Preventing Malnutrition through Adequate Management of Gastrointestinal Dysmotility in Systemic Sclerosis Patients: A Literature Review

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ABSTRACT

Gastrointestinal dysmotility in systemic sclerosis occurs as the end result of extensive fibrosis of the gastrointestinal tract. The entire length of the tract from the esophagus to the anorectum could be affected, exerting various gastrointestinal symptoms. Clinical manifestations attributed to gastrointestinal dysmotility are associated with significant distress and an increased risk of nutritional impairment, reducing the quality of life of systemic sclerosis patients. One of the most commonly overlooked gastrointestinal implications in systemic sclerosis is malnutrition. Once malnutrition ensues in the course of systemic sclerosis, the detrimental effects attributed to nutritional decline are difficult to reverse and pose an increased risk of mortality. Adequate management through timely diagnosis of gastrointestinal dysmotility and utilization of malnutrition screening tools for systemic sclerosis patients could prevent the progression to malnutrition and its negative impacts.

Keywords: *gastrointestinal dysmotility, systemic sclerosis, malnutrition*

ABSTRAK

Dismotilitas gastrointestinal pada sklerosis sistemik terjadi akibat fibrosis ekstensif pada traktus gastrointestinal. Seluruh bagian dari saluran cerna dari esofagus hingga anorektum dapat terlibat, menimbulkan berbagai gejala gastrointestinal yang variatif. Manifestasi klinis akibat dismotilitas gastrointestinal diasosiasikan dengan gangguan fungsi dan gangguan penyerapan nutrisi yang berdampak pada penurunan kualitas hidup pasien sklerosis sistemik. Salah satu komplikasi keterlibatan saluran cerna pada sklerosis sistemik yang sering terlewatkan dalam penilaian klinis adalah malnutrisi. Manifestasi malnutrisi dalam perjalanan penyakit sklerosis sistemik sulit dikembalikan pada status semula sebelum malnutrisi terjadi. Malnutrisi juga diasosiasikan dengan peningkatan risiko mortalitas pada pasien sklerosis sistemik. Manajemen dismotilitas gastrointestinal melalui diagnosis yang tepat sasaran dan penggunaan instrumen skrining malnutrisi dapat mencegah timbulnya malnutrisi dan dampak buruk yang terkait.

Kata kunci: *dismotilitas gastrointestinal, sklerosis sistemik, malnutrisi*

INTRODUCTION

Systemic sclerosis (SSc) is an autoimmune disease with the hallmark features of progressive fibrosis, presence of autoantibody, and vasculopathy.[1] Pathogenesis of SSc stems from the dysregulation of innate and adaptive immune systems, combined with the degenerating effects of fibroblast dysfunction which leads to abnormal collagen deposition in multiple organs.[2] Clinical manifestations of systemic sclerosis are heterogenous in nature and can often be observed simultaneously throughout multiple body systems.[3]

Gastrointestinal (GI) system is affected in approximately 90% of SSc patients and the manifestations of GI involvement can be observed throughout the entire length of GI tract, from the oral cavity to the anorectum.[4] Studies showed that 75–98% of SSc patients reported at least one GI symptom and that around 10% SSc patients presented with only gastrointestinal complaints at initial visit.[5] A smaller fraction of cases of SSc with GI involvement (8%) presents with severe manifestations, which is attributed to 3–4% mortality and significant decrease in the 9-year survival rate in SSc.[4,6] A study conducted by McMahan et al also found that severe GI manifestations in SSc are especially prevalent in male SSc population with a concomitant history of myopathy and sicca symptoms.[7]

GI disorders contribute to 5–10% of mortality in SSc.[8] Most complications of SSc in the gastrointestinal system can be traced back to hypomotility disorder which is the end-result of structural changes of the gastrointestinal histological architecture due to extensive fibrosis and autoantibody deposition.[9] One of the complications that is easily overlooked in SSc is malnutrition, which warrants the utilization of malnutrition screening tool.[6,10] The prevalence of malnutrition in studies on SSc has fluctuating rates, but findings have consistently revealed that malnutrition is strongly associated with an increase in morbidity and decreased quality of life of SSc patients.[9,11] Many studies also include malnutrition as one of the criteria of severe GI involvement along with the need of hyperalimentation, episodes of pseudo-obstruction, and significant weight loss.[12] Once malnutrition ensues in the course of SSc, it is difficult to reverse the deteriorating effects that resulted from the nutritional declines.[6] The need of parenteral nutrition in patients with severe malnutrition is also associated with higher mortality rate.[13]

ETIOPATHOGENESIS OF GASTROINTESTINAL DYSMOTILITY IN SYSTEMIC SCLEROSIS

Even though gastrointestinal dysmotility accounts for the majority of symptoms observed in SSc patients, there has not been many extensive studies which could elucidate the complex pathogenesis of GI dysmotility in SSc completely.[14] The initial event which precipitates multiple organ dysfunction in SSc, including the GI system is vasculopathy.[15] Endothelial dysfunction and ischemia due to the alteration of microvasculature promote production of reactive oxygen species, which facilitates inflammation through the recruitment of inflammatory cells and activation of cytokine cascade.[14] The amalgamation of immune cell dysfunction and release of pro-fibrotic cytokines contribute to excessive fibroblast activation and aberrant deposition of collagen in the extracellular matrix of susceptible tissues.[4] In terms of alteration of gene expression from molecular level, studies have found that some particular subtypes of micro-RNAs (miRNAs), which have a role in gene regulation and expression, might contribute to the progression of fibrosis and vasculopathy in SSc.[16] Many recent studies have also linked the alteration of gut flora composition in SSc, which plays an important role of nitric oxide (NO) regulation, to the manifestations of GI dysmotility.[17]

The alternate proposed mechanism of GI dysmotility progression in SSc that has been widely accepted is that the condition originates from the autonomic dysfunction associated with neuropathy, which leads to atrophy of GI smooth muscle cells and hypomotility through impaired peristaltic movement.[9,10,18] The postulate is also supported by the finding of muscarinic acetylcholine receptor 3 (M3-R) antibody in SSc, an autoantibody produced from aberrant humoral response, which precipitates the irreversible structural changes in the neuromuscular junction of myenteric plexus, rendering the smooth muscle of GI tract unresponsive to external stimuli.[18,19] The notion is further supported by another study by Kumar et al which showed mitigated progression of nerve and smooth muscle dysfunction on the GI tract by the administration of IVIg that binds to M3-R antibody in an animal model.[14]

ESOPHAGEAL DYSMOTILITY IN SYSTEMIC SCLEROSIS

Esophageal symptoms are the most common GI symptoms reported by SSc patients, with a prevalence ranging between 40–80%.[20] Dysmotility which typically manifests as dysphagia and gastroesophageal reflux disease (GERD) which presents as heartburn or regurgitation are the two major spectrums of esophageal symptoms observed in SSc.[14] Moreover, esophageal involvement in SSc often follows a refractory course with worse degree of symptoms severity, which often warrants an aggressive approach and surgical intervention.[20,21] Complication of GERD such as peptic stricture, Barrett's esophagus, and esophageal carcinoma can develop in the course of the disease, but the incidence is within the similar range found in common population without SSc.[22] Aside from the increased morbidity, microaspiration of gastric acid to the esophagus has been postulated to be one of the possible mechanisms which is responsible for the development of interstitial lung disease (ILD) in SSc patients.[23]

One third of patients of SSc with GI symptoms are often initially asymptomatic, especially in the early course of disease, which often results to delay in early diagnosis.[24,25] Studies even documented that more than 75% of SSc patients have esophageal dysmotility confirmed by manometry in the absence of symptoms.[20,26,27] In terms of diagnosis, classic manometry has been the mainstay of modality used to diagnose esophageal dysmotility in SSc , which typically reveals the characteristic findings of hypotensive lower esophagus sphincter (LES) and distal aperistaltis. However, recently high-resolution manometry (HRM) has been more favored due to its ability to accurately record the pressure of every segmental part of the esophagus.[20,28]

Culmination of esophageal dysmotility, hypotensive LES, gastroparesis, and impaired saliva production in SSc, leads to the development of GERD with persistent symptoms.[22] Although GERD in SSc can be definitively diagnosed by using the esophageal pH monitoring method with or without impedance, this modality is generally reserved when clinically diagnosed GERD fails to improve with empirical proton-pump inhibitors (PPI) therapy.[29] Esophagogastroduodenoscopy (EGD) can also be performed to evaluate the complications of GERD and is preferred to evaluate the symptom of dysphagia in SSc patients.[20,29] In remote areas with limited diagnostic modalities, GERD questionnaire (GERD-Q) can be utilized as well to diagnose GERD in SSc patients. A study by Chunlertrith et al showed that a lower cut-off point with GERD-Q score of 4 or higher has a high sensitivity for GERD diagnosis among SSc populations.[30,31]

In terms of esophageal dysmotility management in SSc, there is no specific treatment available, but prokinetics, such as metoclopramide, domperidone, and erythromycin are commonly prescribed for symptom control.[22,32] Besides the conflicting results from multiple studies about the beneficial effect of prokinetics in SSc and the fact that prokinetic agents do not prevent the progression of dysmotility, the use of prokinetic warrants a close observation due to the cardiac side effects that this particular class of drug commonly possesses.[10] Other drug option, such as buspirone is also considered one of the potential therapies as studies have shown that Buspirone can alleviate symptoms by increasing the resting low esophageal sphincter (LES) pressure.[33] Dietary adjustment with small frequent feedings accompanied with water consumption between bites and avoidance of sticky food can be instituted in patients with solid dysphagia.[34]

Dietary and lifestyle changes, such as avoidance of alcohol, tobacco, and high-fat meals should be firstly incorporated along with the pharmacological approach for GERD treatment in SSc.[32] The use of PPI for GERD management in SSc is often limited as only half of the patients respond to the standard dose of PPI. Failure of symptom control with standard dose of PPI often requires higher doses of PPI, coupled with increased frequency of PPI administration to two times a day, and switching to other PPI drugs on subsequent visits.[10] Studies have also shown that symptom of heartburn tends to persist in 77.4% GERD patient with SSc despite prolonged treatment with conventional PPI.[35] Addition of histamine-2 blocker (H2-blocker) at night can be tried when standard management with PPI does not result in symptom remission.[10] SSc patients with Raynaud's phenomenon often consumes calcium channel blocker (CCB) which could contribute to the persistence of GERD symptoms despite adequate therapy.[17]

When GERD follows a refractory course and pharmacological management fails, endoscopic surgical procedures may be attempted.[4,10] Unfortunately, there has not been a consensus and standardized algorithms regarding the surgical management of GERD in special population in SSc.[22] A study by Aiolfi et al proposed the algorithm for recalcitrant GERD in SSc which puts emphasis on the findings of long-segment fibrosis through endoscopy. GERD patient with long-segment fibrosis generally requires esophagectomy, while patients with no long-segment fibrosis require

further gastric emptying study with scintigraphy for evaluation. Minimally invasive fundoplication should be recommended to patients with normal gastric emptying study, while short-limb Roux-en-Y gastric bypass (RYGB) procedure should be reserved for patients with delayed gastric emptying.[36]

GASTROPARESIS IN SYSTEMIC SCLEROSIS

Gastroparesis is one of the two most common stomach impairments seen in SSc aside from gastric antrum vascular ectasia (GAVE).[37] Half of SSc patients develop gastroparesis which generally manifests as early satiety, bloating, nausea, and vomiting.[3,4] Early detection and evaluation with scintigraphy or endoscopic capsule is deemed essential because as nerve damage progresses through the course of disease, prokinetic agents will be less effective in controlling the symptoms.[37] In underweight and malnourished patients with gastroparesis, thorough evaluation of serum vitamin levels is also recommended as concomitant vitamin deficiencies is also commonly observed.[38] Moreover, inadequate control of gastroparesis can cause dehydration and electrolyte imbalance which requires urgent repletion and correction.[32]

Four-hour solid phase gastric emptying scintigraphy is considered the gold standard to diagnose and evaluate the degree of severity of gastroparesis.[39] However, recent study showed that diagnosis of gastroparesis with scintigraphy on both solid and liquid study may provide more clinically relevant considerations in optimizing the management of gastroparesis, rather than either alone.[18,40] In terms of treatment for gastroparesis, modification of diet by promoting small frequent meals with soluble fibers and avoidance of fatty food consumption can be instituted initially to ameliorate delayed gastric emptying which exacerbate the symptoms.[4,32] Metoclopramide remains the first-line drug for gastroparesis in SSc. Metoclopramide must be prescribed with caution due to its side effects of QT interval prolongation, for which a baseline electrocardiogram (ECG) evaluation is recommended prior to its initiation.[10,32] Second-line drugs include domperidone and erythromycin can be tried, especially when the evaluation of gastric emptying revealed motility compromise with solid food in particular.[4] Adequate treatment of concomitant GERD should be addressed as uncontrolled GERD symptoms could exacerbate symptoms of gastroparesis.[10] Administration of some drugs which are associated with impairment of GI smooth muscle motility, such as opioid medication and PDE-5 inhibitor should also be promptly evaluated.[17]

Later stages of gastroparesis are difficult to control with medications and enteral nutrition via percutaneous gastrostomy or jejunostomy might be the best option, especially when patients are in an increased risk of malnutrition with loss of 10% body weight in a period of 3–6 months.[32] Enteral nutrition can be started at 25 to 50 mL/hour with progressive increment of 10 to 25 mL/hour as tolerated.[38] Gastric peroral endoscopic myotomy (G-POEM) might also be considered as a potential option.[41] If the patient is not a suitable candidate for gastrostomy, total parenteral nutrition (TPN) might be considered as last resort. TPN alone carries multiple risks of morbidity, but combination of both enteral and parenteral nutrition is associated with increased survival.[38,42]

DISMOTILITY OF THE SMALL INTESTINE IN SYSTEMIC SCLEROSIS

Studies have found that about 40–90% of SSc patients reported symptoms associated with intestinal dysmotility, which prolonged course causes retention of materials in the small intestine. Retention of material further promotes colonic bacteria migration and colonization in the small intestine, creating the small intestinal bacterial overgrowth (SIBO).[32] Aside from the dysmotility which is caused by histopathological tissue alteration and deposition of polyglucosan inclusion bodies in SSc, hypochloremia which is associated with PPI use in SSc is also a risk factor for SIBO development.[43] Common symptoms of SIBO include post-prandial bloating, excessive flatulence, abdominal pain, nausea, vomiting, along with signs of malabsorption such as steatorrhea and loss of weight despite adequate oral intake.[18,44] Deficiencies of fat-soluble vitamins, vitamin B-12, and iron are also common, which should be evaluated at initial diagnosis.[32,43]

Culture of jejunal aspirate remains the gold standard for the diagnosis of SIBO. However, due to the invasive nature of the procedure, breath test is more favorable in clinical practice, despite having lower sensitivity.[18,32,45] Glucose and lactulose are commonly used as substrates for breath test in detecting SIBO. GI microbes metabolize the substrates, producing hydrogen and methane as the byproducts, which are partially absorbed by the GI tract into the vasculature and eventually exhaled through lungs for measurement.[43,44]

Rifaximin is the favorable choice of antibiotic in SIBO due to its poor systemic absorption and

low toxicity profile compared to other antibiotics.[46] Rifaximin is also associated with preservation of normal colonic flora such as lactobacilli and bifidobacteria.[43] Other broad-spectrum antibiotics which can be used include amoxicillin, tetracycline, ciprofloxacin, and metronidazole.[32] Antibiotics are generally prescribed for 2 weeks and the use of rotating regimen of antibiotics is encouraged to minimize the development of antibiotic resistance.[18] The role of probiotics administration remains controversial in SIBO, however some studies reported improvement of symptoms with consumption of probiotics.[44] In rare occasion when chronic intestinal dilation from small intestine dysmotility and overproduction of gas from colonization of bacteria persist, progression into pneumatosis cystoides intestinalis (PCI) can be imminent. The formation of gas-filled cysts within intestinal wall in PCI can cause pneumoperitoneum when perforated.[10]

Other small intestine dysfunction which can be observed in SSc is chronic intestinal pseudo-obstruction (CIPO).[10] CIPO is characterized by signs and symptoms of intestinal obstruction which include abdominal pain, nausea, and abdominal distension, in the absence of mechanical occlusion.[4,47] Abdominal CT and plain abdominal x-ray which reveal non-specific bowel obstruction can be ordered to exclude mechanical obstruction.[47] Patient with CIPO should be admitted for hospital care and is initially treated with bowel rest, intravenous hydration, electrolyte repletion, and broad-spectrum antibiotics.[24] Studies have shown that pharmacological approach to CIPO with prokinetics and cisapride has not exhibited excellent response.[32] Octreotide use in treating CIPO among SSc patients has also been investigated by multiple studies, revealing marked symptom improvement, especially when combined with erythromycin.[4] CIPO usually resolves with conservative treatment, however surgical approach can be conducted as last resort, although not typically preferred due to the high rates of re-operation following the surgical intervention.[32,47] After period of bowel rest and symptoms improvement, nutritional support through enteral and eventually oral feeding can be started, along with periodic measurement and repletion of electrolytes, vitamins, and minerals.[47]

COLONIC DYSMOTILITY IN SYSTEMIC SCLEROSIS

Colonic involvement which typically manifests as constipation and diarrhea, is observed in 20–50% of SSc patients.[4] Extensive fibrosis of colonic wall and atrophy of colonic smooth muscle contributes to development of colonic hypomotility in SSc, which is commonly observed as constipation in the early course of colonic involvement.[32] SSc patients also often reported symptoms of incomplete evacuation of stool, abdominal discomfort, and hard stool which are attributed to constipation.[24] As the colonic dysmotility progresses, stasis of the colon contributes to precipitation of SIBO, which shifts symptoms of constipation to malabsorptive diarrhea.[10] Fibrosis of the lymphatic system and chronic intestinal ischemia are also attributed with development of diarrhea.[4] Coupled with fecal incontinence, which is a prevalent anorectal involvement in SSc, diarrhea is associated with decreased quality of life in SSc patients.[32]

New onset of constipation in SSc patients requires further investigation to rule out other pathologic changes such as malignancy, strictures, and diverticulosis.[4,37] Furthermore, alarming symptoms of constipation such as weight loss and rectal bleeding are often observed in SSc, which can mask the other pathologic processes.[4] Evaluation of electrolyte serum levels and avoidance of drugs contributing to constipation such as CCB and opioid should also be considered in constipation.[18] In terms of management, adequate hydration and moderate fiber supplementation are generally recommended to alleviate symptoms. However, it should be noted that fiber consumption is also associated with gastroparesis exacerbation, worsening of bloating and excessive flatulence, and precipitation of fecal impaction.[4,20] Stimulant laxatives, such as senna and bisacodyl are preferred initially, as osmotic laxative can worsen concomitant electrolyte imbalance and renal function.[4] Addition of stool softener or prokinetics with stimulant laxative can also be considered.[24,37] Constipation is generally resolved with dietary changes and pharmacological approach, but surgery might be considered in refractory cases.[32]

Evaluation of diarrheal symptoms in SSc should include additional workup to exclude other causes of diarrhea, which include infection, celiac disease, amyloidosis, and microscopic colitis.[10,32] Anti-diarrheal agent like loperamide can be prescribed to alleviate the symptom, but the risk of pseudo-obstruction with loperamide use should be adequately evaluated. Bile acid sequestrants can also be used to ameliorate steatorrhea due to fat malabsorption in SIBO.[32]

MALNUTRITION IN SYSTEMIC SCLEROSIS

Proper management of GI manifestations in SSc is essential because refractory gastroparesis, SIBO, and CIPO are highly associated with malnutrition.[18,48] Although there are multiple GI symptoms that are associated with malnutrition, studies found that poor appetite is strongly attributed to increased risk of malnutrition in SSc.[49] Other factors such as fatigue and mood disturbances, which are commonly observed in SSc patients, also contribute to the development of malnutrition and declining functional status.[11] Microstomia and xerostomia in SSc patients are also associated with poor oral intake and malnutrition, which is why routine dental evaluation for SSc patients is encouraged.[52]

Malnutrition is also found to be more prevalent in one particular subtype of SSc, diffuse SSc.[50] Furthermore, interstitial lung disease (ILD) which is commonly diagnosed in diffuse SSc, also has a strong positive correlation to malnutrition.[34,50] Other study by Yalcinkaya et al showed possible association of severe skin involvement and capillary rarefaction (reduction of vascular density) in SSc with increased risk of malnutrition and severe GI manifestation.[51]

Malnutrition affects the clinical outcome of SSc patients. The fact that malnutrition contributes to 20% of associated mortality in SSc highlights the importance of proper its early screening in order to streamline an early intervention.[6,18,34] Along with various malnutrition screening tools, routine anthropometry including body weight measurement, along with BMI calculation, and assessment of nutritional intake should also be documented at first visit and followed on subsequent visits.[52–54] American Society of Parenteral and Enteral Nutrition (ASPEN) recommended serum measurements of hemoglobin, vitamin B12, folic acid, fat-soluble vitamins, prealbumin, and albumin in SSc patients to assess deficiencies associated with nutritional impairment in SSc.[10] Patient with moderate risk of malnutrition needs to be assessed on their dietary intake for three consecutive days. If dietary intake is adequate, patient can be reassessed in 2–3 months. However, patient with high risk of malnutrition requires thorough evaluation with collaboration nutritional support team to establish nutritional repletion goals.[52]

Multiple studies with focus on SSc and malnutrition adopted various criteria to define malnutrition, which reflected the discrepancy in malnutrition prevalence among studies, which is between 8–55%.[6,9,11] Although most conducted studies utilized criteria formulated by European Society for Clinical Nutrition and Metabolism (ESPEN), a study by Rosato et al showed that by implementing the criteria of malnutrition developed by Global Leadership Initiative on Malnutrition (GLIM), malnutrition in SSc was twice as prevalent.[55] Similar findings were also reported by Wojteczek et al.[56] The use of other instruments for malnutrition diagnosis such as subjective global assessment (SGA) and simplified nutritional appetite questionnaire (SNAQ) were also documented in some studies.[56,57] Comparison of multiple instruments was scrutinized by Wojteczek et al showed that malnutrition prevalence of 17.9% through the fulfillment of the criteria formulated by ESPEN 2015, 16.1% with SNAQ, 23.2% in 7-SGA, and 62.5% with GLIM.[56]

In terms of malnutrition screening tools, many expert panels who formulated nutritional guidelines including ASPEN recommended the use of malnutrition universal screening tool (MUST) as malnutrition screening tool in all SSc patients at initial visit and it is recommended to be repeated annually afterwards.[10,56] MUST has been ubiquitously used across multiple studies and has proved to have great validity and high reproducibility rate among healthcare workers.[49] However, studies have found that risk determined with MUST had not always been accurate in every condition, especially in complex chronic inflammatory disease with prominent GI involvement like SSc.[6,49] Study from Bagnato et al showed the incidence of malnutrition in 29% of SSc patients in 12 months with none to low risk determined from MUST which prompted the formulation of a new instrument, namely predictor of malnutrition in systemic sclerosis (PREMASS) scoring system. PREMASS which can predict development of malnutrition among SSc patients has clear timeframe, which is within 12 months, with positive predictive value of 62% and negative predictive value of 97%. PREMASS assesses various indicators which have been associated with malnutrition in SSc, which include adiponectin/leptin ratio, presence of SCl-70 antibody, and forced vital capacity (FVC).[6]

Patients at risk for malnutrition whose body weight keeps declining despite supportive treatment and dietary modification should be considered for enteral nutrition.[18] Early collaboration with nutritionist that is also recommended as macronutrient and micronutrient deficiencies is common in SSc patients with GI dysmotility manifestation.[12,32] The need of prolonged enteral feeding as nutritional therapy in patients with malnutrition leads to a strong consideration for percutaneous gastrostomy or percutaneous jejunostomy, which the latter is preferred due to lower

Table 1. Evaluation of GI dysmotility in SSc

Dysmotility in SSc	Manifestations	Diagnostic modalities	Management	Special considerations
Esophagus	GERD	Empirical diagnosis GERD-Q (limited setting) Definitive diagnosis: Esophageal pH monitoring Evaluation of complication such as peptic stricture and Barret's Esophagus: Endoscopy	Lifestyle and diet Modification Empirical PPI therapy PPI + H2RA Surgical approach if refractory	1. Avoidance of CCB 2. Treat adequately to prevent ILD precipitation
	Dysphagia	Manometry	Diet modification Prokinetics	1. ECG evaluation and QTc measurement before administration (Metoclopramide) 2. Adequate GERD treatment 3. Avoidance of opioid and PDE-5 inhibitors
Gaster	Gastroparesis	Scintigraphy	Diet modification Prokinetics nutritional deficiencies replenishment G-POEM (later stage)	1. Small frequent meals and avoidance of high-fat foods 2. ECG evaluation 3. Malnutrition screening and vitamin deficiencies evaluation
Small Intestine	SIBO	Definitive diagnosis: Jejunal aspirate culture Other modality: Breath test	Cyclical antibiotics Malnutrition evaluation Fat-soluble vitamin, B12, iron evaluation	1. Role of probiotics is still controversial 2. PPI use can precipitate SIBO
	CIPO	Abdominal x-ray, CT abdomen (nonspecific findings, exclude mechanical obstruction)	Hospital admission IV hydration Bowel rest Prokinetics Octreotide	1. Electrolyte evaluation and repletion 2. Nutritional repletion
Colon	Constipation	Clinical diagnosis, but workup to exclude structural changes should be performed initially, especially in presence of alarming symptoms	Adequate hydration Stimulant laxative Bulk-forming agent Prokinetics	1. Fiber consumption should be monitored in concomitant gastroparesis 2. Regular electrolyte measurement and kidney function evaluation with stimulant laxative use
	Diarrhea	Consideration to rule out infection and other associated gut pathology	Anti-diarrheal agent Bile acid sequestrant (steatorrhea)	1. Use of anti-diarrheal agent should be monitored to prevent precipitation of bowel obstruction

GERD: gastroesophageal reflux disease; GERD-Q: GERD questionnaire; CCB: calcium channel blocker; ILD: interstitial lung disease; PPI: proton-pump inhibitor; ECG: electrocardiogram; SIBO: small intestinal bacterial overgrowth; CIPO: chronic intestinal pseudo-obstruction; CT: computerized tomography

risk of aspiration.[10,52] In cases of refractory nutritional improvement, the adoption of parenteral nutrition approach should be instituted and monitored closely by multidisciplinary team due to the high risk of catheter-related sepsis and thrombosis.[4,52]

CONCLUSION

Manifestations of gastrointestinal dysmotility in systemic sclerosis can lead to the development of malnutrition, which affects a multitude of clinical outcomes in systemic sclerosis patients. Adequate management of gastrointestinal dysmotility, coupled with collaborative efforts with nutritionist and routine utilization of malnutrition screening tools should be implemented and integrated into the standardized care of systemic sclerosis patients to prevent the ensuing of malnutrition in the course of systemic sclerosis.

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