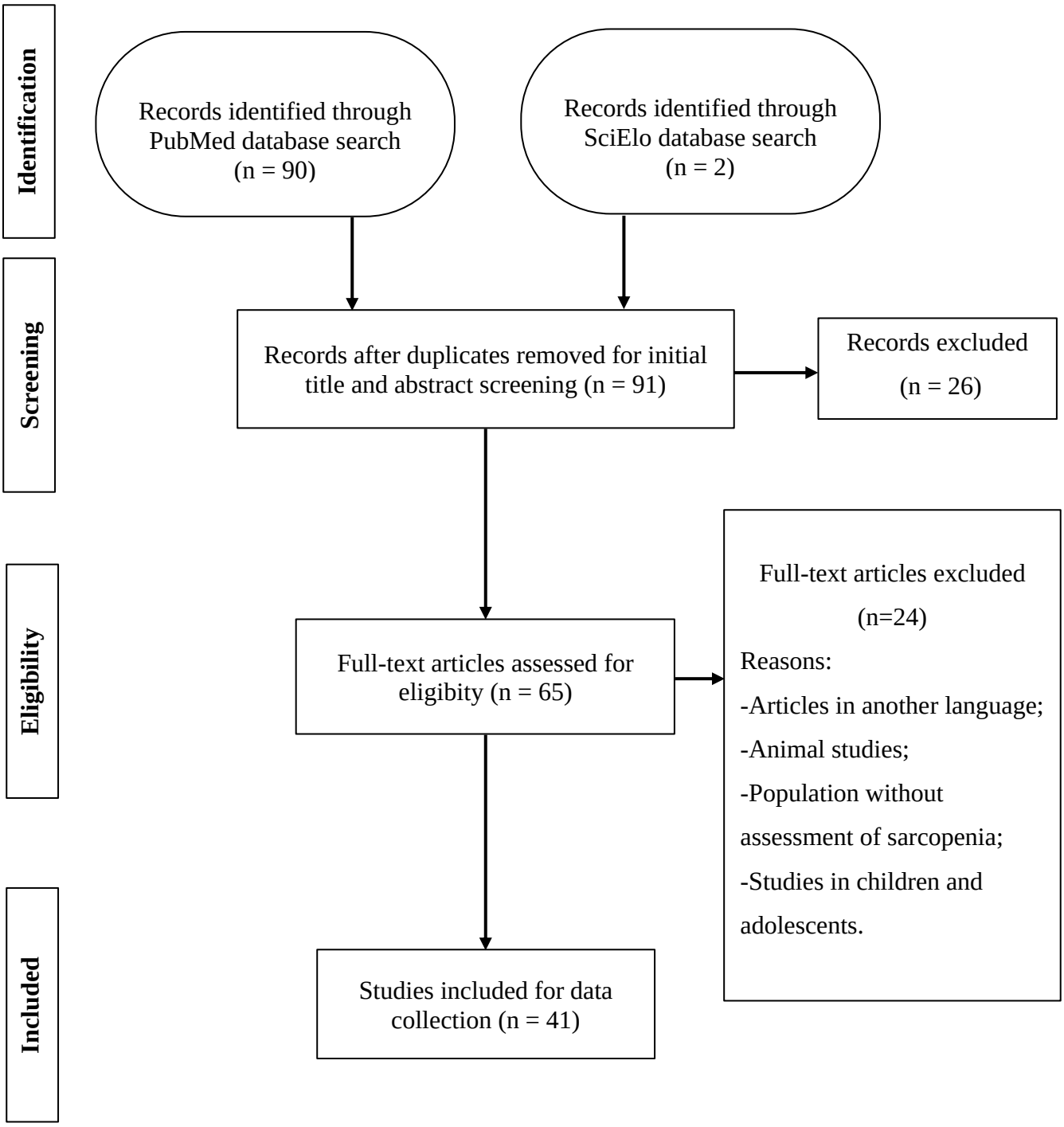

Figure 1. PRISMA flow diagram adapted from Page MJ *et al.* (2021) (38).

3. Inflammatory bowel disease and nutrition disorders

The prevalence and incidence of IBD has increased significantly worldwide in recent decades (18,28).

In IBD, inflammation is present, due to the increased production of pro-inflammatory cytokines, and in particular, tumor necrosis factor alpha (TNF- α) (39), that play an important role in triggering metabolic disorders (17). Once these, they connect to the receptors present on myocytes, activating the nuclear factor kappa of the B cells (NF-κB), inducing muscle cell death and inhibiting the release of insulin-like growth factor-1 (IGF-1), preventing muscle formation (anabolism) (17) and increasing muscle proteolysis (catabolism) (17,35).

In IBD, one of the disease's main symptoms is the significant change in the patients' body composition (7). It is estimated that around 20 to 75% of patients present weight loss (17), which is usually marked by the onset of malnutrition and/or secondary to sarcopenia (7,16). This is due to the presence of inflammation, the action of pro-inflammatory cytokines (16) and established medications that cause loss of appetite, poor absorption of nutrients, loss of nutrients, increased energy requirements (7), nausea, abdominal pain and diarrhoea (5).

Therefore, it is common for IBD patients to present themselves with malnutrition and sarcopenia (7,16) due to ingestion deficiencies, malabsorption and metabolic disorders (17,28). It is reported by a study that up to 60% of IBD patients (35) have MM depletion when compared to healthy individuals (5,11).

IBD patients therefore have many nutritional disorders, in particular, vitamin deficiencies (vitamin B12, A, D, K and folic acid) and minerals (iron, calcium, selenium, zinc, magnesium) more specifically in patients with CD (17).

Another symptom reported by 40% of IBD patients is fatigue (41). Because of this, IBD patients are less physically active and are more prone to malnutrition and the use of corticosteroids, risk factors for increased loss of muscle mass and strength, that is, sarcopenia (41,42).

The assessment of nutritional status and nutritional therapy play a crucial role in the clinical care of IBD patients, as this can prevent several adverse consequences (5,17).

3.1. Risk factors for the development sarcopenia in IBD patients

3.1.1. Inflammation

Chronic inflammation present in IBD is a major factor in the development of muscle atrophy, because there is an increase in pro-inflammatory cytokines, such as TNF-α, and an alteration in protein turnover, leading to muscle protein degradation and reduction of myofibrillar proteins (35,39). This breakdown of muscle proteins arises because hormones and cytokines that regulate a coordinated signaling network act to reduce synthesis and increase protein degradation (2).

3.1.2. Malnutrition

One of the risk factors for the presence of sarcopenia in IBD patients is based on an inadequate diet (1), since IBD patients have a high lack of appetite (18,39). Inappropriate food intake leads to the unavailability of essential proteins for muscle growth donated through food, as an insufficient intake of proteins (often observed in aging and chronic inflammatory diseases) leads to undernutrition, protein degradation and reduction of anabolic processes leading to muscle atrophy, since there is no supply of anabolic stimuli, nor of amino acids necessary for the synthesis of muscle proteins (1,39).

In IBD patients, the loss of MM and strength has consequences in functional capacity (16). Also, the loss of MM has an impact on the course of the disease, on the response to specific therapies, on surgery outcomes (11) and influences the risk of disability and mortality (3,39,43,44). Thus, the presence of sarcopenia is associated with an increased risk of severe post-operative complications (7,11,45), such as blood transfusions and Intensive Care Unit (ICU) hospitalization (1).

A recent study developed by Pizzoferrato *et al.* (2019) reporte a weak correlation between body mass index (BMI) and the presence of sarcopenia in IBD patients (7). These results can be explained by the fact that sarcopenia can develop in individuals presenting low or normal BMI, as well as in those presenting overweight or obesity (8,44,47,48). Thus, a mere assessment of the BMI in IBD patients can be misleading (18). In fact, IBD patients may be sarcopenic even without being visibly undernourished (5) since the reduction in muscle mass can be compensated by the increase in fat mass (FM) (8,49,50). This situation, along with the loss of MM and strength may predispose to sarcopenic

obesity in IBD patients, which further aggravates their prognosis (46,51), particularly in CD patients (17).

Thus, the loss of MM and strength must be assessed independently of patient's BMI (2,18,52,53). This is corroborated by results from several studies: a study conducted by Flores *et al.*(2015), in 581 patients diagnosed with IBD, showed that up to 32.7% patients are obese and, in particular, up to 30.3% and 35.2% of patients with CD and UC, respectively (54). In addition to this, Adams *et al.* (2017) (24), in a study performed in 90 patients, reported that 41.5% and 20% of sarcopenic IBD patients had normal and high BMI, Steed *et al.*(2009) (55) showed that about 25% to 30% of IBD patients are obese or overweight and Palmese *et al.* (2021) reports that patients with CD, affected by sarcopenia, mostly present sarcopenic obesity in nutritional assessment tests (11).

Malnourished IBD patients have reduced MM by up to 60% compared to patients with a normal nutritional status (3), and this reduction increases the risk of adverse outcomes (31), such as a higher rate of complications and infections (33), increased length of hospital stay, higher risk of hospital readmission and increased mortality rate (34).

3.1.3. Malabsorption

One of the characteristics of IBD is malabsorption resulting from an overgrowth of bacteria in the small intestine, which is related to the presence of chronic inflammation at the intestinal level and/or intestinal surgery (ileal resection) (5).

This bacterial growth causes malabsorption, as it accelerates intestinal transit (reducing digestion and nutrient absorption by reducing the contact time of luminal content with the mucosal surface), producing active metabolites that contribute to increase the discomfort, resulting in increased stool volume and diarrhoea (17). Mucosal alterations (impaired epithelial transport and reduced epithelial integrity) lead to malabsorption (responsible for vitamin deficiencies) which contributes to the presence of malnutrition in IBD patients (5).

During the active and remission phase of the disease in patients with CD and UC, there is the release of inflammatory cytokines by the cells of the intestinal mucosa, which some studies have linked to a cause of malabsorption, which leads to sarcopenia due to degrading muscle protein (2). This malabsorption condition usually worsens during hospitalization, contributing to a phenomenon called "post-hospital syndrome", which

means that after hospital discharge there is a greater probability of morbidity and hospital readmission (6).

3.1.4. Vitamin D deficiency

This deficiency is common and highly prevalent in IBD patients (6). This is related to malabsorption (5), inadequate daily intake, diarrhea, state of inflammation (2), low exposure to sunlight and treatment with steroids (11,18). Vitamin D has numerous benefits, as it decreases inflammatory markers, increases muscle growth markers such as IGF-1, and decreases catabolic markers such as C-Reactive Protein (CRP) (6) (a high level, greater than 10 milligrams per liter, is associated and present in IBD patients since high levels of CRP are present when there is inflammatory activity) (42,50).

Some studies indicate that vitamin D levels may be involved in the pathogenesis of IBD, as they are related/associated with the activity of the pathology (2,5). IBD patients are at increased risk of deficiency of this vitamin, since the study by Martín *et al.* (2019) demonstrated that 67% of IBD patients have a low exposure to sunlight (56), one of the important factors for the synthesis of vitamin D in the skin (1).

In this sense, the change in vitamin levels can generate a risk factor for IBD, since it preserves the integrity and healing capacity of the mucosa, its deficiency (low levels) can increase the risk of damage from impairment of the mucosal barrier, causing a more violent/aggressive course of the pathology (2,18).

Furthermore, vitamin D deficiency (serum levels lower than 25-hydroxyvitamin D (25(OH)D) concentrations) seems to be related to atrophy and fibrosis of type IIA muscle cells - "fast twitch fibers", leading to loss of MM (39), since, vitamin D is one of the factors involved in the proliferation, differentiation and regeneration of muscle cells (11) and inhibits the expression of myostatin (1,57).

Although the mechanism by which vitamin D affects muscle homeostasis is not yet known, it appears to be mediated by the vitamin D receptor (VDR) (expressed in skeletal muscle cells), and its expression decreases with age and in IBD (39).

Activation of VDR can decrease the expression of NF-kB, Toll-Like Receptor (TLR) 2 and TLR4, resulting in decreased production of TNF-α and activation of muscle contraction and mitochondrial function (39). As proof of this, changes in vitamin D levels (low level) seem to be related to an increased likelihood of developing sarcopenia and sarcopenic obesity (1,11).

The prevalence of this vitamin deficiency is higher in CD (duodenal and jejunal disease) affecting approximately 70% of patients and up to 40% of patients with UC (5). IBD patients who are malnourished, the majority are affected by this deficiency, approximately 90% (2,5).

A prospective study by Ananthakrishnan *et al.* (2012) performed with 72 women, showed that higher plasma vitamin D levels are associated with a considerable reduction in the risk of developing CD, but not UC (58), as maintaining vitamin D levels at the recommended or high values leads to improved function. of the epithelial barrier, promoting the production of anti-inflammatory cytokines, T cell development (18), and appears to play a relevant role in modulating innate immunity as well as adaptive immunity (2).

3.2. Identification of sarcopenia in IBD patients

The assessment of nutritional status in IBD is essential to identify nutritional disorders, including sarcopenia, in order to establish an adequate intervention (2,21).

It has been reported that approximately 80% of patients with CD require surgery (59), however, this has a high risk of complications such as wound infection, anastomotic leakage and intra-abdominal sepsis, especially in cases of low immunity, malnutrition and sarcopenia (8). Therefore, a comprehensive nutritional assessment is crucial in IBD patients (8). This assessment should include the clinical history, physical examination, anthropometric measurements, laboratory markers, body composition and functional capacity (3).

According to the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines, all patients newly diagnosed with IBD should be evaluated for the presence of malnutrition, as well as those who will undergo surgery (3). For this assessment, a validated nutritional screening tools should be used (3,48,60,61).

To identify sarcopenia in IBD patients, based on the EWGSOP, it is recommended to monitor the algorithm called Find cases- Assess-Confirm- Severity (F - A - C - S) which contains four steps to screening and diagnosis of sarcopenia (6,9).

The first step, called Find cases, aims to identify individuals at risk for sarcopenia, where the use of the SARC-F questionnaire is recommended (9). This questionnaire, also recommended by the EWGSOP2 as a way of screening patients with characteristic signs of sarcopenia, has the advantage of its high specificity to predict the reduction in muscle

strength, high applicability and low cost, which makes it possible to be used in hospital and community settings (9,10).

The second stage, Assess, in which the determination of muscle function and performance is recommended (6,7), measured through the Hand Grip Strength (HGS). HGS is an easy-to-perform technique (2) with the aid of a dynamometer (1).

The penultimate step is to confirm the presence of sarcopenia (9,10) by measuring muscle mass (quantity or quality) (47). Computed Tomography (CT) (63) and Magnetic Resonance Imaging (MRI) (3), despite their high accuracy and precision (2), have limited use in clinical practice (5) due to lack of portability, high cost, low practicality, the need for trained professional and exposure to x-rays and contrast medium (7).

Dual Energy X-ray Absorptiometry (DEXA) is considered the gold standard for the assessment of muscle mass (1,5). However, this technique requires high costs due to the need for a suitable location, sophisticated equipment and a trained evaluator (64). Bioelectrical Impedance Analysis (BIA) is considered a valid alternative for DEXA is clinical practice for the assessment of muscle mass (2,5). Anthropometry, particularly mid-arm muscle circumference and calf circumference, despite being susceptible to bias, is also used in clinical practice to estimate muscle mass (9).

Sarcopenia severity can be determined (9,10), based on performance measures such as the Short Physical Performance Battery (SPPB), Walking speed and Timed-Up and Go Test (TUG) (1,14).

3.3. Management strategies: prevention and treatment of sarcopenia in IBD patients

3.3.1. Nutrition

According to Beaudart *et al.* (2016) (62), the recommendation of protein for sarcopenia patients is 1.2-1.4 gram per kilogram of body weight, similar to the recommendations of the ESPEN, which indicates that daily protein intake should be 1.2-1.5 gram per kilogram body weight in IBD patients (1,65).

On the other hand, it has been shown that increased protein intake through food or protein supplementation improves anabolism and reduces muscle loss (1), resulting in better muscle strength and function and a decrease in the incidence of sarcopenia (43).

IBD patients usually present diminished oral intake (5). Nutritional interventions can improve clinical outcomes. In order to maintain and restore nutritional status,

nutritional therapy (enteric nutrition (EN), oral nutritional supplements or tube feeding) is recommended (5,18).

Based on the study of Frolkis *et al.* (2013) (66), this reported that 70% of patients with CD need to undergo surgery during their lifetime and according to the guidelines of the European Chron's and Colitis Organization (ECCO) (67), preoperative nutritional assessment should be performed in all patients with CD who need surgery (17). This statement can be justified by the fact that one of the most considered problems in surgical patients is the presence of malnutrition and/or sarcopenia (18). Thus, nutritional counseling before and after surgery significantly improves the clinical results of these patients, since there is a strong association between malnutrition/sarcopenia and unsatisfactory postoperative results (17). Considering that a greater amount of MM can be a protective factor against morbidity in the period after surgery (26).

Therefore, an early administration of nutritional support in the preoperative period is relevant, in order to reduce the risk of postoperative complications regardless of the administration route (3,5).

Despite the high importance in the correction of possible nutritional imbalances to reduce postoperative complications, no clinical trial has yet been carried out to indicate which of the nutritional supplementation routes will be the most advantageous to be performed before surgery. However, it has been shown that EN and parenteral nutrition (PN) before surgery reduce postoperative complications (18). EN has been shown to reduce morbidity and the onset of postoperative infectious complications in patients with CD being the reason why it should be preferred as nutritional support, while PN should be reserved for those patients who are unable to tolerate EN (3,18).

EN appears to exert an anti-inflammatory effect on the intestinal mucosa, due to the help on reducing the production of Interleukin (IL) -6 cytokines and the increasing of IGF-1 production (5).

It was also shown that patients who were treated with exclusive enteral nutrition (EEN) preoperatively, about 25% with CD did not have to undergo surgery (68), and those who underwent surgery had a lower rate of complications (18). The British Society of Gastroenterology (BSG) suggests EEN as therapy for up to 8 weeks in patients with mild to moderate CD who do not want to take corticosteroids (5). The induction of EEN in patients hospitalized with IBD demonstrated in a study that about 25% of these patients could avoid surgery due to its remission (18,66).

Regarding nutritional follow-up in the postoperative period of IBD patients with intestinal resections (69) (decreased surface area for nutrient absorption and increased dysmotility) it is essential to reduce the risk of onset or progression to malnutrition and/or sarcopenia (3,70).

Enteral feeding should always be preferred over PN due to the lower incidence of complications and lower costs (5). However, PN may be advised in case of failure or inability to tolerate EN or the presence of some clinical conditions that contraindicate the use of the enteral route (severe intestinal hemorrhage, high-output intestinal fistula or ostomy, obstruction and ischemia intestinal), since long-term PN and especially total parenteral nutrition (TPN) is associated with thromboembolic (thrombophlebitis, deep vein thrombosis and pulmonary embolism) and infections (5,18).

3.3.2. Physical activity

Physical activity is the most efficient way to increase MM, as well as being a vital factor in improving well-being and being an additional therapeutic factor (1,18).

One study has shown that performing 2–3 times a week of resistance training lasting 45–60 min has been found to decrease IL-6 concentrations, thus decreasing inflammation, increasing MM, strength, and improved muscle protein synthesis (1). But it can also be concluded that performing low-intensity physical activity (walking) for three weeks improved the quality of life among patients suffering from CD (1,10,71).

3.3.3. Vitamin D

Recently, it was demonstrated by Rondanelli *et al.* (2016) (72), that vitamin D supplementation has an anabolic effect, leading to a significant increase in muscle, and decreasing the prevalence of sarcopenia (6,72).

Thus, it becomes relevant in clinical practice, the indication for screening for vitamin D deficiency in all patients considered at risk (11) so that there is correction for adequate levels of the vitamin, as a way to prevent and treat inflammatory activity and sarcopenia in IBD patients (6).

Recently, it has been advised that serum 25(OH)D concentrations may be a better indicator than total 25(OH)D for assessing the levels of this vitamin, especially in patients with CD (11). Although the most used way to assess vitamin D in clinical management is to determine the serum concentrations of vitamin D (25(OH)D) in circulation, there is

still no agreement among the scientific societies on the normal serum levels of 25(OH)D (11). Taking into account the guidelines of the Endocrine Society, it is considered an insufficiency of this vitamin when the serum 25(OH)D is between 21–29 ng / mL (525–725 nmol / L) and deficiency if it is below 20 ng / mL (50 nmol / L) (11). Frigstad *et al.* (2016) (73), demonstrated that IBD patients have lower concentrations compared to healthy individuals and that vitamin D levels below 20 ng/mL have been reported in about 53% of patients with CD and 44% of patients with UC (1,74).

On IBD patients with low concentrations of this vitamin, the supplementation is essential (1,39). Vitamin D supplementation in combination with physical activity has shown beneficial effects in the prevention and treatment of sarcopenia in sarcopenia IBD patients (1), improving and increasing the number and diameter of type IIA muscle cells, increasing muscle strength (11), mass and function of these patients compared to the control group, leading to a reduction in falls mainly in elderly patients (39).

3.3.4. Omega 3 polyunsaturated fatty acids

Correct levels of omega 3 fatty acids, fibers and antioxidants are beneficial for IBD, as it leads to reduced inflammatory risk due to decreased macrophage activation, reduced production of pro-inflammatory cytokines such as IL- 6 and TNF-α, and the increased production of anti-inflammatory cytokines, such as IL-10 (18).

4. Discussion

IBD patients present intake deficiencies, malabsorption and metabolic disorders (7) which impact disease activity (5) and cause and predispose for malnutrition and sarcopenia (75).

Sarcopenia can affect IBD patients at any age (1), considerably increasing the risk of adverse outcomes such as length of hospital stay (75), morbidity and mortality (7). In IBD patients, it became relevant to pay attention to the presence of sarcopenia, due to the negative impact it has on the course of the pathology (75).

Thus, it is crucial to be alert to the risk factors that lead to the development of sarcopenia in IBD patients, such as inadequate diet (insufficient protein intake resulting in muscle atrophy) (39), vitamin D deficiency that increases inflammatory markers and inhibits muscle growth markers (45), as well as malabsorption resulting from the growth of bacteria in the small intestine (1) and the development of visceral fat (59), which, when

associated with the presence of chronic inflammation characteristic of DII leads to increased levels of inflammatory cytokines, resulting in loss of muscle mass and reduced strength (47).

Sarcopenia in IBD patients is associated with an increase in the rate of postoperative complications (17). The early identification of sarcopenia and other nutrition disorders is crucial in IBD patients, so that there is a timely and adequate nutritional intervention to prevent further adverse outcomes (48).

Despite the importance of regular assessment and monitoring of body composition in IBD patients to screen for sarcopenia, this procedure is not routinely performed (14).

There is also a consistent body of evidence showing that sarcopenic IBD patients may present a normal or even high BMI (17). Thus, there is a need to carry out a formal assessment of sarcopenia in all patients and not just those who are visibly undernourished (5). Thus, the change in body composition may not be recognized through traditional assessment in clinical practice (weight and BMI), since the decrease in MM can be compensated by the increase in FM, leading to the non-identification of sarcopenia in IBD patients, leaving those at risk (59).

Nutrition support, including oral nutritional supplements and EN (5) are among the most used strategies to treat malnutrition in IBD patients. Moreover, vitamin D (1)and omega 3 (18) fatty acids supplementation have also been associated to a decrease in inflammatory activity. Notwithstanding this, there are no specific guidelines concerning the prevention or treatment of sarcopenia in IBD patients. Therefore, the association of different strategies and also regular physical activity appear to be the most effective ways to increase muscle mass and function (71).

In IBD patients, a comprehensive and frequent nutritional assessment is a key strategy to the early identification of nutrition disorders, including sarcopenia. Strength and muscle mass assessment should be performed regularly.

Regarding the prevention and treatment of sarcopenia in IBD patients, nutritional intervention should be individualized according patient’s needs.

In conclusion, the current evidence about sarcopenia in IBD is still scarce. Nevertheless, the early identification of sarcopenia in IBD patients if of utmost importance for an effective intervention. Further research is needed in order to establish specific guidelines for the identification of sarcopenia in IBD patients and also to reach a consensus on the most effective nutritional strategies.

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