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Article Title: The Role of Diet in Inflammatory Bowel Disease Onset, Disease Management, and Surgical Optimization

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Abstract

The concept of using diet as therapy in inflammatory bowel disease (IBD) is of interest to clinicians and patients. Once considered to play a minor role, diet is now known to affect not only disease onset but may also serve as a therapeutic tool for inducing and maintaining remission and improving surgical outcomes. Further research is needed to fully elucidate how, when, and in whom diet therapies may be best applied to improve clinical and disease outcomes. The aim of this review is to summarize current research findings and serve as a tool to help facilitate patient-clinician conversations.

Keywords: diet, IBD, nutrition, surgery, remission

Introduction

The interaction between diet and human health holds significant importance for both medical professionals and patients.[1] This relationship is highlighted in the context of the pathogenesis and treatment of inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC). With the global prevalence of IBD continuing to rise, there is a growing burden on individuals and healthcare systems.[2-3] Understanding the role of diet in IBD regarding its development and treatment may allow for attenuation of the incidence, enhance clinical outcomes, and alleviate the large financial burden associated with managing IBD. This qualitative review addresses the role of diet in the etiology of IBD, as a primary or ancillary therapy and in the perioperative patient.

Impact of Diet on the Development of Inflammatory Bowel Disease (IBD)

To understand the impact of diet on IBD, it is crucial to comprehend the current IBD paradigm, which revolves around the interplay of the intestinal microbiome, mucosal barrier, and the gastrointestinal immune system (see Figure 1). Diet significantly influences all three of these elements. A Westernized diet, characterized by high levels of fats, added sugars, meat, and ultra-processed foods (UPFs), has been shown to disturb the intestinal microbiome, leading to dysbiosis characterized by decreased biodiversity, a decrease commensal bacteria and an increase in proinflammatory organisms.[4] Environmental factors such as diet dominate over genetics in shaping the intestinal microbiome.[5-6] Furthermore, specific components of the Westernized diet, such as select food additives, have been shown to disrupt mucosal barrier function, thus facilitating interaction between the intestinal immune system and the microbiome.[7]

From an epidemiological standpoint, many common dietary components have been implicated in the development of IBD (see Table 1). Food processing has developed and allowed for innovations in preparation, preservation, nutrient availability, and creation of novel food products. The availability of UPFs has increased dramatically over the last 50 years. UPFs now constitute nearly half of the energy intake in Westernized nations, making them a key element of the Western diet. UPFs are distinguished by their high levels of salt, fat, sugar, and various food additives, coupled with low levels of protein, fiber, vitamins, and minerals.[8] Epidemiological investigations have unveiled links between UPF consumption and IBD. In a prospective cohort study encompassing 116,087 participants from diverse income brackets, greater intake of UPFs correlated with an elevated risk of IBD. Moreover, the study identified associations between IBD risk and the consumption of specific types of UPFs, such as processed meats, sugary beverages, refined sweets, fried foods, and salty snacks. These findings were seen for both CD and UC.[9] A subsequent larger prospective study of US health professionals involving 245,112 participants corroborated the association between UPF consumption and the risk of CD but did not find a similar link for UC.[10] When these studies were combined with the results of three others in a meta-analysis, greater consumption of UPF was associated with an approximately 70% increased incidence of CD but no increased risk of UC.[11]

Increased consumption of dietary fiber has been suggested to reduce the risk of IBD. However, only a limited number of prospective studies have explored the relationship between long-term dietary fiber intake and the incidence of CD or UC. Data from the Nurses' Health Study, found that sustained dietary fiber intake, particularly from fruits, is linked to a decreased risk of CD, although not UC.[12] Analysis of data from the European Prospective Investigation into Cancer (EPIC) study, conducted within a large European population aimed to investigate the association between fiber intake and the onset of CD and UC.[13] The findings did not demonstrate an association between dietary fiber intake and risk of the development of UC. Specifically, the study found that non-smokers with greater intake of cereal fiber had lower odds of developing CD while no such association was seen for smokers, suggesting that one environmental exposure may impart risk that is not able to be overcome by a dietary exposure. Nonetheless, further research is warranted to explore whether certain types of fiber may confer a protective effect, particularly in relation to smoking status in CD.

Oxidative stress has been alluded to in the development of IBD. This raises the question of whether dietary polyphenols, known for their antioxidant properties, could protect against the development of IBD. A study involving 401,326 individuals aged 20 to 80 utilized validated food frequency questionnaires to assess baseline dietary polyphenol intake.[14] Overall, total polyphenol intake showed no significant association with either CD or UC. A significant inverse association was found between flavones and resveratrol intake and CD. No significant associations between polyphenol subtypes and UC were detected.

In the Nurses' Health Study, the impact of energy-adjusted cumulative average total fat intake, as well as specific types of fat and fatty acids, were assessed on the risk of developing CD and UC. Results indicated that a higher intake of dietary long-chain n-3 polyunsaturated fatty acids (PUFAs) was linked with a decreased risk of UC. Conversely, a high consumption of trans-unsaturated fats, which are more common in UPFs, was potentially associated with an increased risk of UC.[15]

While specific dietary components of the Westernized diet have found signals with regards to development of inflammatory bowel disease (IBD), broader “patterns” of dietary intake also provide unique insights. Data from three large prospective cohorts, including 166,903 women and 41,931 men, were analyzed to assess the effects of “dietary inflammatory potential” on the risk of CD and UC. Empirical dietary inflammatory pattern (EDIP) scores were calculated based on frequency/quantity of consumption from 18 food groups obtained via food frequency questionnaires. Self-reported cases of CD and UC were confirmed through medical record review. Over 4,949,938 person-years of follow-up, 328 cases of CD and 428 cases of UC were documented. Dietary inflammatory potential was not associated with the risk of developing UC. However, participants in the highest quartile of cumulative average EDIP scores (reflecting higher dietary inflammatory potential) had a 51% higher risk of CD compared to those in the lowest quartile. Moreover, individuals who shifted from a low to high inflammatory potential diet or consistently consumed a proinflammatory diet had a significantly greater risk of CD. Unfortunately, those who moved from a high to low inflammatory potential diet did not appear to be protected from developing CD.

Nonetheless, these findings underscore the possibility that dietary patterns with low inflammatory potential may reduce the risk of CD, highlighting potential avenues for preventive interventions in IBD management.[16]

Given a significant higher risk (>4.5 fold) of the development of IBD in offspring of mothers with IBD, the opportunity to intervene with diet to mitigate risk holds promise. Breast milk, rich in essential micronutrients and macronutrients, offers significant health benefits to offspring, with breastfeeding often associated with a protective effect against IBD in many studies. While findings across studies have been mixed, a systematic review and meta-analysis of 35 studies revealed that breastfeeding was linked to a decreased risk of both CD and UC.[17] Investigating the influence of maternal nutrition during pregnancy on offspring outcomes, the Modulating Early Life Microbiome through Dietary Intervention in Pregnancy (MELODY) trial is currently underway. This trial explores the effects of an anti-inflammatory dietary intervention during pregnancy on the gut microbiome of pregnant women with CD, compared to those on a regular diet and healthy controls, and its impact on the gut microbiome and fecal calprotectin of their offspring. Positive findings from this trial could present a valuable strategy for modulating the gut microbiome and potentially reducing intestinal inflammation and IBD.[18]

Using Diet as Therapy to Manage IBD

Patients show a great interest in dietary therapies as a treatment of IBD. Unfortunately, many alter their diet without the guidance of their medical team, potentially increasing risk for over-restriction of diet at best, and malnutrition at worst. Therefore, it is crucial that clinicians can competently speak about the role of diet in the management of IBD so that the most appropriate diet advice is provided. Table 2 summarizes the different evidence-based diets commonly used for managing IBD.

Enteral nutrition formula, a medical food, has been used in IBD in various forms since the 1970's. Exclusive Enteral Nutrition (EEN), a diet that is solely comprised of a complete nutrition formula with the exclusion of all other foods and beverages except water, has been shown to be more effective for inducing short-term remission and promoting mucosal healing in mild-moderate pediatric CD than corticosteroid therapy.[19] EEN is used as first line therapy for pediatric CD and spares the patient exposure to corticosteroid therapy during a critical period of growth. Data is less robust for adults with CD, which may be due to lower adherence rates, but EEN shows similar effectiveness when issues of compliance are mitigated. Additionally, prospective studies suggest EEN is effective in complicated CD, with favorable outcomes for fistula closure and reducing strictures.[20-22] The role of EEN in active UC is not well established, but a recent randomized clinical trial suggests that 7 days of EEN may help augment response to steroid therapy in severe acute UC and reduce rates for 6-month colectomy and rehospitalization.[23] With the recognition that enteral nutrition formulas benefit the disease course in CD and can help meet nutrition needs (which influences immunity

and response to pharmacologic therapy), it is reasonable to discuss EEN as a therapeutic approach with IBD patients who are receptive to EEN or in those who are intolerant to or desire avoidance of steroids.

The efficacy of EEN to induce remission and promote mucosal healing seems counterintuitive considering data on UPFs increasing the risk of IBD. However, this highlights the current knowledge gap regarding the mechanism of action of EEN. A recent pilot trial aimed to investigate the impact of a less processed, whole-foods based smoothie in pediatric CD and found reductions in clinical symptoms and fecal calprotectin, similar to results achieved with EEN.[24] These data, along with evidence that enteral nutritional formula composition in terms of protein source and fat content does not impact efficacy,[19] support the hypothesis that the mechanism may be related more to the food that is excluded than the EEN formula itself. Further studies are needed to fully understand what makes EEN so effective and how (or if) it can be replicated using a whole-foods approach. UPF are not created equal and there are likely elements of UPFs that may promote or be of detriment to human health. What is known is that enteral nutrition formula appears to be beneficial for patients with IBD.

An alternative to EEN is Partial Enteral Nutrition (PEN), where an enteral nutrition formula is used to replace about half of a patient's nutritional needs. PEN can be a useful strategy for maintenance of remission in CD. A randomized controlled trial of patients with Crohn's disease found significantly lower relapse rates in the PEN arm (34% relapse) compared to patients not on PEN (64% relapse) after a 1.5-year period.[25] PEN has also been shown to augment response to biologic therapy as well as reduce risk for loss of response in patients with CD.[26-28] Further exploring this concept of using

enteral formula or PEN as a “combination therapy” with biologics, a recent prospective trial of adults with active CD found PEN combined with a TNF (tumor necrosis factor) inhibitor is more effective for inducing clinical and endoscopic remission, while significantly improving psychological burden and quality of life.[29]

PEN has also been studied along with an exclusion diet called the Crohn’s Disease Exclusion Diet (CDED). CDED is a defined diet, rich in fruits, vegetables, resistant starch, and low in red meat, wheat, dairy, ultra-processed foods and food additives. CDED has been shown to be effective for inducing remission in CD and has been found to be more tolerable than EEN.[30-31] CDED is a 3-phase diet that encourages the patient to move through each phase as remission is achieved, with the eventual destination being a more liberalized and sustainable diet approach that is intended to maintain remission. A small randomized controlled study in adults suggests that the CDED may be equally or only modestly less effective without the formula/PEN component, an important discussion point for clinicians to address with patients during the shared decision-making process.[32] Long term studies on the diet’s effectiveness are needed.

The Specific Carbohydrate Diet (SCD) has been proposed as a whole-foods approach for managing IBD. SCD was first developed in the early 1900’s by Dr. Sidney Haas[33] and was initially used to successfully treat children with celiac disease until the discovery of gluten as the dietary antigen that damages the small bowel. SCD was later popularized by Elaine Gotschall, who found success with using the diet as therapy for her daughter who had ulcerative colitis. Ms. Gotschall wrote the book, *Breaking The Vicious Cycle*, which outlines specifics about the diet that clinicians and patients use as

a resource. SCD is a grain-free, soy-free, lactose-free diet low in processed foods, and rich in animal proteins, fish, fruits, non-starchy vegetables, certain legumes, and fermented dairy. Patients with IBD who adhere to the SCD report improvements in abdominal pain, diarrhea, nocturnal bowel movements, and weight.[34] Small studies of pediatric patients with active CD on SCD have found improvements in clinical symptoms, biochemical markers of inflammation, stool calprotectin[35] and mucosal improvements (capsule endoscopy).[36] In the largest pediatric study on SCD to date, researchers compared SCD to a more liberal "modified SCD (MSCD)" and found no significant difference in symptoms or inflammation; however, some patients had improvements in symptoms and fecal calprotectin when compared to usual diet [37]. Data on SCD in adults is limited, but a case series of 50 adults with IBD on SCD revealed a mean time to improvement of 29 days on SCD, a high rate of compliance (95%), and a high quality of life (mean SIBDQ score of 60).[38]

Given these early promising data for SCD and the popularity of this diet in the IBD community, researchers conducted a large randomized controlled trial (n=194) to better examine the effects of 12 weeks of either a SCD or a Mediterranean style diet in adults with mild to moderate Crohn's disease.[39] Findings from this trial revealed no significant difference in rates of patients achieving symptomatic remission (46% in SCD vs 43% in those on Mediterranean diet), or fecal calprotectin response (34% on SCD vs 30% on Mediterranean diet). However, both diets had little effect on c-reactive protein response (5% in those on SCD vs 3% in those on Mediterranean diet). Because SCD is gluten and lactose free, the investigators hypothesized that SCD might have a beneficial effect on symptoms by reducing certain FODMAPs. However, subgroup analyses of

those patients with or without elevated inflammatory markers at baseline or recent abnormal colonoscopy found similar results to the overall analysis. Thus, at least in patients with mild to moderate symptoms, there was no evidence of a benefit of SCD over Mediterranean diet in this trial. An important caveat of the trial is that all participants were provided with meals that were prepared without additives. As such, to the extent that there is benefit to an additive-free diet, it may have masked a potential therapeutic advantage of SCD relative to a Mediterranean style diet. These findings can help inform discussions around expectations of diet therapy, and which diet approach may be best.

In patients who have achieved remission, a plant-forward approach or Mediterranean Diet Pattern (MDP) has been a suggested diet strategy.[40] An MDP consists of a diet rich in olive oil, fruits, vegetables, whole grains, legumes, beans, nuts and seeds, moderate in dairy, seafood and poultry, and low in meat, eggs, processed meats and sweets. Patients following an MDP appear to spend longer times in remission and have lower fecal calprotectin levels. A prospective study of 693 patients with IBD (CD and UC) in remission found that those who adhered to a MDP along with physical activity had a lower risk of disease exacerbation, suggesting these healthy lifestyle interventions can mitigate disease activity.[41] A cross-sectional trial in children on biologic therapy who were mostly in remission found that a MDP was associated with lower fecal calprotectin levels.[42] And a prospective study of patients with UC after pouch surgery found an inverse association with MDP adherence and onset of pouchitis.[43] Given the many benefits a plant-based diet can have on overall health (cardiac,

metabolic, reduction in cancer risk, etc), and the low rates of fiber in the typical Western diet, an MDP should be encouraged in IBD.

While some of these diets are less adaptable (EEN), a registered dietitian can help patients modify these diets to best meet the person's individual needs, considering important factors such as intestinal anatomy and absorptive capacity, disease phenotype (e.g. stricturing), food access/availability, culinary skills, cultural and religious background, and food tolerance/preference.

Leveraging Diet to Optimize Surgical Outcomes

Malnutrition and high dose systemic corticosteroids are important risk factors for surgical complications.[44-49] Nutrition is an important preoperative intervention to reduce complications and potentially reduce the extent of bowel resected. The European Crohn's and Colitis Organization (ECCO) recommends nutritional assessment prior to surgery and optimization in patients with identified deficiencies through enteral or parenteral support.[50] However, when enteral nutrition is possible, it is the preferred method.

Multiple observational studies support the benefit of preoperative enteral nutrition for patients with Crohn's disease. A recent systematic review and meta-analysis of 14 observational studies of EEN in the preoperative setting included data on 874 patients treated with EEN and 1044 control patients.[51] In the pooled analysis, patients treated with EEN prior to surgery had a 2.1-fold lower rate of intra-abdominal septic complications and a 1.6-fold lower rate of skin and soft tissue infections. In contrast to the favorable association of EEN with infectious outcomes, preoperative treatment with

parenteral nutrition was not associated with a reduction in infectious complications. Neither nutritional therapy was associated with a reduction in the extent of bowel resection.

There are multiple mechanisms by which EEN could reduce the risk of surgical complications. The patients in the EEN group had higher C reactive protein (CRP) and lower albumin concentrations at the time of initial evaluation, suggesting that they were potentially at higher risk of complications.[51] However, after nutritional optimization, the albumin concentration increased, and the CRP concentration decreased. EEN also serves as a mechanism to reduce corticosteroid dose, which would be expected to reduce the rate of infectious complications. In several of the studies included in the meta-analysis, the authors note that the EEN was used in conjunction with efforts to reduce the dose of corticosteroids.[52-58] EEN may also give time for penetrating complications to be better controlled, which may make surgery safer and perhaps allow for minimally invasive approaches rather than open operations.

There are several questions related to nutritional support prior to IBD surgery that remain to be answered (see Table 3). The results of the observational studies showing reduced complications in Crohn's disease surgeries needs to be validated in prospective randomized trials. How long patients need to be treated with nutritional therapy to reduce the risk of surgical complications has not been fully elucidated. In the prior studies, nutrition therapy was typically used for four to six weeks, but it is possible that even shorter durations may be effective. Similarly, whether PEN is as effective as EEN needs to be determined. There are far less data on nutritional optimization prior to surgery for ulcerative colitis, although it is logical that correcting severe nutritional

deficiencies would be beneficial. Unfortunately, many surgeries for ulcerative colitis are more urgent, taking place during a hospitalization for severe acute exacerbation. Finally, the degree of malnutrition that warrants nutritional optimization before IBD surgery has not been well defined. The risks associated with parenteral nutrition, such as line infection, may outweigh the benefits for patients with only mild malnutrition.[59] These risks are lower when enteral nutrition is able to be used. While we wait for the answers to these questions, it is reasonable to follow recommendations from medical societies for nutrition optimization of surgical patients: screen patients for malnutrition and anemia, carbohydrate load immediately prior to surgery, and advance diet to regular as soon as possible in the post-operative setting with or without a nutrition supplement shake to help meet nutrient needs during a critical time for recovery.[60-61]

Conclusion

Our understanding of the impact of diet on IBD onset and disease management is evolving and more evidence suggests a variety of approaches to integrate diet as sole or complementary therapy to benefit the patient and disease outcomes. These diet therapies are important to consider when having discussions with patients and developing treatment plans.

Figure 1: Inflammatory Bowel Disease Paradigm. The development of inflammatory bowel disease is shaped by a complex relationship between the intestinal microbiome, mucosal barrier, and immune system, highlighting the intricacy of disease mechanisms within the gut microenvironment. Dysbiosis, which disrupts the mucosal barrier and compromises its integrity, triggers an immune response characterized by mucosal inflammation. This inflammatory process is cyclical, with continued mucosal damage further exacerbating inflammation, thereby perpetuating the cycle and contributing to the pathology of inflammatory bowel disease.

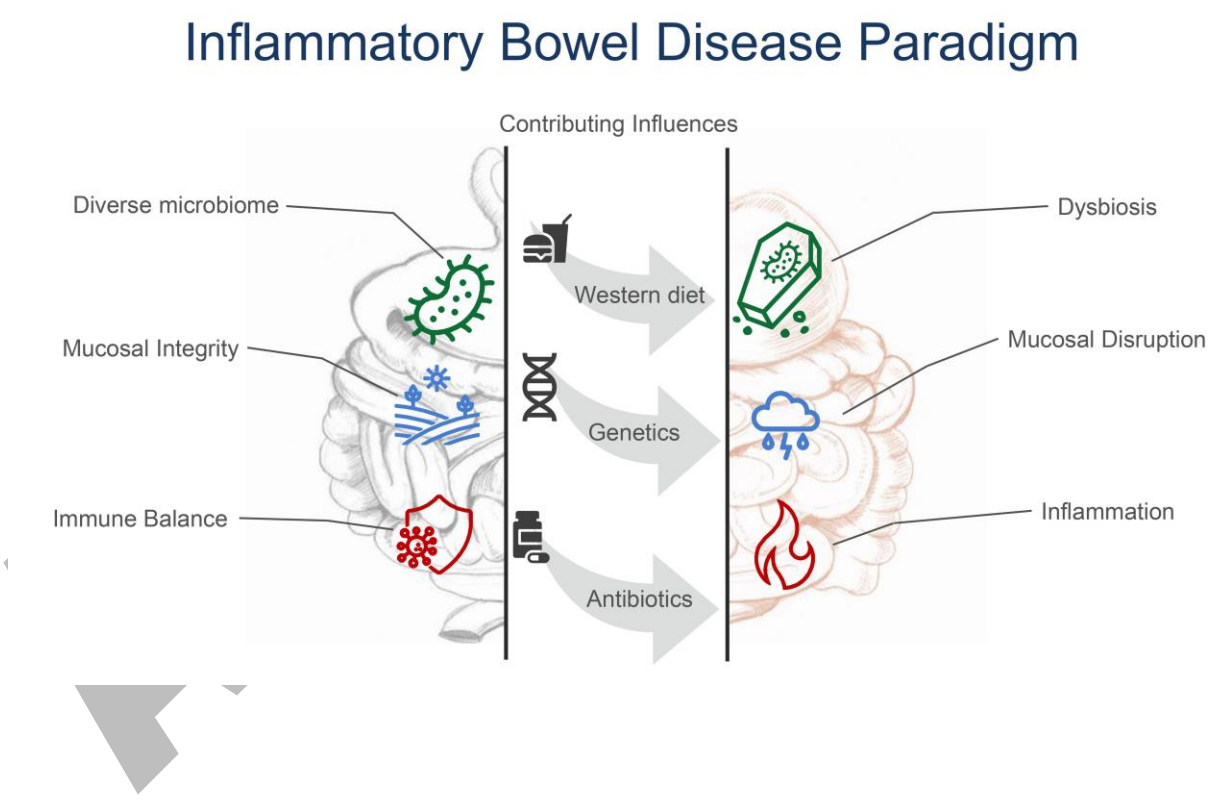

Table 1: Role of Diet in Inflammatory Bowel Disease (IBD) Onset, Disease Management, Perioperative Optimization

	Crohn's Disease	Ulcerative Colitis
Diet Components Suggested to Influence Disease Onset	• UPFs (processed meats, sugary beverages, refined sweets, fried foods, and salty snacks) may increase risk[9] • Fiber[12], flavones and resveratrol[14] may decrease risk • Diet with high inflammatory potential (EDIP) may increase risk[16] • Breastfed infants may have a decreased risk[17]	• UPFs (processed meats, sugary beverages, refined sweets, fried foods, and salty snacks) may increase risk[9] • Dietary long chain n-3 polyunsaturated fatty acids may decrease risk[15] • Trans-unsaturated fats may increase risk[15] • Breastfed infants may have a decreased risk[17]
Diets to Manage IBD (See table 2 for more details on diet therapies)	• EEN induces remission[19] • EEN promotes fistula closure, reduces strictures[20-22] • PEN may help maintain disease remission[25] • In combination with biologic therapy, PEN may augment response to medication and improve medication durability[26-28] • CDED induces remission and is better tolerated than EEN[30-31] • MDP may help maintain remission[40]	• EEN may augment response to steroid therapy and reduce rates for colectomy and rehospitalization[23] • MDP may help maintain remission[40] and reduce risk of pouchitis[42]

Perioperative Nutrition Optimization Strategies	• Screen for malnutrition and anemia, carb load prior to surgery, advance diet as soon as able after surgery, add ONS for additional nourishment as needed[59-60] • EEN before surgery reduces risk for infection[50] • EEN before surgery can be considered as steroid sparing agent[51-57]	• Screen for malnutrition and anemia, carb load prior to surgery, advance diet as soon as able after surgery, add ONS for additional nourishment as needed[59-60]

Legend: UPF = ultra-processed foods; EDIP = Empirical dietary inflammatory pattern; EEN = exclusive enteral nutrition; PEN = partial enteral nutrition; CDED = Crohn's disease exclusion diet; MDP = Mediterranean diet pattern; ONS = oral nutrition supplement

Table 2: Summary of Different Diet Therapies Commonly Used In IBD

Diet	Definition	Advantage	Disadvantage	Adherence	Tolerability
EEN (Exclusive Enteral Nutrition)	100% of nutrition from a complete, balanced formula	Most effective diet therapy for inducing remission in mild-moderate Crohn's disease.[19]	Compliance may be challenging. Avoidance of solid foods is not easy and can affect many aspects of a person's life. Lack of consensus for how to wean off this diet, and what to transition to.	Adherence is typically higher in children than adults – this may be because children often have a multidisciplinary support team, whereas adults do not	EEN has been shown to be less tolerated than PEN/CDED (73% vs 97%).[30]
PEN (Partial Enteral Nutrition)	~50% of nutrition from a complete, balanced formula, and ~50% from foods	PEN is less disruptive to what is typically considered a normal diet.	Long-term consumption of formula.	When compared to CDED, adherence to PEN is lower (86% vs 63%)[32]	Tolerance has been reported to be higher with PEN (97%) compared to EEN (73%)[30]
CDED	A 3-phase diet that becomes more liberal over time.	As effective as EEN for inducing steroid free remission at 6 weeks.[30]	There are many rules to this diet that may limit feasibility, including consumption of	When compared to PEN, adherence to CDED is higher (63% vs 86%)[32]	Tolerance has been reported to be higher

	This diet is free of ingredients thought to contribute to inflammation (red meat, wheat, ultraprocessed foods) and rich in foods thought to promote gut health, such as fruits, vegetables, and resistant starch.		mandatory foods (banana, potatoes, apples, chicken, eggs), avoidance of disallowed foods. The full diet (all 3 phases) is >/=9 months, eventually allowing dining at restaurants up to a couple of times per week. Lack of long-term data on diet, as well as consensus on how to wean/transition off.		with CDED (97%) compared to EEN (73%)[30]
Mediterranean Diet	Diet rich in plant foods (fruits, vegetables, legumes, grains, nuts, seeds, herbs, spices) and olive oil, with limited amounts of fish/seafood,	Liberal diet approach that is adaptable in many situations (travel, eating out, different food preferences, etc.). Beyond IBD, this eating approach has been shown to decrease all-cause	This diet reflects the culture, cuisine, and foods available to people living along the Mediterranean coast, and thus may be difficult to apply to other populations.	Compared to SCD, adherence rates to a Mediterranean diet were found to be similar at 6 weeks (68% vs 64%)[38]	Findings from studies show a Mediterranean diet is well tolerated and improves symptoms in IBD.[38, 62]

	dairy, eggs, chicken, and infrequent red meat and sweets	mortality, decrease risk for heart disease and cancer risk.[61]			
SCD	Diet free of grains, soy, lactose, food additives; rich in fruits, non-starchy vegetables, meats, poultry, fish, certain legumes, fats, nuts, certain seeds, and fermented dairy.	Small studies show clinical and mucosal improvements in IBD. A large RCT found symptomatic improvement, and improvements in quality of life on SCD. [34-38]	There are many food rules with this diet that may make starting it and maintaining it difficult. It may be challenging to follow when traveling. It hasn't been shown to be more effective than a Mediterranean diet for clinical symptoms or fecal calprotectin response.[38]	A survey of adults on SCD reported high adherence rates (95%).[37] Compared to a Mediterranean diet, adherence rates to a SCD were found to be similar at 6 weeks (68% vs 64%).[38]	It appears to be well tolerated[38]

Table 3: Unanswered Questions Related to Nutrition Optimization Prior to Surgery

• Can perioperative nutrition optimization be done safely? • Should all patients be nutritionally optimized, or just those with a degree of malnutrition? Who benefits most? • Would PEN vs EEN pre-operatively yield similar results? • What is the optimal duration for nutrition optimization pre-operatively to improve post-operative outcomes? • What else can we be doing now to improve surgical outcomes?

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