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Stephanie L. Gold, MD is an Instructor of Medicine at the Icahn School of Medicine at Mount Sinai and a gastroenterologist at the Mount Sinai Hospital, with a focus on inflammatory bowel disease (IBD) and nutrition. Dr. Gold's clinical interests include nutrition optimization for patients with IBD and the use of diet as an adjunct therapy. She established a unique Nutrition-IBD clinic where patients have access to an in-depth nutrition and muscle health assessment as well as dietary guidance and support to complement their IBD care. Her research interests include improving the identification of malnutrition, micronutrient deficiencies and sarcopenia in patients with IBD.

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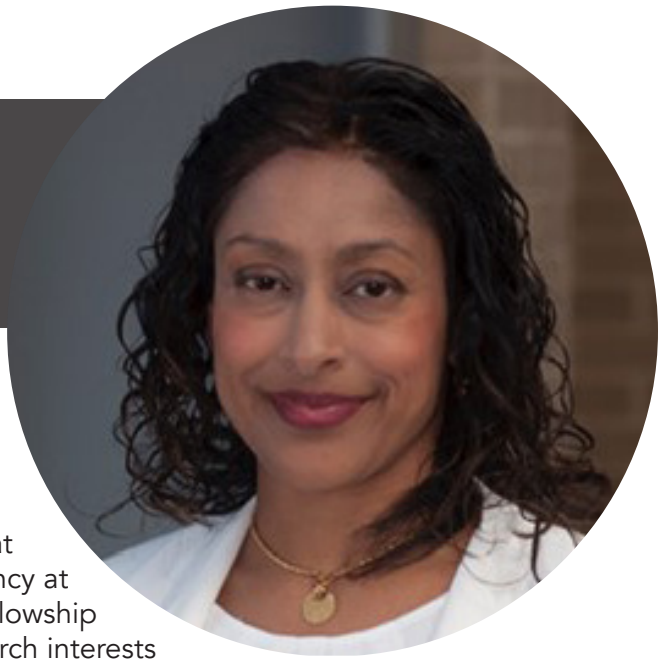

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Malnutrition Assessment in Patients with Inflammatory Bowel Disease

Introduction

Inflammatory bowel disease (IBD) affects over 6.8 million people worldwide and is highly associated with the development of malnutrition.[1] Malnutrition in patients with Crohn's disease (CD) and ulcerative colitis (UC) is often due to the following: decreased oral intake; food avoidance; side effects of medications; malabsorption; chronic enteric losses; altered anatomy from luminal surgery; and increased nutritional needs in the setting of active inflammation and a high catabolic state.[2,3] Approximately 20%-80% of patients with IBD are estimated to be malnourished at some point during their disease course; this wide range is likely secondary to significant heterogeneity in the definition of malnutrition in the literature, and due to the lack of robust, validated tools to identify individuals who are malnourished.[4] While malnutrition is traditionally thought of as under-nutrition or protein calorie malnutrition, there are other nutrition phenotypes of significance in patients with IBD including micronutrient deficiencies, sarcopenia and obesity (over-nutrition).[4,5] Malnutrition is associated with poor outcomes in patients with IBD, including a high number of disease flares; impaired response to biologics; increased surgical complications; hospitalizations; and impaired quality of life, independent of disease activity.[3,6,7] Given the significant prevalence of malnutrition, the impact it can have in patients with IBD, and its responsiveness to therapeutic interventions, it is crucial to accurately assess the nutritional status of patients at the time of diagnosis and regularly thereafter.

Malnutrition risk assessment and diagnostic tools

Malnutrition screening is a rapid, non-invasive technique to assess patients for nutritional risk that can be completed by any member of the clinical team in order to determine which patients are at increased risk of becoming malnourished and would therefore benefit from a referral to a dietitian. There are numerous questionnaire-based malnutrition risk assessment tools available, the majority of which were developed for the general population, and two that were designed specifically for patients with IBD. While there

is no "gold standard" or universally accepted malnutrition screening or diagnostic tool, the Malnutrition Universal Screening Tool (MUST) has been validated in an IBD cohort and is commonly used clinically and in nutrition studies. The MUST takes into account body mass index (BMI), recent unintentional weight loss and an acute illness evaluation.[8] Of interest, the MUST can be completed by either the provider or the patient and can usually deliver similar results, increasing the ease of use in a busy clinical setting. Although the MUST was designed for use in the geriatric population, it has been used in several IBD nutrition studies in both the outpatient and hospital setting with non-geriatric patients.[4,9-11] Additionally, two nutrition screening tools were designed specifically for patients with IBD: the Malnutrition Inflammatory Risk Tool (MIRT) and the Saskatchewan IBD Nutrition Risk Tool (SaskIBD-NR). These tools include disease specific features including gastrointestinal symptoms, as well as markers of systemic inflammation; however, to date, neither tool has been adopted for routine use.[4]

Traditionally, malnutrition is diagnosed utilizing criteria from the European (ESPEN) and American (ASPEN) nutritional societies, as well as the Subjective Global Assessment (SGA).[12-14] Similar to the MUST, the SGA can be completed by the provider or patient, and studies have shown that the patient reported SGA has a high sensitivity for identifying malnutrition risk.[8] The malnutrition diagnostic tools are generally more comprehensive than the screening tools mentioned above; however, the ESPEN, ASPEN and SGA were similarly designed for use in the general population and they are weighted towards low BMI and unintentional weight loss. However, patients with IBD can be malnourished despite a normal or elevated BMI and therefore these tools may lead to an underestimate of malnutrition in this unique patient population.[15,16] Given this, the Global Leadership Initiative on Malnutrition (GLIM) published a novel set of criteria for identifying malnutrition that is more comprehensive than the ESPEN or ASPEN criteria.[17] The GLIM includes etiologic criteria for malnutrition such as weight loss, BMI and reduced muscle mass as well as phenotypic criteria such as reduced intake, inflammation and malabsorption.[17] Although the GLIM has been studied in surgical IBD patients, there is no data on its use with IBD patients in an outpatient setting. Despite this, the nutrition research community is advocating for universal acceptance of the GLIM to provide a standardized and comprehensive tool that includes a broad definition of malnutrition and considers both inflammation and malabsorption.

Micronutrient assessment

Micronutrient deficiencies are commonly seen in patients with protein calorie malnutrition; however, these deficiencies can similarly occur in patients who are well nourished. In fact, in Western countries, the diets are often rich in energy and low in nutrients, resulting in "hidden hunger" or isolated micronutrient deficiencies.[18] Traditionally, deficiencies in vitamin B12, vitamin D, folate and iron are commonly associated with CD; however, deficiencies in other vitamins and minerals can contribute to significant symptoms and complications.[5] For example, in patients with large volume diarrhea or high output ileostomies, it is important to test for zinc and magnesium deficiencies, as these can lead to worsening of diarrhea, muscle weakness and poor appetite.[5,19] Moreover, in patients with a history of ileal resection, vitamins B1 and B12, and folate levels should be assessed to prevent neurological complications, fatigue, and paresthesias.[19] Finally, micronutrient deficiencies can occur secondary to specific medication use, such as vitamin B6 deficiency with isoniazid use, fat soluble vitamin loss in those on cholestyramine, and folate deficiency in patients on methotrexate as well as sulfasalazine.[5,19] While there are many studies evaluating micronutrient deficiencies in those with IBD, there are two excellent review articles which highlight the identification and management of the common and less common deficiencies in IBD patients and these can be a great resource for IBD providers.[5,19]

Micronutrients are typically assessed in the serum or plasma and these levels are thought to represent a measure of the total body nutrient stores. However, recent clinical studies have demonstrated that many of the nutrients are, in fact, acute phase reactants and therefore serum levels are significantly impacted by

systemic inflammation. In patients with IBD, this can result in inaccurate testing, making it difficult to provide supplementation. Therefore, researchers are looking for other modalities to accurately assess nutrient levels in patients with systemic inflammation, including testing of hair, sweat and even urine. While these micronutrient assessment techniques are only being used in research today, the authors are hopeful for their use in the future.

Sarcopenia assessment

Sarcopenia, a loss of muscle mass or function, is intimately linked to malnutrition and is independently associated with disease complications in patients with IBD. Sarcopenia is traditionally diagnosed utilizing the psoas muscle area or total skeletal muscle area on computerized tomography (CT) or magnetic resonance imaging (MRI) at the level of the third lumbar vertebrae (L3). While this is the gold standard, given the cost of an MRI or CT, the time it takes to obtain a scan and potential radiation exposure, cross-sectional imaging is not used routinely in clinical practice to assess for sarcopenia. Therefore, novel, bedside measures of muscle mass and function have been proposed, including handgrip strength (HGS) evaluation, mid-upper arm circumference (MUAC), and bioelectrical impedance analysis. Studies have demonstrated that HGS and MUAC are significantly lower in patients with active or inactive IBD vs healthy controls and that these metrics are more predictive of nutritional status than BMI in patients with CD.[20] While these tools provide a rapid assessment of muscle health, they have yet to be validated in the IBD population and thus are not routinely used.[21] In the geriatric literature, ultrasound of the thigh and upper extremity muscles has been proposed as an accurate point-of-care modality to measure muscle mass.[22] Learnings from geriatrics include the importance of measuring the cross-sectional area of the muscle and the pennation angle, echogenicity and fascicle length.[22] Unfortunately, normative values for these muscle metrics are not clearly defined, which limits the use of these techniques to identify sarcopenia at the current time. While albumin has traditionally been associated with malnutrition and sarcopenia, many studies have demonstrated that low albumin is likely a marker of IBD activity (given its role as an acute phase reactant) and less likely a reliable marker of low muscle mass or function.[23,24] Future studies evaluating this relationship between albumin as well as total protein with sarcopenia and identifying novel serum markers associated with sarcopenia will be helpful in advancing this field. Looking forward, with the discovery of these easy-to-use, inexpensive and non-invasive muscle assessment modalities and defined normative values in a healthy population, it is hoped that sarcopenia evaluation will become more ubiquitous for those with IBD.

Conclusion and Practical Implementation of Nutrition Screening and Assessment in IBD

Although there is still a great deal to discover about malnutrition evaluation in patients with IBD, it is important to highlight a few practical guidelines for clinical care today. First, all patients with IBD should be screened for malnutrition at the time of diagnosis and regularly thereafter utilizing the MUST or SaskIBD-NR.[4,8] Patients identified as being moderate or high risk for malnutrition should undergo further evaluation (micronutrient testing, as well as muscle health evaluation) and be referred to a registered dietitian with experience managing patients with IBD. Second, all patients should be weighed at every clinic visit, as this is a crucial "vital sign" to assess for malnutrition risk. With the shift toward telemedicine, it is important to ask patients about their weight when they are not seen in the clinic and to schedule routine in-person visits in order to obtain an accurate objective weight, and to establish a trend for these values longitudinally. To establish a diagnosis of malnutrition, the GLIM offers a comprehensive strategy that includes malabsorption and reduced oral intake, as well, as markers of muscle health, in addition to the more traditional measures of BMI and unintentional weight loss. However, the abridged SGA can be successfully completed by the patient (unlike the GLIM which requires a provider) and therefore may be a valuable tool to identify malnutrition in a busy clinic practice. Finally, regardless of disease activity and malnutrition risk, micronutrient levels should be measured at the time of diagnosis and at routine follow-up visits. While vitamin D, vitamin B12 and iron

deficiencies are commonly seen in IBD patients, it is important to consider zinc, vitamin B1, vitamin A, folate, and vitamin C deficiencies as well.[5] In addition to the above, it is crucial to ask all patients with IBD about dietary avoidances, restrictions and patterns of eating, as these can help identify patients on highly restrictive diets.

Conclusion:
Malnutrition is a common complication in patients with IBD and is associated with poor outcomes independent of disease activity. Thorough malnutrition screening at the time of diagnosis and routinely thereafter of all patients with IBD, utilizing available screening and diagnostic tools as well as micronutrient assessments and dietary pattern evaluations are crucial to identify those at risk for developing IBD and nutrition related disease complications.

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Financial Disclosures:
None

Screening Item		Points
BMI	>20	0
	18.5-20	1
	<18.5	2
Weight Loss (3 months) %	<5	0
	10-May	2
	≥10	3
CRP (mg/)	<5	0
	5-50	2
	≥50	3

Table 1: *Malnutrition Inflammation Risk Tool*

Screening Item		Score
Have you experienced nausea, vomiting, diarrhea or poor appetite for greater than two weeks?	No symptoms	0
	1-2 symptoms	1
	≥3 symptoms	2
Have you lost weight in the last month without trying?	No	0
	Yes	2
	Unsure	1
If YES (you have lost weight in the last month without trying), how much weight have you lost?	<5 lbs	0
	5-10 lbs	1
	10-15 lbs	2
	>15 lbs	3
Have you been eating poorly because of a decreased appetite?	No	0
	Yes	2
Have you been restricting any foods or food groups?	No	0
	Yes	2

Table 2: *Saskatchewan IBD Nutrition Risk Tool (SaskIBD-NR)*

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- Patients with known hypersensitivity or any components to STELARA®/STELARA® I.V.
- Severe infections such as sepsis, tuberculosis and opportunistic infections

Relevant warnings and precautions:

- Potential to increase the risk of infections and reactivate latent infections
- STELARA®/STELARA® I.V. should not be given to patients with any clinically important active infection. Patients should be evaluated for tuberculosis infection prior to therapy and monitored for active tuberculosis during and after treatment
- Potential to increase the risk of malignancy
- All patients, in particular those greater than 60 years of age, those with a medical history of prolonged immunosuppressant therapy or those with a history of PUVA treatment, should be closely monitored for skin cancer
- Hypersensitivity reactions including serious allergic reactions (anaphylaxis and angioedema), allergic alveolitis and eosinophilic pneumonia
- May cause allergic reactions in individuals sensitive to latex
- Concurrent use with live viral or bacterial vaccines is not recommended
- Caution should be exercised when considering concomitant use of immunosuppressive agents and STELARA®/STELARA® I.V.
- May affect allergy immunotherapy
- If reversible posterior leukoencephalopathy syndrome is suspected, administer appropriate treatment and discontinue STELARA®/STELARA® I.V.
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Reference

1. STELARA/STELARA I.V. Product Monograph. Janssen Canada Inc., September 9, 2021.