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Research Article

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# Malabsorption Syndromes' Influence on Chronic Wound Healing in Patients with Gastrointestinal Resection

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## Introduction

A gastrointestinal resection is a procedure where part of the gastrointestinal tract is removed. In patients with gastrointestinal stromal tumors, resections are performed when there are signs of bleeding, necrosis, heterogeneous echogenicity, and ulceration [1]. For Crohn's disease patients, treatment is required if complications appear such as perforation, persisting or recurrent obstruction, abscess, dysplasia, cancer, or intractable hemorrhage [2]. Moreover, patients with upper gastrointestinal cancers may have adenocarcinoma, adenoma, or lymphoma [3]. In a meta-analysis observing ulcerative colitis (UC) and crohn's disease (CD) patients, the 5-year cumulative risks of colectomy in UC patients was approximately 7% and the risk of surgery in CD patients was around 18% [4]. According to the American College of Surgeons National Surgery Quality Improvement Program (ACS-NSQIP), colectomy and small intestine resection pose risks to patients due to the high morbidity and mortality rates [5]. Patients who have undergone gastrointestinal resection are at risk of short and long term outcomes. Notably, short term outcomes include anastomotic leakage, infections, and reoperations [6]. In addition, long term outcomes include diarrhea, appetite loss, bowel dysfunctions and eating restrictions, significantly affecting quality of life [7].

Loss of absorptive surface area in the gastrointestinal tract will reduce nutrient absorption. The American Gastroenterological Association states certain areas lost in the intestine can lead to vitamin B12 deficiency or fat malabsorption [8]. Furthemore, the disruption of tight junction proteins like claudin-2 and claudin 15 will disrupt glucose absorption [9]. In patients who have undergone a total gastrectomy or extensive small bowel resection will have the highest nutritional risk. Patients that underwent Total gastrectomy will experience lean body mass loss, overall weight loss, and micronutrient deficiencies [10]. Similarly, patients who have had Extensive small bowel resection will experience short bowel syndrome and will need long term-parenteral nutrition [11]. This reliance on nutritional delivery will negatively impact the patient's quality of life. With the progression of surgical techniques and postoperative medical treatment, the long term survival rate of patients has increased, however, the long-term complications from the surgeries have a higher likelihood of posing risks. Certain conditions from the surgeries can arise, such as exocrine pancreatic insufficiency (EPI), bile acid malabsorption (BAM), and small intestinal bacterial overgrowth (SIBO) [12]. Although patients are surviving longer, these factors significantly decrease their ability to live a balanced day-to-day life.

A crucial consequence of malnutrition is the weakening of the immune response, which will reduce the body's ability to fight infections and increase the risk of postoperative complications like an intra-abdominal abscess [13]. Malnutrition will affect the body's ability to produce collagen, causing delayed wound healing [14]. A consequence of malnutrition in these patients results in longer hospital stays [15]. In patients who underwent rectal cancer surgery, malnutrition was linked to a higher 30-day mortality rate and other complications [15]. As discussed prior, malnutrition can impair wound healing and collagen synthesis. Immunonutrition can enhance phagocytic activity, which will increase the number of T-helper cells, which is vital for immune surveillance [16]. The objective of this systematic review is to analyze evidence linking chronic wound healing to malabsorption. The review will examine how physiological issues impact wound healing and the potential therapeutic treatments. Understanding the relationship between malabsorption and wound healing will provide strategies on better post operative care and improved healing outcomes in patients who have undergone gastrointestinal resection.

## Methodology

This narrative literature review was conducted to integrate current knowledge and outlooks related to malabsorption, wound healing, and gastrointestinal resection. An extensive search of peer-reviewed literature was conducted using the following databases: PubMed, Scopus, Web of Science, and the Cochrane Library, in order to identify relevant studies on malabsorption, wound healing, and gastrointestinal resection.

The search strategy encompassed combinations of relevant keywords, such as "malabsorption," "gastrointestinal resection," "wound healing," "nutritional deficiency," and "postoperative complications." Studies published in English and within the last thirty years were prioritized to maintain relevance and reflect current understanding. However, seminal or highly cited older studies were included when appropriate.

Inclusion criteria comprised studies that focused on human subjects and employed rigorous methodologies, such as randomized controlled trials (RCTs), systematic reviews, and meta-analyses. Studies with these methodologies were prioritized. Additionally, studies discussing malabsorption, wound healing, and gastrointestinal resection were also emphasized. Exclusion criteria for the search included non-English studies and non-peer-reviewed articles and publications, opinion pieces, case reports (except those incorporated within larger studies), conference abstracts without full data, articles lacking scientific rigor or relevance to the review focus, and animal studies, besides those that directly compared findings to current human data.

Data extraction focused on study design, patient characteristics and demographics, approaches to nutritional assessment, wound healing outcomes (such as time to closure, infection rates, and scar formation) and interventions (including dietary changes, nutritional supplementation, and enteral or parenteral nutrition). The quality of evidence was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework.

To refine the search, a Boolean strategy was employed incorporating combinations of keywords derived from the research focus. Terms such as *"malabsorption syndrome," "gastrointestinal resection," "chronic wound healing,"* and *"postoperative complications"* were combined with nutritional-related terms including *"nutritional deficiency," "micronutrient deficiency," "zinc deficiency," "vitamin A,"* and *"vitamin C."* Additional keywords included *"collagen synthesis," "angiogenesis," "immune function," "enteral nutrition," "parenteral nutrition," "nutritional supplementation," "arginine," "glutamine,"* and *"hydroxymethylbutyrate (HMB)."* Terms related to specific clinical contexts, such as *"surgical wound healing," "inflammatory bowel disease,"* and *"malnutrition,"* were also incorporated into the search. Boolean operators (AND, OR) were used to combine terms and narrow results to studies specifically addressing both malabsorption and wound healing mechanisms or outcomes.

The quality of studies was assessed with priority given to study design, ranking randomized controlled trials (RCTs) highest, followed by cohort studies and case reports. Literature was thematically organized and critically examined to identify key patterns in nutritional deficiencies, wound healing mechanisms, and postoperative outcomes. Rather than providing a comprehensive systematic review, this narrative synthesis aims to interpret the most impactful findings that contribute to current understanding of malabsorption, wound healing, and gastrointestinal resection, while also highlighting knowledge gaps and emerging concepts.

## Pathophysiology and Mechanisms: How Malabsorption Impairs Wound Healing

Individuals who have undergone gastrointestinal resection, whether it be for disease, a malignant tumor, or a benign condition, face an increased risk of nutritional deficiencies depending on the location of anatomical loss. Resection of the duodenum, for instance, which is the primary site of absorption of iron and fat-soluble vitamins, can lead to deficiencies in these nutrients [17]. Patients undergoing weight-loss surgical procedures also run the risk of nutritional deficiencies. Though multiple types of weight-loss surgeries exist, malabsorptive types bypass portions of the small intestine essential for nutrient absorption, raising the risk for nutritional deficiencies [20]. Gasmi et al (2022) further describe how undigested food entering the ileum suppresses pancreatic secretion, increasing malabsorption. Nutritional deficiencies can manifest as a range of clinical presentations. Deficiencies in vitamin C or zinc, for example, can lead to impaired wound healing [20]. The onset of nutritional deficiencies following gastrointestinal resection or weight-loss surgeries, along with the adverse consequences, highlights the importance for patient monitoring and appropriate supplementation post-procedure.

Patients with an underlying disease, such as irritable bowel disease (IBD) or malignancy, are more likely to experience worsened nutritional outcomes following gastrointestinal resection. Prior to surgery, individuals with IBD or malignancy often present with a combination of malnutrition, immunosuppression, and systemic inflammation [18, 19]. In malignancy, malnutrition may arise from reduced appetite, gastrointestinal function, or nutrient absorption. When coupled with inflammation, this may lead to cachexia, a syndrome characterized by metabolic wasting and muscle imbalance [19]. Surgical intervention may exacerbate these pre-existing issues, further compromising the immune response and delaying wound healing. These factors should be considered when assessing the patient before their procedure, as early intervention may help to enhance outcomes.

Malnutrition affects both collagen synthesis and tissue repair by disrupting the absorption nutrients required for the production and stabilization of collagen fibers. Collagen, an essential structural protein, is made up of glycine, proline, and hydroxyproline [21, 22]. The formation of this triple-helix protein depends on various cofactors, including vitamins A, C, and essential minerals like iron and zinc [22]. Consequently, deficiencies in any of these nutrients can hinder collagen formation and compromise the structural integrity of tissues. Vitamin C in particular has an important role as a cofactor for the hydroxylation of lysine and proline to hydroxylysine and hydroxyproline, two proteins that enhance the stability of collagen through cross-linking [26]. Further, vitamin A inhibits collagenase [26], preventing the breakdown of collagen. Without adequate levels of these nutrients, the body's ability to synthesize collagen is compromised.

Proteins are broken down into essential amino acids for tissue growth, repair and maintenance, as well as maintaining intravascular oncotic pressure [26]. Sufficient protein intake is, therefore, essential for effective wound healing and fluid homeostasis, preventing pathological conditions such as edema. Protein provides amino acids for collagen synthesis, an important component in the formation of granulation tissue, a temporary, highly vascular tissue involved in tissue repair [22].

Therefore, protein deficiency can impair granulation tissue formation, leading to delayed healing. That being said, it is important to note that the utilization of certain proteins requires other nutrients as cofactors [26]. This should be considered when assessing a patient's nutritional status to determine whether protein deficiency is the primary issue or a deficiency in another nutrient is impairing the healing process.

Deficiencies in vitamin A, iron, and zinc impact angiogenesis, whether that is inhibiting or promoting the process. Vitamin A is known to promote angiogenesis and epidermal proliferation [23, 26]. Although a deficiency in vitamin A may impair angiogenesis, a zinc deficiency may produce symptoms that closely resemble a vitamin A deficiency. Zinc is required for the synthesis of the transport proteins for vitamin A absorption, as well as the vitamin A metabolic pathway [26]. Additionally, zinc itself has a direct role in angiogenesis by stimulating the production of vascular endothelial growth factor (VEGF) [24]. While vitamin A and zinc support angiogenesis, it is iron deficiency that promotes this process. Iron is required for hemoglobin synthesis and delivery of oxygen to the tissues, and its deficiency can result in tissue hypoxia [26]. Several mechanisms have been proposed to explain how iron impacts angiogenesis. Iron deficiency stabilizes hypoxia-inducible factor 1-alpha (HIF-1α), supporting the transcription VEGF [24, 25]. Similarly, excess iron generates reactive oxygen species, which also increase HIF-1α levels [25]. The pro-angiogenic effects of micronutrients are complex and can be influenced by both deficiencies and excesses, highlighting the importance of balanced nutrient levels in regulating angiogenesis.

Malnutrition significantly impairs cellular immunity and the inflammatory response, both of which are important for wound healing. Deficiencies in essential nutrients disrupts immune cell function. As a result, the inflammatory response is diminished, impairing the recruitment of immune cells and weakening the overall immune defense. Vitamin A plays an important role in immune modulation by promoting cytokine production, supporting B- and T-cell maturation, and enhancing macrophage and NK cell activity [27]. Additionally,vitamin A promotes the regeneration of mucosal epithelial cells [27]. A deficiency in vitamin A will lead to a depressed innate and adaptive immune response. Vitamin C is an essential antioxidant that neutralizes reactive oxygen species, downregulates pro-inflammatory cytokines, and suppresses activation of the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signaling pathway, a central regulator of inflammation, with zinc acting in a similar anti-inflammatory manner [27]. Because essential nutritional deficiencies have a profound impact on the immune response, it is important to address said deficiencies to optimize a patient's outcome. Ensuring proper nutrition supports immune function and enhances the body's ability to repair and regenerate tissue.

## Factors Influencing the Severity of Malabsorption

Different nutrients are absorbed into the bloodstream at different segments of the GI tract. Most absorption of macronutrients (proteins, carbohydrates, and lipids) occurs in the small intestine, while the colon absorbs water and electrolytes. Starting proximally, the mouth, esophagus, and stomach are involved in food digestion rather than absorption. The gastric parietal cells of the stomach fundus and body produce intrinsic factor, which binds to cobalamin (B12), allowing for B12 absorption in the terminal ileum of the small intestine [28]. Moving distally, the duodenum is the first segment of the small intestine and the first site of absorption for several vitamins and minerals. These include iron, calcium, phosphorus, magnesium, copper, selenium, thiamin B1, riboflavin B2, niacin B3, biotin B7, folate B9, and the fat-soluble vitamins A, D, and E, and K. The jejunum is the second segment of the small intestine. In addition to the water and fat-soluble vitamins, iron, and calcium absorbed by the duodenum, the jejunum also absorbs pantothenic acid B5, pyridoxine B6, ascorbic acid C, zinc, and macronutrients: lipids, monosaccharides, and small peptides. The ileum is the terminal segment of the small intestine. Like the other segments, the ileum absorbs magnesium and vitamins B9, C, K and D. The ileum is the only segment that absorbs vitamin B12 and bile salts and acids [29]. Finally, the large intestine absorbs water, electrolytes, vitamins, and short-chain fatty acids. Potassium, sodium, and chloride are transported across the colonic lumen, creating an osmotic gradient that brings water into the bloodstream as well. Additionally, colonic bacteria produce vitamin K and B vitamins that are absorbed in the colon [30].

Different resection types correlate with deficiencies in the nutrients absorbed by the resected GI segments. These include vitamin deficiencies, mineral deficiencies, and malnutrition. For example, duodenal resection without supplementation can result in iron deficiency, hypocalcemia, fat-soluble vitamin deficiency, and deficiencies in vitamins B1, B9, and B12 [31]. However, small intestinal resection does not always result in nutrient deficiencies. There is overlap in the nutrients absorbed by the three segments, and the remaining intestines compensate for the resected segment through small bowel adaptation to increase the absorptive surface [32]. Therefore, resection length is an important prognostic factor, as the absorptive capacity of the small intestine is preserved in patients with over 50% left. If the resection is extensive, patients will suffer from fat and carbohydrate malabsorption and depend on parenteral nutrition [31]. As mentioned previously, the malabsorptive state caused by extensive GI resection is referred to as short bowel syndrome. Since bile salts and vitamin B12 are absorbed exclusively in the terminal ileum, resection of >60cm of this segment will cause B12 deficiency and bile salt malabsorption [33]. Colonic resection does not greatly impair nutrient absorption, but it does cause chronic salt and water losses [34].

Individuals with preexisting conditions such as Inflammatory Bowel Disease (IBD) and cancer cachexia are at an increased risk of becoming malnourished. IBD patients often have decreased oral food intake, increased GI losses, and malabsorption secondary to mucosal damage. IBD patients experience nausea and abdominal pain, leading to appetite loss [35]. Additionally, mucosal damage impairs the transport of nutrients, fluid, and electrolytes across the intestinal lumen, leading to malabsorption and diarrhea [36]. Cancer cachexia also contributes to malnutrition by reduced oral intake, increased metabolism, and inflammation. Both systemic tumor effects and cancer treatment such as chemotherapy can cause nausea, vomiting, and pain, leading to decreased oral intake [37]. However, the malnutrition observed in cancer cachexia is mostly due to tumor-derived factors, hormones, and inflammatory cytokines increasing metabolic demand [38].

The main comorbid conditions affecting malabsorption include GI disorders, pancreatic disease, liver disease, heart failure, diabetes, cancer, and chronic infections. In addition to IBD and short bowel syndrome discussed above, celiac disease also causes malabsorption because immune-mediated damage to the villi reduces the absorptive surface of the small intestines [39]. Patients with chronic pancreatitis produce less pancreatic lipase, so they suffer from fat maldigestion and fat-soluble vitamin deficiencies [39]. Liver disease such as cirrhosis causes reduced bile salt synthesis, and bile duct damage or obstruction impairs secretion of bile salts, which also cause fat maldigestion and fat-soluble vitamin deficiencies [36]. Chronic heart failure leads to splanchnic venous congestion and intestinal hypoperfusion, which cause malabsorption and contribute to cardiac cachexia [40]. Diabetes can cause gastroparesis, which slows gastric transit, causing Small Intestinal Bacterial Overgrowth (SIBO). Food stagnation leads to an overgrowth of bacteria $>10^5$ colony forming units (cfu)/mL of bacteria in the proximal small intestine. These bacteria break down bile salts, causing fat malabsorption [41]. Cancer contributes to malnutrition as discussed above, and GI cancers in particular can cause malabsorption by damaging the intestinal lining. Lastly, GI infections that cause malabsorption include Tropical sprue, Whipple's disease, Giardiasis, and *H. pylori* duodenitis [36].

Malabsorption is more common in the elderly than the younger age groups, although the mechanisms causing malabsorption are different. Digestive enzyme production is mostly preserved with age, and aging alone does not significantly decrease pancreatic, biliary, or intestinal function [42]. However, comorbid conditions such as heart failure, diabetes, and cancer are more common in the elderly population. Additionally, the elderly are more likely to be on medications that affect GI transit such as opioids, PPIs, and calcium channel blockers. SIBO secondary to slowed GI transit is a common cause of malabsorption in this population [43]. In the young, malabsorption is typically secondary to congenital or early-onset conditions such as cystic fibrosis, celiac disease, or lactase deficiency.

Finally, a strong baseline nutritional status protects against the effects of malabsorption by delaying malnutrition. Individuals with sufficient stores of macro and micronutrients can better tolerate nutrient losses from temporary malabsorption [44]. They also have improved immune function and enhanced GI tract tissue integrity. Alternatively, patients with poor baseline nutritional status suffer from a negative feedback loop that leads to persistent malnutrition. Deficiencies in vitamins A, D, C, E, B6, and B12 as well as folate, zinc, iron, copper, and selenium have been shown to impair immune cell function and decrease antibody production [45, 46].

## Assessment of Nutritional Status in Postoperative Patients

An abundance of nutritional screening and assessment tools have been utilized to evaluate nutritional risk, however, there is still no consensus on the most recommended [47]. A few of the most used nutritional screening tools include the Nutritional Risk Screening 2002 (NRS-2002), Subjective Global Assessment (SGA), and Mini Nutritional Assessment (MNA). Each of these examples is implemented in their unique setting and patient population. The NRS-2002 is most often utilized in the inpatient setting to identify patients who are at risk of malnutrition. Nutritional risk screening using the NRS-2002 has been assessed and validated in hundreds of studies, strongly correlates with complications, and is reliable [47, 48]. On the other hand, SGA is used in many different settings within a hospital clinical practice and combines a medical history review with a physical examination. SGA is unique in that it includes subjective evaluations, which can be useful in certain instances. However, it does not account for biochemical values, and its sensitivity, precision, and reproducibility have not been extensively proven [48]. Lastly, MNA is often used with geriatric patients and includes diverse components (loss of appetite, altered sense of taste and smell, loss of thirst, frailty, depression) in addition to anthropometric measurements, nutritional habits, general condition, and self-evaluation. A study published by Raslan et al. (2010) evaluated the ability of the NRS-2002 and MNA to predict unfavorable clinical outcomes (e.g., complications, very long hospital stays, and death). They reported similar performance in predicting negative clinical outcomes between the two, but NRS-2002 seemed to provide the best yield [49]. This demonstrates the effectiveness of both tools, however, the NRS-2002 appears to have a better performance compared to MNA. Nutritional screening is crucial to identify patients at risk and should be performed in a systematic way using the most appropriate tool for the setting and patient.

The timing of screening is an important consideration so that appropriate interventions can be administered promptly. Most studies recommend screening patients preoperatively. For instance, patients undergoing gastrointestinal surgery should be screened at least ten days before the procedure due to research findings of how malnutrition significantly impacts surgical outcomes [50]. Benoist et al. (2015) found that there is a 20% reduction in postoperative morbidity when preoperative nutritional management occurs. In addition, there is evidence that preoperative screening can predict postoperative complications. A 2023 prospective study with 126 patients who underwent general and gastrointestinal surgery demonstrated that preoperative nutritional risk was associated with a greater development of complications and length of stay [51]. Thus, early screening in the preoperative period is essential to lower the risk of morbidity and mortality postoperatively.

Risk stratification is utilized so that interventions can be prioritized for patients in most need of care. This consists of categorizing individuals into nutritional groups based on their level of nutritional risk. Four nutritional groups can be established based on the presence of malnourishment, the presence of risk factors for malnutrition, and whether the planned surgical intervention is at a high risk of morbidity [50]. Group I contains non-malnourished patients, AND no risk factor for malnutrition, AND surgery not at high risk of morbidity; Group II contains non-malnourished patients, AND at least one risk factor of malnutrition present, OR surgery at high risk of morbidity; Group III contains malnourished patients AND surgery not at high risk of morbidity; Group IV contains malnourished patients AND surgery at high risk of morbidity [50]. By categorizing individuals into these four nutritional groups, it enables a more efficient use of resources and a prioritization of correct interventions. Ultimately, those at most risk for malnutrition in terms of present status, risk factors, and surgical procedures should be prioritized for interventions.

Biomarkers such as albumin, prealbumin, transferrin, and serum zinc are frequently used in the assessment of nutritional status. Most studies report concerns regarding their reliability, especially in states of starvation [52], anorexia nervosa [53], and

in the functionally impaired elderly [54], however, they continue to be used. The capacity of each biomarker to reflect nutritional status can be influenced by their half-lives and certain environments. The half-lives of albumin and prealbumin have an impact on the evaluation of long-term and short-term nutritional status. For example, albumin has a half-life of approximately 20 days, while prealbumin has a half-life of two to three days. Given the differences, the shorter half-life of prealbumin makes it a better indicator of acute changes in nutritional status [55]. Additionally, there is controversy surrounding the use of transferrin as a marker for nutritional status. Some studies have found transferrin useful, while others have not as their levels are influenced by iron status [55]. Lastly, serum zinc is useful in many enzymatic reactions and immune functions. Although serum zinc may be used to evaluate nutritional status, it is not as often utilized, as albumin and prealbumin are more widely used [56]. Albumin, prealbumin, transferrin, and serum zinc can all be utilized to assess nutritional status but need to be evaluated with an understanding of their limitations.

Albumin, prealbumin, and transferrin are negative acute-phase proteins, which means their levels are influenced by inflammatory states and physiological dysfunction. This directly alters their dependability as a diagnostic test, as decreased levels may not be secondary to malnutrition, rather, certain inflammatory states. For instance, albumin exhibits decreased levels in states of infection, burns, fluid overload, hepatic failure, cancer, and nephrotic syndrome [56]. Prealbumin shows decreased levels in renal dysfunction, corticosteroid therapy, physiological stress, infection, and liver dysfunction [56]. Transferrin levels are influenced by liver disease, fluid status, stress, and illness [56]. Given the circumstances that can influence levels of these biomarkers, it brings about reliability concerns during inflammatory states. In addition, the role of zinc in immune function can lead to a decrease in levels during inflammation [57]. This has the potential to lead to inaccuracies in the diagnosis of malnutrition if biomarker levels are evaluated during an inflammatory state. Due to this, the interpretation of these biomarkers must be performed cautiously in the context of inflammation and acute-phase response.

The major consensus throughout the literature is that albumin, prealbumin, transferrin, and serum zinc are not reliable on their own, but should be used as a complement to medical history and physical examination [56]. This is where the utilization of the Subjective Global Assessment (SGA) is useful as it allows clinicians to evaluate for changes in subcutaneous fat, overall body muscle mass, muscle strength, and overall functional status. For instance, in a prospective study of 154 patients with esophageal cancer, the physical examination was the only tool that strongly correlated with malnutrition [56]. This highlights the importance of physical examination in diagnosing malnutrition because it allows clinicians to detect subtle presentations that may not be revealed in lab tests. Ultimately, biomarkers may provide insight into the nutritional status of a patient, however, physical examination is a better tool for diagnosing malnutrition post-GI resection.

## Nutritional Interventions and Their Impact on Wound Healing

Supplements such as arginine, glutamine, vitamin C, and zinc, primarily used in combination, show good clinical results in patients with wounds or those predisposed to such skin lesions [58].

Proteins are directly involved in the tissue repair process and cellular renewal. Nitrogen must be properly regulated through increased protein synthesis. Protein deficiency is associated with impaired wound healing and a higher rate of complications. In this context, arginine either alone or in combination with antioxidants, as well as enteral therapy for the treatment of pressure ulcers, accelerates the healing process and reduces the length of hospital stay. Furthermore, it is also associated with a reduction in the area and depth of the lesion [59].

Vitamin C is associated with collagen synthesis and the reduction of reactive oxygen species. It also contributes to calcium metabolism and the immune response. Its deficiency leads not only to wound complications but also to the formation of abnormal scars [58].

Zinc plays an important role in wound healing. When used topically, it acts as an antiseptic and anti-inflammatory agent. Zinc oxide at 1% increases mitotic rates and re-epithelialization [60].

Nutrient supplementation is recommended after intestinal resection, especially for oncologic patients. Thus, oral diet supplementation becomes necessary to achieve an adequate amount of nutrients in both the immediate postoperative period and in the long term. Enteral or parenteral nutrition is recommended if oral diet supplementation alone becomes insufficient, as the diet will be adapted depending on the individual case and each surgery's tolerance [61].

The implementation of this treatment plan within 24 hours after surgery has been shown to improve intestinal motility, stimulate protein synthesis, and maintain muscle function. In postoperative ileus, early enteral feeding reduces infection rates and shortens the length of hospital stay. In contrast, in upper gastrointestinal tract surgeries, oral nutrition is delayed due to the risk of complications such as aspiration pneumonia. Therefore, it is important to understand that enteral nutrition is often preferred due to the higher protein availability and shorter healing time, especially in extensive surgeries [61].

In addition to the aforementioned benefits, there are noticeable improvements directly related to skin wound healing, such as increased collagen synthesis, enhanced immune response, and a reduction in both the size and depth of skin lesions [60].

Systematic reviews [59], scoping review [60] and review articles [58, 61] have compared nutritional supplementation with no supplementation, as well as diets rich in sugars and fats. As a result, it is possible to observe a lower reabsorption of essential nutrients and a decrease in the immune response in these cases. These are essential factors for a better prognosis in patients with skin lesions and show a significant difference in response to the proposed treatment.

## Discussion and Future Directions

MS is highly prevalent in patients post gastrointestinal resection and this may directly affect wound healing as patients would experience deficiencies in nutrients and minerals essential for the healing process. These deficiencies disrupt collagen synthesis, angiogenesis, and immune functions of the body. Current studies support that adequate nutrition is essential for wound healing as it necessitates proficiency in cellular activities, including the production of nucleic acids, proteins, and other elements needed in the development and differentiation of functional tissue [58, 62].

The studies reviewed had several limitations including small sample sizes that reduced statistical power and significant potential for confounding variables in the samples such as age, sex, race, and socioeconomic status that limited the ability to draw causal interpretations. The use of different methodologies and inconsistencies in MS diagnostic and measurement criteria across studies contributes to additional biases. Differences in the type and location of patients' gastrointestinal resection procedures as well as their dietary restrictions following the procedure could also lead to varying degrees of nutritional deficiency, making it difficult to compare outcomes across studies.

To address current limitations, future research should include more randomized clinical trials and longitudinal studies to assess the impact of MS and possible nutrition interventions on wound healing. Additionally, it is necessary to introduce standardized nutritional assessment methods to improve comparability across studies [63].

To optimize wound healing in patients with MS following GI resection, individualized nutritional plans may be integrated into surgical recovery. The involvement of dietitians, surgeons, and gastroenterologists in the nutritional management of patients may play a significant role for timely intervention for deficiencies that impair healing. Embedding proactive nutritional strategies into surgical care would reduce complications and enhance wound healing [58].

## References

1. Koo, D. H., Ryu, M. H., Kim, K. M., Yang, H. K., Sawaki, A., Hirota, S., Zheng, J., Zhang, B., Tzen, C. Y., Yeh, C. N., Nishida, T., Shen, L., Chen, L. T., & Kang, Y. K. (2016). Asian Consensus Guidelines for the Diagnosis and Management of Gastrointestinal Stromal Tumor. *Cancer research and treatment*, *48*(4), 1155–1166. https://doi.org/10.4143/crt.2016.187
2. Lichtenstein, G. R., Loftus, E. V., Isaacs, K. L., Regueiro, M. D., Gerson, L. B., & Sands, B. E. (2018). ACG Clinical Guideline: Management of Crohn's Disease in Adults. *The American journal of gastroenterology*, *113*(4), 481–517. https://doi.org/10.1038/ajg.2018.27
3. Dorcaratto, D., Heneghan, H. M., Fiore, B., Awan, F., Maguire, D., Geoghegan, J., Conlon, K., & Hoti, E. (2015). Segmental duodenal resection: indications, surgical techniques and postoperative outcomes. *Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract*, *19*(4), 736–742. https://doi.org/10.1007/s11605-015-2744-0
4. Tsai, L., Ma, C., Dulai, P. S., Prokop, L. J., Eisenstein, S., Ramamoorthy, S. L., Feagan, B. G., Jairath, V., Sandborn, W. J., & Singh, S. (2021). Contemporary Risk of Surgery in Patients with Ulcerative Colitis and Crohn's Disease: A Meta-Analysis of Population-Based Cohorts. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, *19*(10), 2031–2045.e11. https://doi.org/10.1016/j.cgh.2020.10.039
5. Schilling, P. L., Dimick, J. B., & Birkmeyer, J. D. (2008). Prioritizing quality improvement in general surgery. *Journal of the American College of Surgeons*, *207*(5), 698–704. https://doi.org/10.1016/j.jamcollsurg.2008.06.138
6. Singh, B., Fisher, O. M., Singh, G., Lansom, J., Bock, M., Kozman, M., Alzahrani, N., Liauw, W., & Morris, D. L. (2019). Short- and Long-Term Outcomes of Patients Requiring Gastrectomy During Cytoreductive Surgery and Intraperitoneal Chemotherapy for Lower-Gastrointestinal Malignancies: A Propensity Score-Matched Analysis. *Annals of surgical oncology*, *26*(11), 3627–3635. https://doi.org/10.1245/s10434-019-07510-9
7. Van Erning, F. N., Nieuwenhuijzen, G. A. P., van Laarhoven, H. W. M., Rosman, C., Gisbertz, S. S., Heisterkamp, J., Lagarde, S. M., Slingerland, M., van den Berg, J. W., Kouwenhoven, E. A., Verhoeven, R. H. A., & Vissers, P. A. J. (2023). Gastrointestinal Symptoms After Resection of Esophagogastric Cancer: A Longitudinal Study on Their Incidence and Impact on Patient-Reported Outcomes. *Annals of surgical oncology*, *30*(13), 8203–8215. https://doi.org/10.1245/s10434-023-13952-z
8. Iyer, K., DiBaise, J. K., & Rubio-Tapia, A. (2022). AGA Clinical Practice Update on Management of Short Bowel Syndrome: Expert Review. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*, *20*(10), 2185–2194.e2. https://doi.org/10.1016/j.cgh.2022.05.032
9. Wada, M., Tamura, A., Takahashi, N., & Tsukita, S. (2013). Loss of claudins 2 and 15 from mice causes defects in paracellular Na+ flow and nutrient transport in gut and leads to death from malnutrition. *Gastroenterology*, *144*(2), 369–380. https://doi.org/10.1053/j.gastro.2012.10.035
10. Aoyama, T., Sato, T., Segami, K., Maezawa, Y., Kano, K., Kawabe, T., Fujikawa, H., Hayashi, T., Yamada, T., Tsuchida, K., Yukawa, N., Oshima, T., Rino, Y., Masuda, M., Ogata, T., Cho, H., & Yoshikawa, T. (2016). Risk Factors for the Loss of Lean Body Mass After Gastrectomy for Gastric Cancer. *Annals of surgical oncology*, *23*(6), 1963–1970. https://doi.org/10.1245/s10434-015-5080-4
11. Carbonnel, F., Cosnes, J., Chevret, S., Beaugerie, L., Ngô, Y., Malafosse, M., Parc, R., Le Quintrec, Y., & Gendre, J. P. (1996). The role of anatomic factors in nutritional autonomy after extensive small bowel resection. *JPEN. Journal of parenteral and enteral nutrition*, *20*(4), 275–280. https://doi.org/10.1177/0148607196020004275
12. Khaw, R. A., Nevins, E. J., & Phillips, A. W. (2022). Incidence, Diagnosis and Management of Malabsorption Following Oesophagectomy: a Systematic Review. *Journal of gastrointestinal surgery: official journal of the Society for Surgery of the Alimentary Tract*, *26*(8), 1781–1790. https://doi.org/10.1007/s11605-022-05323-y
13. Hashash, J. G., Elkins, J., Lewis, J. D., & Binion, D. G. (2024). AGA Clinical Practice Update on Diet and Nutritional Therapies in Patients with Inflammatory Bowel Disease: Expert Review. *Gastroenterology*, *166*(3), 521–532. https://doi.org/10.1053/j.gastro.2023.11.303

14. Munoz, N., Litchford, M., & Cereda, E. (2022). Nutrition and Wound Care. *Physical medicine and rehabilitation clinics of North America*, *33*(4), 811–822. https://doi.org/10.1016/j.pmr.2022.06.007
15. Wolf, J. H., Ahuja, V., D'Adamo, C. R., Coleman, J., Katlic, M., & Blumberg, D. (2020). Preoperative Nutritional Status Predicts Major Morbidity After Primary Rectal Cancer Resection. *The Journal of surgical research*, *255*, 325–331. https://doi.org/10.1016/j.jss.2020.05.081
16. Suzuki, D., Furukawa, K., Kimura, F., Shimizu, H., Yoshidome, H., Ohtsuka, M., Kato, A., Yoshitomi, H., & Miyazaki, M. (2010). Effects of perioperative immunonutrition on cell-mediated immunity, T helper type 1 (Th1)/Th2 differentiation, and Th17 response after pancreaticoduodenectomy. *Surgery*, *148*(3), 573–581. https://doi.org/10.1016/j.surg.2010.01.017
17. Utrilla Fornals, A., Costas-Batlle, C., Medlin, S., Menjón-Lajusticia, E., Cisneros-González, J., Saura-Carmona, P., & Montoro-Huguet, M. A. (2024). Metabolic and Nutritional Issues after Lower Digestive Tract Surgery: The Important Role of the Dietitian in a Multidisciplinary Setting. *Nutrients*, *16*(2), 246. https://doi.org/10.3390/nu16020246
18. D'Andrea, A. P., Khetan, P., Miller, R., Sylla, P., & Divino, C. M. (2020). Outcomes After Bowel Resection for Inflammatory Bowel Disease in the Era of Surgical Care Bundles and Enhanced Recovery. Journal of Gastrointestinal Surgery, 24(1), 123–131. https://doi.org/10.1007/s11605-019-04362-2
19. Arends, J. (2024). Malnutrition in cancer patients: Causes, consequences and treatment options. *European Journal of Surgical Oncology*, *50*(5), 107074. https://doi.org/10.1016/j.ejso.2023.107074
20. Gasmi, A., Bjørklund, G., Mujawdiya, P. K., Semenova, Y., Peana, M., Dosa, A., Piscopo, S., Gasmi Benahmed, A., & Costea, D. O. (2022). Micronutrients deficiencies in patients after bariatric surgery. *European Journal of Nutrition*, *61*(1), 55–67. https://doi.org/10.1007/s00394-021-02619-8
21. Guo, S., & DiPietro, L. A. (2010). Factors Affecting Wound Healing. *Journal of Dental Research*, *89*(3), 219–229. https://doi.org/10.1177/0022034509359125
22. Chu, A. S., Delmore, B., & Chiu, E. S. (2024). High-Quality Dietary Protein: The Key to Healthy Granulation Tissue. *Advances in Skin & Wound Care*, *37*(10), 520. https://doi.org/10.1097/ASW.0000000000000210
23. Zinder, R., Cooley, R., Vlad, L. G., & Molnar, J. A. (2019). Vitamin A and Wound Healing. *Nutrition in clinical practice: official publication of the American Society for Parenteral and Enteral Nutrition*, *34*(6), 839–849. https://doi.org/10.1002/ncp.10420
24. Dürig, J., Calcagni, M., & Buschmann, J. (2023). Transition metals in angiogenesis – A narrative review. *Materials Today Bio*, *22*, 100757. https://doi.org/10.1016/j.mtbio.2023.100757
25. Saghiri, M. A., Asatourian, A., Orangi, J., Sorenson, C. M., & Sheibani, N. (2015). Functional role of inorganic trace elements in angiogenesis—Part I: N, Fe, Se, P, Au, and Ca. *Critical Reviews in Oncology/Hematology*, *96*(1), 129–142. https://doi.org/10.1016/j.critrevonc.2015.05.010
26. Grada, A., & Phillips, T. J. (2022). Nutrition and cutaneous wound healing. *Clinics in Dermatology*, *40*(2), 103–113. https://doi.org/10.1016/j.clindermatol.2021.10.002
27. Munteanu, C., & Schwartz, B. (2022). The relationship between nutrition and the immune system. *Frontiers in Nutrition*, *9*. https://doi.org/10.3389/fnut.2022.1082500
28. Ogobuiro I, Gonzales J, Shumway KR, et al. Physiology, Gastrointestinal. [Updated 2023 Apr 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537103/
29. Basile EJ, Launico MV, Sheer AJ. Physiology, Nutrient Absorption. [Updated 2023 Oct 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK597379/
30. Azzouz LL, Sharma S. Physiology, Large Intestine. [Updated 2023 Jul 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK507857/
31. Gorospe, E. C., & Oxentenko, A. S. (2012). Nutritional consequences of chronic diarrhoea. Best Practice & Research. Clinical Gastroenterology, 26(5), 663–675. https://doi.org/10.1016/j.bpg.2012.11.003
32. Szczygiel, B., Jonkers-Schuitema, C. F., & Naber, T. (n.d.). Basics in Clinical Nutrition: Nutritional support in extensive gut resections (short bowel). E-SPEN, the European E-Journal of Clinical Nutrition and Metabolism, 5(1), e63–e68. https://doi.org/10.1016/j.eclnm.2009.06.021
33. Nightingale J. M. (2001). Management of patients with a short bowel. World journal of gastroenterology, 7(6), 741–751. https://doi.org/10.3748/wjg.v7.i6.741
34. Christl, S. U., & Scheppach, W. (1997). Metabolic consequences of total colectomy. Scandinavian journal of gastroenterology. Supplement, 222, 20–24. https://doi.org/10.1080/00365521.1997.11720712
35. Balestrieri, P., Ribolsi, M., Guarino, M. P. L., Emerenziani, S., Altomare, A., & Cicala, M. (2020). Nutritional Aspects in Inflammatory Bowel Diseases. Nutrients, 12(2), 372. https://doi.org/10.3390/nu12020372
36. Ensari A. (2014). The Malabsorption Syndrome and Its Causes and Consequences. Pathobiology of Human Disease, 1266–1287. https://doi.org/10.1016/B978-0-12-386456-7.03804-1
37. Van Cutsem, E., & Arends, J. (2005). The causes and consequences of cancer-associated malnutrition. European Journal of Oncology Nursing: Supplement 2, 9, S51–S63. https://doi.org/10.1016/j.ejon.2005.09.007
38. Argilés, J. M. (2005). Cancer-associated malnutrition. European Journal of Oncology Nursing: Supplement 2, 9, S39–S50. https://doi.org/10.1016/j.ejon.2005.09.006
39. Nolan, J. D., Johnston, I. M., & Walters, J. R. F. (2012). Physiology of malabsorption. Surgery (Oxford), 30(6), 268–274. https://doi.org/10.1016/j.mpsur.2012.02.013
40. Valentova, M., von Haehling, S., Bauditz, J., Doehner, W., Ebner, N., Bekfani, T., Elsner, S., Sliziuk, V., Scherbakov, N., Murín, J., Anker, S. D., & Sandek, A. (2016). Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. European Heart Journal, 37(21), 1684–1691. https://doi.org/10.1093/eurheartj/ehw008
41. Rana, S. V., Malik, A., Bhadada, S. K., Sachdeva, N., Morya, R. K., & Sharma, G. (2017). Malabsorption, Orocecal Transit Time and Small Intestinal Bacterial Overgrowth in Type 2 Diabetic Patients: A Connection. Indian journal of clinical biochemistry: IJCB, 32(1), 84–89. https://doi.org/10.1007/s12291-016-0569-6

42. Schiller, L. R. (2020). Maldigestion Versus Malabsorption in the Elderly. Current Gastroenterology Reports, 22(7). https://doi.org/10.1007/s11894-020-00771-5
43. Holt, P. R. (2007). Intestinal Malabsorption in the Elderly. Digestive Diseases, 25(2), 144–150. https://doi.org/10.1159/000099479
44. Biesalski Hans, & Jana, T. (2018). Micronutrients in the life cycle: Requirements and sufficient supply. NFS Journal, 11, 1–11. https://doi.org/10.1016/j.nfs.2018.03.001
45. Sinha, P., & Guerrant, R. L. (2024). The Costly Vicious Cycle of Infections and Malnutrition. *The Journal of infectious diseases*, *229*(6), 1611–1613. https://doi.org/10.1093/infdis/jiad513
46. Mora, J. R., Iwata, M., & von Andrian, U. H. (2008). Vitamin effects on the immune system: vitamins A and D take centre stage. Nature reviews. Immunology, 8(9), 685–698. https://doi.org/10.1038/nri2378
47. Sun, Z., Kong, X. J., Jing, X., Deng, R. J., & Tian, Z. B. (2015). Nutritional Risk Screening 2002 as a Predictor of Postoperative Outcomes in Patients Undergoing Abdominal Surgery: A Systematic Review and Meta-Analysis of Prospective Cohort Studies. *PloS one*, *10*(7), e0132857. https://doi.org/10.1371/journal.pone.0132857
48. Reber, E., Gomes, F., Vasiloglou, M. F., Schuetz, P., & Stanga, Z. (2019). Nutritional Risk Screening and Assessment. *Journal of Clinical Medicine*, *8*(7), 1065. https://doi.org/10.3390/jcm8071065
49. Raslan, M., Gonzalez, M. C., Dias, M. C., Nascimento, M., Castro, M., Marques, P., Segatto, S., Torrinhas, R. S., Cecconello, I., & Waitzberg, D. L. (2010). Comparison of nutritional risk screening tools for predicting clinical outcomes in hospitalized patients. *Nutrition (Burbank, Los Angeles County, Calif.)*, *26*(7-8), 721–726. https://doi.org/10.1016/j.nut.2009.07.010
50. Benoist, S., & Brouquet, A. (2015). Nutritional assessment and screening for malnutrition. *Journal of visceral surgery*, *152 Suppl 1*, S3–S7. https://doi.org/10.1016/S1878-7886(15)30003-5
51. Power, S., Maarof, A., Power, A., Feehan, S., & Whelan, M. (2024). Nutritional risk predicts postoperative complications and length of stay, whereas sarcopenia risk predicts need for step-down care in a mixed elective surgery population. *Journal of human nutrition and dietetics: the official journal of the British Dietetic Association*, *37*(1), 308–315. https://doi.org/10.1111/jhn.13256
52. Lee, J. L., Oh, E. S., Lee, R. W., & Finucane, T. E. (2015). Serum Albumin and Prealbumin in Calorically Restricted, Nondiseased Individuals: A Systematic Review. *The American journal of medicine*, *128*(9), https://doi.org/10.1016/j.amjmed.2015.03.032
53. Haluzík, M., Kábrt, J., Nedvídková, J., Svobodová, J., Kotrlíková, E., & Papezová, H. (1999). Relationship of serum leptin levels and selected nutritional parameters in patients with protein-caloric malnutrition. *Nutrition (Burbank, Los Angeles County, Calif.)*, *15*(11-12), 829–833. https://doi.org/10.1016/s0899-9007(99)00177-x
54. Kuzuya, M., Izawa, S., Enoki, H., Okada, K., & Iguchi, A. (2007). Is serum albumin a good marker for malnutrition in the physically impaired elderly?. *Clinical nutrition (Edinburgh, Scotland)*, *26*(1), 84–90. https://doi.org/10.1016/j.clnu.2006.07.009
55. Keller, U. (2019). Nutritional Laboratory Markers in Malnutrition. *Journal of Clinical Medicine*, *8*(6), 775. https://doi.org/10.3390/jcm8060775
56. Bharadwaj, S., Ginoya, S., Tandon, P., Gohel, T. D., Guirguis, J., Vallabh, H., Jevenn, A., & Hanouneh, I. (2016). Malnutrition: laboratory markers vs nutritional assessment. *Gastroenterology report*, *4*(4), 272–280. https://doi.org/10.1093/gastro/gow013
57. Gammoh, N. Z., & Rink, L. (2017). Zinc in Infection and Inflammation. *Nutrients*, *9*(6), 624. https://doi.org/10.3390/nu9060624
58. Brown, K. L., & Phillips, T. J. (2010). Nutrition and wound healing. *Clinics in dermatology*, *28*(4), 432–439. https://doi.org/10.1016/j.clindermatol.2010.03.028
59. Blanc, G., Meier, M. J., Stocco, J. G., Roehrs, H., Crozeta, K., & Barbosa, D. A. (2015). Efetividade da terapia nutricional enteral no processo de cicatrização das úlceras por pressão: revisão sistemática [Effectiveness of enteral nutritional therapy in the healing process of pressure ulcers: a systematic review]. *Revista da Escola de Enfermagem da U S P*, *49*(1), 152–161. https://doi.org/10.1590/S0080-623420150000100020
60. Miranda, L. S. G., Amado, J. D. N., & Alves, P. J. P. (2023). Importância da nutrição na cicatrização de feridas: uma scoping review. Revista Feridas. https://revistaferidas.congressonursing.com.br/index.php/revistaferidas/031161
61. Wobith, M., & Weimann, A. (2022). Postoperative Nutrition Management: Who Needs What?. Visceral medicine, 38(5), 354–362. https://doi.org/10.1159/000526665
62. Wild, T., Rahbarnia, A., Kellner, M., Sobotka, L., & Eberlein, T. (2010). Basics in nutrition and wound healing. *Nutrition (Burbank, Los Angeles County, Calif.)*, *26*(9), 862–866. https://doi.org/10.1016/j.nut.2010.05.008
63. Van der Heide F. (2016). Acquired causes of intestinal malabsorption. *Best practice & research. Clinical gastroenterology*, *30*(2), 213–224. https://doi.org/10.1016/j.bpg.2016.03.001.