Journal of Enterocolitis

Review

Sarcopenia and Its Effect on Inflammatory Bowel Disease

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Cite this article as: Akpınar MY. Sarcopenia and its effect on inflammatory bowel disease. *J Enterocolitis.* 2022;1(2):28-32.

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Received: May 11, 2022 **Accepted:** July 22, 2022

DOI:10.5152/Jenterocolitis.2022.220913

Abstract

Malnutrition and sarcopenia are common conditions in inflammatory bowel disease. Both Crohn's disease and ulcerative colitis are characterized by chronic inflammation; additionally, strictures and fistulas can be seen in Crohn's disease. These conditions, individually or together, are causative factors for diminished oral intake, micronutrient deficiencies, protein-energy malnutrition, and/or sarcopenia. Malnutrition is considered poor prognostic criteria for inflammatory bowel disease in terms of disease course, hospitalization, need for surgery, and surgical complications. Sarcopenia is a syndrome characterized by progressive skeletal muscle deficiency which can be responsible for higher hospitalization rates, increase in bone fractures, and impairment of immune system functions. It seems that assessment of sarcopenia in patients with inflammatory bowel disease is essential since sarcopenia is considered a poor prognostic factor such as in many other chronic disease. In the last decade, studies investigating sarcopenia in inflammatory bowel disease were markedly increased. According to these studies, sarcopenia is a common condition in inflammatory bowel disease, and it can be classified as a poor prognostic factor for inflammatory bowel disease like malnutrition. Here, we want to review studies in the literature to clarify the frequency of sarcopenia and its potential effects on disease course in inflammatory bowel disease.

Keywords: Crohn's disease, inflammatory bowel disease, sarcopenia, prognosis, ulcerative colitis

INTRODUCTION

Malnutrition is an important and common condition in terms of disease course and response to therapy in inflammatory bowel disease (IBD).[1] Its prevalence ranges between 5 and 75% according to different studies and different patient populations. It is obvious that the nature of IBD and its therapy, either medical or surgical, are potential risk factors for malnutrition.[2] Malnutrition can manifest in various forms like micronutrient deficiencies, protein-energy type malnutrition, and sarcopenia in patients with IBD. Because of all these reasons, early recognition of malnutrition is important.

Sarcopenia is a condition which is characterized by skeletal muscle deficiency. When sarcopenia was first identified, it was considered a consequence of aging. Nowadays, it is well known that there are so many chronic inflammatory diseases which are associated with sarcopenia. The existence of sarcopenia is associated with increased morbidity and mortality in these chronic diseases. Sarcopenia is also common in IBD. The frequency of sarcopenia was found at 50% frequency in an IBD-associated retrospective study.[3] Like in other chronic inflammatory diseases, sarco penia-associated studies in the IBD population increased over time.[4] Current literature confirms that sarcopenia is a poor prognostic factor in terms of disease course, response to therapy, and postsurgical complications of IBD. Herein, we want to review studies which investigate sarcopenia in IBD and create awareness of the prognostic importance of sarcopenia in IBD.

MALNUTRITION IN INFLAMMATORY BOWEL DISEASE

Malnutrition is a serious condition and one of the major complications in IBD with a reported frequency between 20 and 70%.[5] Patients with Crohn's disease (CD) tend to have malnutrition more frequent than patients with ulcerative colitis (UC) (65–70% and 18–62%, respectively).[6] Malnutrition can present with protein-energy deficiencies, which is the most common form, micronutrient deficiencies and related symptoms, or sarcopenia. Several disease and treatment-related factors increase the probability of malnutrition in IBD. Active disease conditions, both in UC and CD, cause malnutrition.[7] In the active phase, especially in moderate-to-severe disease attacks, diarrhea, pain, and vomiting are frequent symptoms, and they can cause reduced oral intake. In this phase, if nutritional support is not enough to maintain daily calorie requirements, severe malnutrition can occur. Affected bowel segment, solely, can be a determinant of malnutrition. If this segment is too long, like in CD with long segment terminal ileitis, absorptive functions of the bowel can be diminished. Surgery can be a causative factor of malnutrition in IBD. Large segment bowel resections are treatment options in terms of treatment of primary disease and its complications in CD.[8] Extensive resections, especially in the ileum, can also impair absorption. Beyond these causative factors, epithelial dysregulation can also impair absorption.[9]

Malnutrition can affect the course of IBD negatively.[10] It is well known that malnutrition can impair immune functions and delay the wound healing process. The clinical aspect of this process is diminished response to medical therapy. Surgical outcomes are worse in patients with malnutrition.[11] Also, quality of life generally decreases in patients with malnutrition and overall life expectancy is shortened. Therefore, appropriate diagnosis and correction of malnutrition in IBD are essential.

Prevention of malnutrition is mandatory in the first step. Especially in patients with a higher risk of malnutrition, screening and documentation of malnutrition are crucial to prevent future complications. According to the European Society for Clinical Nutrition and Metabolism practical guideline in 2020, patients in the active phase must be followed up closely and dietary recommendations, medical nutrition support, and/or surgical approaches for nutrition must be applied to eligible patients.[12]

DEFINITION AND DIAGNOSIS OF SARCOPENIA

According to European Working Group on Sarcopenia in Older People (EWGSOP2), sarcopenia is a progressive and generalized skeletal muscle disorder that is associated with increased likelihood of adverse outcomes including falls, fractures, physical disability, and mortality.[13] Operational definition of sarcopenia can be considered according to 3 criteria which are listed in Table 1. If there is criteria 1, the diagnosis of sarcopenia is probable. If there are both criteria 1 and 2, the diagnosis of sarcopenia is confirmed. If a patient has all 3 criteria, then sarcopenia is defined as severe.

In the lifelong period, muscle strength and mass have a dynamic phase. In early adulthood, they increase and receive a stable phase in midlife and adults. After that, both of them start to decrease. After the fifth decade of life, 15% of muscle strength decreases annually.[14,15] From this perspective, sarcopenia can be considered a physiologic condition attributable to aging and this is true. Sarcopenia can be associated with aging in most of the patients; however, some other diseases can also lead to sarcopenia irrespective of aging, and these are classified as secondary causes of sarcopenia. Malnutrition, chronic inflammatory diseases, neurologic diseases, and inactivity irrespective of etiology can be considered as secondary causes.[16-18]

Suspicion of Sarcopenia in Clinical Practice

Significant proportion of patients with sarcopenia are not aware of their disease because of their asymptomatic conditions.[19] Because of this reality, awareness of physicians about sarcopenia and assessment of sarcopenia properly in this period will help to prevent future complications and improve treatment outcomes. In clinical practice, a wide variety of tests and tools can be useful for the evaluation of sarcopenia. While some of these tests help to identify the patients who suffer from sarcopenia or at risk for sarcopenia, the others are used to diagnose sarcopenia. Questionnaire-based tests are first-line tests to screen patients for sarcopenia. In clinical practice, several tests like SARC-F, Ishii Test, Mini Sarcopenia Risk Assessment Questionnaire, Taiwan Risk Score for Sarcopenia, and Sarcopenia Scoring Assessment Model can be used for this purpose.[20] According to EWGSOP2, SARC-F is the recommended test. It is a questionnaire consisting of 5 questions that is self-reported, inexpensive, and easy to use. This test has low-to-moderate sensitivity and high specifity.

After this first evaluation, some other tests can be helpful to evaluate skeletal muscle strength. They are easy to perform and can guide clinicians for their further investigations about sarcopenia. Low grip strength is one of them. Handgrip strength can be diminished in sarcopenia and it is related to longer hospital stay and mortality. especially in hospitalized patients.[21] Nowadays, calibrated handheld dynamometers can be used to assess this function. Chair stand test also can be performed to assess the strength of the muscles.[22]

Table 1. Operational Definition of Sarcopenia

Probable sarcopenia is identified by Criterion 1. Diagnosis is confirmed by additional documentation of Criterion 2. If Criteria 1, 2, and 3 are all met, sarcopenia is considered as severe
(1) Low muscle strength
(2) Low muscle quantity or quality
(3) Low physical performance

Measuring muscle quantity or mass is helpful to establish the diagnosis of sarcopenia. Multiple methods can be used for determining muscle mass and muscle quantity such as total body skeletal muscle mass, appendicular skeletal muscle mass, or muscle cross-sectional area of specific muscle groups. The gold standard methods for assessment of muscle mass are computed tomography (CT) and magnetic resonance imaging (MRI). However, in clinical practice, they are not usually performed because of their high costs and availability worldwide. Compared to MRI and CT, dual energy X-ray absorptiometry (DXA) is more available, but the results in DXA can be influenced by the hydration status of patients. In addition to classic imaging methods as mentioned earlier, some new tools are more widely being used in clinical practice such as lumbar third vertebra imaging by CT, psoas muscle measurement with CT, and mid-tight muscle measurement.

SARCOPENIA IN INFLAMMATORY BOWEL DISEASE

The first report of sarcopenia in IBD was published in 2008. Schneider et al investigated the frequency of sarcopenia in CD and its relationship with osteoporosis. They found that sarcopenia was higher in younger CD patients.[23] After this study, spotlights on sarcopenia increased with time and a lot of clinical studies were performed to evaluate the frequency of sarcopenia and/or effect of sarcopenia on IBD course. Basically, studies about sarcopenia in IBD can be classified under the following titles: frequency of sarcopenia, effect of sarcopenia on disease course, and relationship between sarcopenia and surgical outcomes.

Frequency of Sarcopenia in Inflammatory Bowel Disaease

In recent years, many studies investigate the frequency of sarcopenia in IBD. According to studies performed in last 5 years, the overall frequency of sarcopenia is between 16% and 70%, irrespective of disease type. The majority of studies were performed on CD patients and the most frequently used diagnostic test was CT. It seems that acute severe disease increases the probability of sarcopenia; two studies in acute severe UC found that the frequency of sarcopenia was 50.2% and 70%. On the other hand, in the remission period, the frequency of sarcopenia seems to decline compared to active disease (Table 2).

Effect of Sarcopenia on Disease Course

According to the literature, sarcopenia affects disease course negatively. Atlan et al investigated sarcopenia and disease severity in pediatric CD and UC in terms of the need for biological therapy and disease exacerbation.[33] They found that sarcopenia is a predictor of severe disease. Other studies also confirmed that sarcopenia is associated with increased hospitalization rate and increased frequency of perianal or enteral abscess.[30]

MAIN POINTS

- Sarcopenia is a common problem in inflammatory bowel disease.
- Sarcopenia can be considered as a poor prognostic factor in terms of disease course and surgical outcomes.
- In patients with sarcopenia, careful diagnostic approach and appropriate management are mandatory to keep patients away from sarcopenia-related complications.

Table 2. Studies Investigating the Frequency of Sarcopenia in Inflammatory Bowel Disease

Author	Country	Year	Disease	Disease Severity	Number of Patients	Assessment Modality	Sarcopenia (%)
Campbell et al[24]	USA	2022	CD and UC	Mixt (Severe is 48.7)	156	CT	24
Yasueda et al[25]	Japan	2022	CD	n/a	56	CT	16
Ünal et al[26]	Turkey	2021	UC or CD	Remission	344	EWGSOP2	41.3
Boparai et al[27]	India	2021	CD	Mixt (Moderate in 38.6%)	44	CT	43
Ge et al[28]	China	2021	UC	Severe	233	CT	50.2
Celentano et al[29]	UK	2020	CD	n/a	31	MRI	38
Lee et al[3]	Korea	2020	CD	n/a	79	CT	50
Grillot et al[30]	France	2020	CD	n/a	88	CT	58
Cushing et al[31]	USA	2018	UC	Severe	89	CT	70
Thiberge et al[32]	France	2018	CD	n/a	149	CT	33.6

CD, Crohn's disease; UC: ulcerative colitis; EWGSOP, European Working Group on Sarcopenia in Older People; MRI, magnetic resonance imaging; CT, computed tomography.

Table 3. Studies Investigating Relationship Between Disease Course and sarcopenia in ınflammatory Bowel Disease

Disease	Country	Year	Disease	Investigated Outcomes	Number of Patients	Results
Atlan et al[33]	Israel	2021	CD and UC	Biological therapy and disease exacerbation		Positive significant relationship between sarcopenia and investigated outcomes
Boparai et al[27]	India	2021	CD	Surgery	44	More patients with sarcopenia underwent surgery ($P = .01$)
Grillot et al[30]	France	2020	CD	Abscesses, hospitalization, and digestive surgery	88	Sarcopenic CD patients had more abscesses, hospitalization rate, and digestive surgery ($P > .05$)
Bamba et al[34]	Japan	2017	CD and UC	Intestinal resection	72	Sarcopenia predicts intestinal resection ($P > .05$)
Zhang et al[35]	Chiana	2017	UC	Disease activity and colectomy	204	Sarcopenia is associated with high disease activity and poor clinical outcome in UC patients
Adams et al[36]	USA	2017	CD	Surgery	90	Sarcopenia was a predictor of surgery in patients with a body mass index ≥ 25

CD, Crohn's disease; UC, ulcerative colitis.

Table 4. Studies Investigating Relationship Between Sarcopenia and Postoperative Complications in Inflammatory Bowel Disease Patients

Author	Country	Year	Disease	Investigated Outcomes	Number of Patients	Results
Trinder et al[37]	Australia	2022	CD and UC	Assess the impact of sarcopenia on postoperative anastomotic leak rates	147	Patients with sarcopenia were more likely to develop a postoperative anastomotic leak, grade IV complications and require total parenteral nutrition
Alipour et al[38]	USA	2021	CD and UC	Sarcopenia defined by Psoas muscle thickness has utility in predicting post-operative outcomes in patients with inflammatory bowel disease	85	A low status of Psoas muscle thickness was not associated with increased postoperative complications
Zager et al[39]	Israel	2021	CD	Correlations of the lean body mass marker and psoas muscle area (PMA), with postoperative outcomes in CD patients undergoing gastrointestinal surgery	121	Psoas muscle area associated with postoperative complications in patients with CD undergoing bowel resection
Celentano et al[29]	UK	2021	CD	The primary outcome was the incidence of 30-day postoperative complications in patients with sarcopenia	31	Psoas muscle cross-sectional area and skeletal mass area can be estimated on magnetic resonance enterography as surrogate markers of sarcopenia
Erős et al[40]	Hungary	2020	CD and UC	Assess whether sarcopenia predicts the need for surgery and postoperative complications in patients with IBD	885	Analysis of adjusted data identified sarcopenia as an independent predictor for both the undesirable outcomes
Galata et al[41]	Germany	2020	CD	Role of the skeletal muscle mass index (SMI) for major postoperative morbidity in patients with Crohn's disease	230	Skeletal muscle index was the only independent risk factor for major postoperative complications
O'Brien et al[42]	Ireland	2018	CD and UC	Outcomes in IBD patients undergoing surgical resection relative to the presence of sarcopenia and myosteatosis	77	Sarcopenia and myosteatosis were associated with hospital readmission within 30 days on univariate analysis
Pedersen et al[43]	USA	2017	CD and UC	Assessed the role of sarcopenia on operative outcomes in IBD	178	In patients younger than 40 years, sarcopenia was an independent predictor of complications
Fujikawa et al[44]	Japan	2017	UC	Association between sarcopenia and surgical site infection after surgery for ulcerative colitis	69	Sarcopenia is predictive of surgical site infection after pouch surgery for ulcerative colitis

CD, Crohn's disease; UC, ulcerative colitis.

As an unexpected and undesirable outcome, the need for surgery was found more common in sarcopenic IBD patients. Bamba et al found that intestinal resection was higher in patients with CD and UC who had sarcopenia.[34] Zhang et al also found similar results in the UC population Table 3.[35]

Interaction Between Sarcopenia and Surgery

The frequencies of postoperative complications and mortality are high in sarcopenic patients regardless of operation type. Sarcopenia's possible effects on outcomes after IBD-related surgery are listed in Table 4. In general, sarcopenia can be defined as a poor prognostic factor for surgical outcomes. It is associated with anastomotic leaks, surgical site infections, and hospital re-admissions. These results were not different between UC and CD.

CONCLUSION

Sarcopenia is common in IBD patients. Clinicians must be aware of the possibility of sarcopenia especially in patients with advanced age, active, and/or long-term disease. According to studies, sarcopenia is a predictor of long hospital stay, increased need for biological therapies, and postoperative complications in IBD patients. Therefore, it is important to recognize sarcopenia timely and properly. With new guidelines, it is clear that diagnosis of sarcopenia can be made by CT and or DXA easily which are widely available. In patients with sarcopenia, multidisciplinary approach is necessary. Optimizing skeletal muscle mass and correcting concomitant malnutrition is important to provide a better response to medical therapies and to avoid potential postoperative complications in IBD.

Peer-review: Externally peer-reviewed.

Declaration of Interests: The author have no conflicts of interest to declare.

Funding: The author declared that this study has received no financial support.

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