

The role of gut microbiota support in the prehabilitation process for patients requiring gastrointestinal surgery

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Abstract

Gastrointestinal surgery complications are common. Implementation of an interdisciplinary prehabilitation program could reduce their frequency and shorten hospital stays. Including gut microbiota support supplements in prehabilitation may be a new strategy to reduce treatment-related morbidity in patients undergoing gastrointestinal surgery. The current state of knowledge and previous studies are very heterogeneous in terms of interventions and results obtained. All studies indicate a positive impact of the use of supplements supporting gut microbiota in the perioperative period on the patient's condition, as well as a reduction in postoperative morbidity, but they do not explain the effect of the microbiota on the entire prehabilitation process. Implementing nutritional interventions together with gut microbiota support supplements from the very beginning of prehabilitation could improve quality of life and reduce complications. The aim of this review is to determine the possibilities of supporting the gut microbiota in the perioperative period for patients requiring gastrointestinal surgery.

Introduction

Millions of surgeries are performed annually worldwide [1]. Each surgery induces psychological and physiological stress that can exacerbate complications, lead to organ dysfunction and dysbiosis, impair cognitive function, and cause disability [2]. Length of hospital stay remains a significant indicator of the financial burden on patients within healthcare systems, especially for planned surgeries. Many medical institutions have introduced Enhanced Recovery After Surgery (ERAS) programs aimed at improving patient outcomes while reducing costs and readmissions [3]. The ERAS protocol primarily focuses on activities determined largely by the surgeon shortly before surgery. Prehabilitation is a multidisciplinary perioperative approach centred on the patient. This process is multifaceted, with the primary goal of optimising the patient's physiological and psychological state before, during, and after surgery. Prehabilitation programs may vary strategically but always share the same objective [4]. The aim of this review is to determine the possibilities of supporting the gut microbiota in the perioperative period for patients requiring gastrointestinal surgery.

Prehabilitation – reducing perioperative stress process

The concept of the ERAS protocol arose from the ongoing search for answers on how to care for patients to reduce surgical stress, accelerate their

recovery, and minimise the risk of postoperative complications [4]. This idea has gained the approval of the world's largest surgical societies. The protocol consists of guidelines related to preoperative education, nutritional optimisation, standardised non-opioid analgesia, balancing perioperative electrolytes and fluids, using minimally invasive surgical techniques, and promoting early mobilisation and feeding [5]. Existing research shows that properly implemented ERAS protocols are safe, reduce hospital stay and the risk of postoperative complications, and lower pain levels while significantly saving hospital costs [6]. The expert panel developing recommendations for the use of prehabilitation unanimously stated that prehabilitation should be a component of comprehensive perioperative care (Table 1) [7]. The primary goal of prehabilitation is to prepare the patient for all factors associated with the planned surgery that negatively and destructively affect homeostasis and bodily function. Given the multidimensional nature of these factors, the patient must be prepared in terms of nutritional status, physical condition, and psychological state. Such preparation requires a multimodal approach and the work of specialists in multidisciplinary teams [8]. A prehabilitation team should consist of a solid team of surgeons, anaesthesiologists, perioperative physicians, physiotherapists, dieticians, psychologists, and specially trained nurses, working in tandem to create a robust system providing support to the patient both at home, in outpatient settings,

Table 1. Integration of additional ERAS Protocol with Prehabilitation – based on Gillis *et al.* 2022, Banasiewicz *et al.* 2023 [4, 7]

Scope	ERAS Protocol	Prehabilitation
Parameter	ERAS Protocol with Prehabilitation – based on Gillis <i>et al.</i> 2022	ERAS Protocol with Prehabilitation – based on Banasiewicz <i>et al.</i> 2023
Preoperative care	Correction of anaemia and malnutrition Smoking cessation Reduction of pharmacological cascade, opioids, and antibiotics Medical leave for the perioperative period	Consultations Dietitian Optimizing nutritional status, treating malnutrition, reducing treatment-related symptoms (nausea, diarrhoea, loss of appetite) Physiotherapist Implementing exercises to enhance cardiorespiratory fitness, maintain muscle mass Psychologist Reducing stress, providing psychological support, and preparing mentally for life after surgery
Perioperative education	Explanation of hospital procedures Preparation for postoperative stages (early mobilisation, early nutrition) Discussion with the patient, answering questions	Detailed explanations from specialists on surgical preparation: Dietitian Explaining the importance of nutritional preparation for surgery Dispelling concerns about restrictive diets or calorie counting Managing self-treatment with supplements; selecting appropriate supplementation Developing individualized nutrition strategies Answering patient questions Monitoring progress through follow-up visits or a mobile app Supporting recovery post-surgery until full rehabilitation Physiotherapist Explaining the importance of physical preparation for surgery Dispelling myths about overly strenuous exercises Creating an accessible exercise program with tailored exercises to strengthen muscles and improve cardiorespiratory function Supervising exercises and tracking progress via mobile apps Supporting post-surgery recovery until full rehabilitation Psychologist Explaining the psychological preparation required for surgery Providing psychological preparation and emotional support Supporting the family and caregivers for patient's social support Supporting post-surgery recovery until full rehabilitation
Additional recommendations	Discussing limitations and recommendations after hospital discharge Providing educational materials (brochures, leaflets) Educating caregivers and family on follow-up recommendations	Personalised gut microbiota supplementation guided by the healthcare team (doctor and dietitian) Assisting in selecting nutritional supplements with pharmacists Referring patients to social support resources with the help of a social worker Organising group sessions with a surgeon for Q&A and communication through a mobile app Securing sperm and egg cells

and during hospitalisation [8]. ERAS protocols, which are becoming increasingly effective, focus primarily on the intraoperative and postoperative periods. To better prepare the patient for planned surgery, which can accelerate the time of total recovery, these protocols can be supplemented with additional elements creating a prehabilitation process that begins several weeks before surgery [4]. The latest Polish recommendations for the use of prehabilitation refer to a period of 4–8 weeks before the planned surgery, depending on the stage of the disease, and risk groups for complications should be identified at the stage of initial qualification for the procedure [7]. Previous studies have limitations and are characterised by low methodological quality due to the multifactorial nature of surgical stress, as well as the heterogeneity of patient populations, interventions, and outcome measures, with a wide range of agreement [9]. Prehabilitation can take the form of classical, extended, and individualised interventions. Classical interventions should include support from a dietitian, physiotherapist, and psychologist. Extended prehabilitation additionally focuses on comorbidities, nutritional interventions, and extended diagnostics. Individualisation, depending on the type of surgery performed, allows all stages of prehabilitation to be tailored to the patient. This may include, among other things, supporting the gut microbiota, securing sperm and egg cells, and selecting appropriate exercises to accelerate post-operative recovery or improve quality of life [7].

Addressing deficiencies and improving nutritional status

Nutritional intervention in prehabilitation aims to restore energy deficits, prevent weight loss, maintain a healthy gut microbiota profile, and improve functional capacity (Figure 1) [10]. To achieve this, a normocaloric diet (25–40 kcal/kg body weight) with a protein intake of 1.2–1.8 g/kg body weight is usually sufficient [7].

Intervention should include dietary counselling, an enriched diet, oral nutritional supplements (ONS), and parenteral support if enteral feeding is not possible. According to ESPEN recommendations, the enteral route is always preferred when possible, and even if patients are on a normal diet, it is often insufficient to meet their energy needs. Therefore, it is recommended that patients receive ONS in the preoperative period, regardless of their nutritional status [11]. Nutritional intervention in the ERAS program is performed late, only in patients with malnutrition identified in screening tests after admission to the ward [12]. Perioperative nutritional optimisation reduces the risk of both infectious and non-infectious postoperative complications. It also reduces the length of hospital stay in patients undergoing surgery for gastrointestinal cancer [13]. In the prehabilitation process, assessment of nutritional

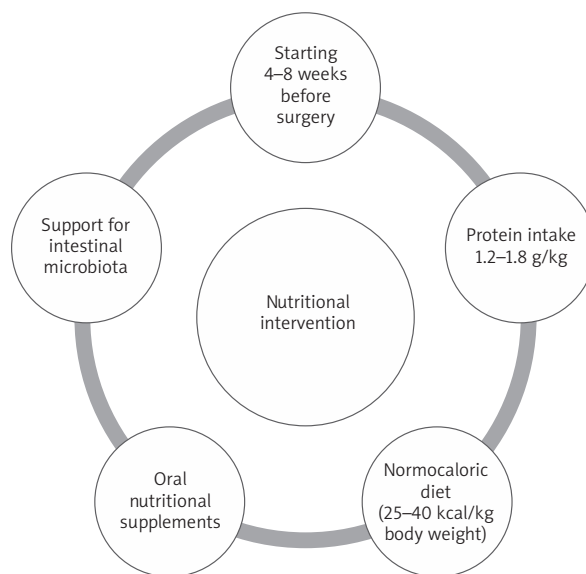


Figure 1. Nutritional intervention in prehabilitation – based on Banasiewicz *et al.* 2023 [7]

status and its modification could begin as early as 8 weeks before surgery, because a 4–5 week prehabilitation process may not be sufficient to increase pre-operative physiological reserves, improve the status of the gut microbiota, and reduce postoperative complications [14]. Prehabilitation allows for the optimisation of modifiable risk factors that increase the occurrence of surgical site infections [15].

The impact of gut microbiota on reducing the risk of postoperative complications

Commensal bacteria also contribute to colonisation resistance against pathogens through competitive inhibition, the production of antimicrobial peptides, and activation of the immune system (Figure 2). Significant changes in the gut microbiome can be detected within a day of changing diet [16]. Despite these constant fluctuations, the overall composition and function of the gut microbiota in healthy individuals most often returns to a stable baseline [17]. However, within just 6 hours of a major physiological injury, the gut microbiota undergoes dramatic changes in both microbial density and function, a condition termed dysbiosis [18]. For example, severe burns, including necessary surgical procedures, can result in a 90% reduction in Bacteroidetes and Firmicutes types and an increase in pathogenic *Gammaproteobacteria* in the intestine [18]. This bloom of pathogenic *Gammaproteobacteria* includes species often responsible for post-operative infections: *Escherichia coli*, *Pseudomonas aeruginosa*, and *Enterococcus faecalis* [19]. After burns, this observation is significant, as it has been established that the intestines are the primary source of pathogens that can cause life-threatening infections [20]. Anasto-

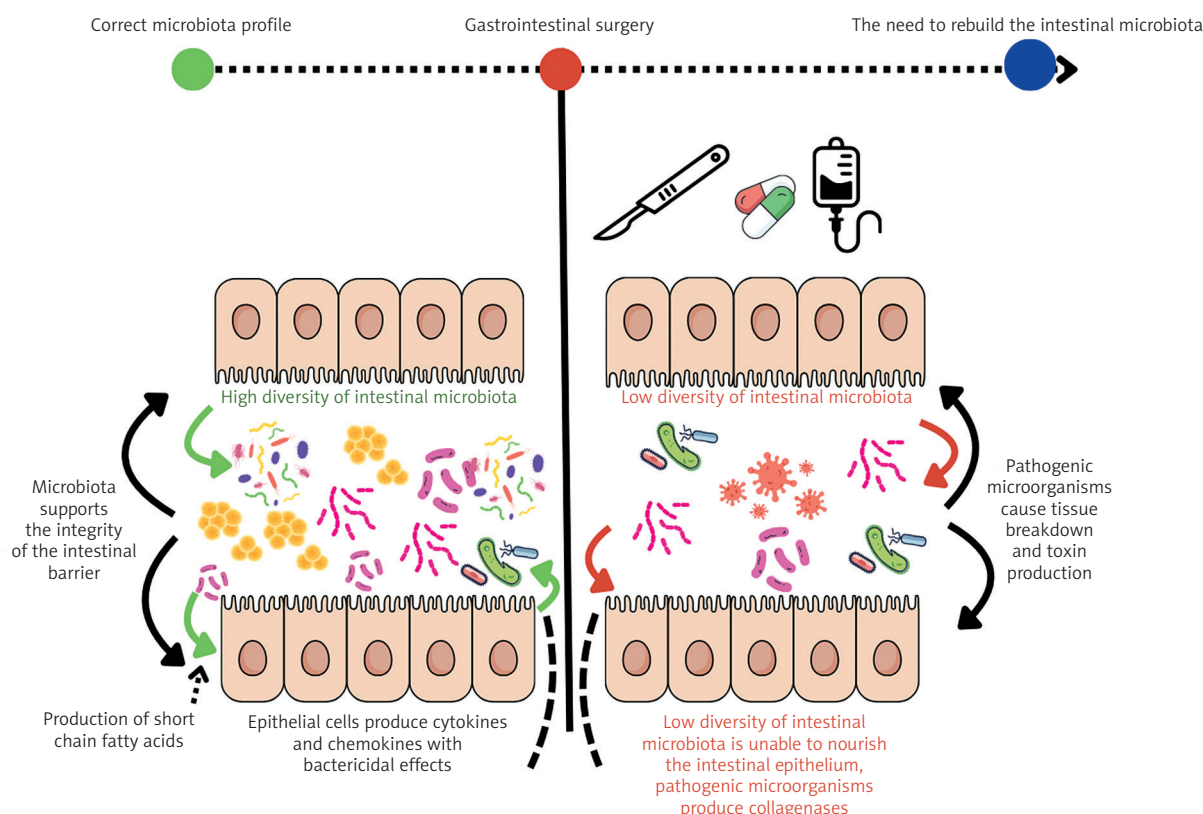


Figure 2. Dysbiosis caused by gastrointestinal surgery – based on Doudakmanis 2021 [29]

motric leakage (AL) is a significant problem in colorectal surgery, and its incidence has remained constant in recent years. In a systematic review conducted by McDermott *et al.*, several regulated and unregulated risk factors for anastomotic leakage were identified, including male sex, smoking, obesity, alcohol, steroid and non-steroid anti-inflammatory drugs, operative time, transfusion, wound contamination, and emergency surgery [21]. Most of these factors can be influenced in the prehabilitation process. Before bowel surgeries, to reduce the risk of anastomotic leakage, oral antibiotic therapy and mechanical bowel preparation are practiced, which according to numerous studies do not bring the expected results [22]. When searching for the causes of this complication, a hypothesis emerged that the gut microbiota may influence impaired healing of the anastomosis [23]. According to numerous studies, anastomotic leakage can be influenced by gut bacteria producing collagenases such as *E. faecalis* and *Proteus mirabilis*, which degrade collagen in anastomosis tissues, inhibiting tissue regeneration and causing leakage of bowel contents into the peritoneum, resulting in peritonitis or sepsis [24, 25]. To reduce the risk of anastomotic leakage, the gut microbiota can be influenced. In studies conducted by Mathew *et al.*, it was shown that a butyrate enema, which is a short-chain fatty acid (SCFA) produced by, among

others, lactic acid bacteria, performed in rats undergoing colon transection and anastomosis increases the mechanical strength of bowel anastomoses [26]. On the other hand, modification of the gut microbiota by faecal microbiota transplantation and the administration of *Parabacteroides goldsteinii* via a feeding tube improved the healing process of the anastomosis in a mouse model, reducing inflammation [27]. A recent study also showed that the gut microbiota transplanted from mice on a Western-style diet to mice on a low-fat, high-fibre diet can modulate the formation and healing of anastomoses [28]. Most of the studies conducted so far have shown low microbial diversity, increased frequency of *Enterobacteriaceae*, and changes in their virulence as the dominant mechanism associated with the occurrence of anastomotic leakage, as well as elevated levels of *Akkermansia* and *Bacteroides* [28]. Open planned abdominal surgery more often than laparoscopic surgery results in impaired intestinal barrier function and bacterial translocation, causing sepsis [29]. Sepsis is one of the worst postoperative complications of the intestines and a major cause of death in burn patients who survive the initial injury [18]. The gut microbiota is associated with the occurrence and development of sepsis, and especially its fermentation product, particularly butyric acid, which plays a major protective role [30].

Table 2. Results of various clinical studies evaluating the effectiveness of probiotics/prebiotics and synbiotics in diseases requiring surgery – based on Zeng 2021 [47]

Type of disease that requires surgery	Intervention	Observed benefits	References
Colorectal cancer	<i>Lactobacillus plantarum</i> , <i>Lactobacillus acidophilus</i> and <i>Bifidobacterium longum</i>	Probiotics can improve the integrity of gut mucosal barrier by benefiting the faecal microbiota, and decreasing infectious complications in patients with colorectal cancer undergoing	Liu <i>et al.</i> (2010) [31]
Colorectal cancer	<i>L. paracasei</i> SD1, <i>L. rhamnosus</i> SD11	The results suggest that both forms of <i>L. paracasei</i> SD1 and <i>L. rhamnosus</i> SD11 could deliver benefits for improvement of CRC conditions by reducing pro-inflammatory cytokines, enhancing anti-inflammatory cytokine IL-10 and IL-12, re-balancing gut microbiota, and reducing the levels of pathogens related to colon cancer, such as <i>F. nucleatum</i> and <i>P. gingivalis</i>	Wanitsuwan <i>et al.</i> (2024) [32]
Colorectal cancer	<i>Bifidobacterium breve</i> , <i>Bifidobacterium longum</i> , <i>Bifidobacterium infantis</i> , <i>Lactobacillus acidophilus</i> , <i>Lactobacillus plantarum</i> , <i>Lactobacillus paracasei</i> , <i>Lactobacillus bulgaricus</i> , <i>Streptococcus thermophilus</i>	No change in progression-free survival was observed in individuals with cancer, suggesting that individual, rather than population-specific, modulation of the microbiome may be necessary	Franko <i>et al.</i> (2024) [33]
Liver transplant	<i>Lactococcus lactis</i> PB411, <i>Lactobacillus casei</i> PB121, <i>Lactobacillus acidophilus</i> PB111 and <i>Bifidobacterium bifidum</i> PB211	This study demonstrates the efficacy of continuous pre-transplant probiotic administration in preventing post-transplant infections and improving early biochemical parameters of graft function. This intervention does not appear to have any benefit with respect to postoperative or pre-transplant mortality	Grat <i>et al.</i> (2017) [34]
Colorectal cancer	<i>Bacillus acidophilus</i> , <i>Bifidobacterium bifidum</i> and <i>Escherichia coli</i>	Preoperative administration of probiotics minimizes postoperative infectious complications, with possible mechanisms attributed to maintenance of gut microbiota and reduction of bacterial translocation. This was an example of enhancing systemic/local immunity while simultaneously reducing the systemic stress response	Zhang <i>et al.</i> (2012) [35]
Gastric cancer	<i>Bifidobacterium longum</i> , <i>Lactobacillus acidophilus</i> and <i>Enterococcus faecalis</i>	Patients receiving chemotherapy following minimal surgery may benefit from appropriate perioperative probiotic supplementation, which may be associated with reduced postoperative infection, improved short-term clinical outcomes, and reduced levels of postoperative inflammatory responses	Liu <i>et al.</i> (2022) [36]
Hip or knee joint replacement, colon cancer surgery	<i>Bifidobacterium longum</i> , <i>Lactobacillus acidophilus</i> and <i>Enterococcus faecalis</i>	Perioperative probiotic treatment may alleviate postoperative cognitive impairment in elderly patients after non-cardiac surgery	Wang <i>et al.</i> (2021) [37]

Table 2. Cont.

Type of disease that requires surgery	Intervention	Observed benefits	References
Obesity (gastric bypass)	<i>Bifidobacterium longum</i> BB536	Administering probiotics may alleviate gastrointestinal symptoms after gastric bypass surgery and improve quality of life, at least initially	Chen <i>et al.</i> (2016) [38]
Gastric cancer (gastrectomy)	<i>Bifidobacterium infantis</i> , <i>Lactobacillus acidophilus</i> , <i>Enterococcus faecalis</i> , and <i>Bacillus cereus</i>	Prophylactic use of probiotics can reduce postoperative inflammation, alleviate metabolic disorders, reduce insulin resistance, restore the balance of the gut microbiota and ultimately promote early recovery of patients	Liu <i>et al.</i> (2023) [39]
Liver cancer, gallbladder cancer, pancreatic cancer	<i>Lactobacillus casei</i> , <i>Bifidobacterium breve</i> + galacto-oligosaccharides	Synbiotic therapy improved and maintained the gut microbiota and environment in elderly Patients who were to undergo gastrointestinal surgery. There is a possibility that synbiotic therapy could have reduced the incidence of infectious complications in these patients	Okazaki <i>et al.</i> (2013) [40]
Oesophageal cancer (oesophagectomy)	<i>Bifidobacterium breve</i> , <i>Lactobacillus casei</i> , galacto-oligosaccharides and galacto-oligosaccharides. The patients in the control group were administered Biofermin-R containing <i>Streptococcus faecalis</i> instead of synbiotics	Perioperative administration of synbiotics in patients after esophagectomy is useful because it inhibits the excessive inflammatory response and alleviates unpleasant abdominal symptoms by changing the gut microbiota	Tanaka <i>et al.</i> (2012) [41]
Colorectal cancer	Fructooligosaccharide (25%), xylooligosaccharide (25%), polydextrose (25%), and resistant dextrin (25%)	Prebiotics can improve serum immunological markers in patients with colon cancer 7 days before surgery. Prebiotics improved the abundance of four commensal microbiomes containing opportunistic pathogens. Surgical stress decreased the abundance of most gut microbiomes in the gastrointestinal tract but increased the abundance of some opportunistic pathogens and commensal microbiomes	Xie <i>et al.</i> (2018) [42]
Colorectal cancer	<i>Pediococcus pentosaceus</i> , <i>Leuconostoc mesenteroides</i> , <i>Lactobacillus paracasei</i> ssp. and <i>Lactobacillus plantarum</i> + b-glucan, inulin, pectin and resistant starch	The use of synbiotics has been shown to improve gastrointestinal symptoms such as diarrhoea, abdominal pain, and bloating in patients who have undergone colectomy for colon cancer	Theodoropoulos <i>et al.</i> (2016) [43]
Colorectal cancer	12.5% glucose solution + <i>Bifidobacterium</i> , <i>Lactobacillus</i> , and <i>Enterococcus faecalis</i>	In the combined probiotics group, the plasma endotoxin, IGF-I, D-lactic acid, and urine L/M concentration were significantly lower than in the glucose solution group ($p < 0.05$). Moreover, the duration of postoperative fever, the mean heart rate 7 days after surgery, and the clinical indices WBC and CRP were significantly shorter and lower in the combined probiotics group than in the glucose solution group ($p < 0.05$)	Xu <i>et al.</i> (2019) [44]

The potential of probiotics, prebiotics, and synbiotics in prehabilitation

The prehabilitation process, due to its individualised nature, can be directed towards supporting the gut microbiota, which plays a crucial role in recovery [7]. The results of human clinical studies related to the influence of perioperative modification of the gut microbiota on the postoperative period show a beneficial effect on reducing the occurrence of postoperative complications and the speed of convalescence (Table 2) [31–44].

Multi-strain probiotics can alleviate postoperative memory deficits induced by general anaesthesia and reduce inflammation associated with postoperative neurocognitive disorders [45]. A systematic review conducted by Chen *et al.* (2022) demonstrated a 37% reduction in the incidence of all postoperative infectious complications in colorectal cancer patients who received probiotics and synbiotics [46]. Probiotic therapy in surgical patients decreases inflammatory markers, prevents gut dysbiosis, and limits non-infectious complications [47]. Probiotics or synbiotics can prevent infections, reduce delayed gastric emptying, and shorten hospital stay and antibiotic use in patients undergoing pancreatoduodenectomy [48]. Similar effects have been observed in liver transplant recipients, where probiotics reduce the risk of postoperative infections and shorten hospital stays and antibiotic durations [49]. Supporting the gut microbiota can accelerate wound healing and improve postoperative peristalsis, reducing diarrhoea and infectious complications [50]. Perioperative administration of probiotics (*Lactobacillus acidophilus*, *Bifidobacterium bifidum*, and *Streptococci*) and synbiotics positively impacts intestinal motility after colorectal surgery, significantly reducing abdominal bloating and postoperative ileus [51]. Probiotic strains like *L. acidophilus* NCFM and *L. salivarius* Ls-33 can induce the expression of pain receptors, reducing normal visceral perception and increasing the pain threshold by 20% after subcutaneous morphine administration (0.1 mg/kg) [52]. Cancer therapies often induce inflammation, cognitive impairment, and diarrhoea. To mitigate these effects or enhance therapeutic efficacy, recent clinical studies focus on faecal microbiota transplantation or probiotic therapy to modulate the gut microbiota [53]. Despite promising results, further research is needed to fully understand the perioperative impact of microbiota-modulating agents. Current studies primarily focus on interventions during or immediately before surgery.

Conclusions

Prehabilitation, a relatively new concept, offers innovative perioperative care. Given the gut microbiota's crucial role, interventions starting at the be-

ginning of prehabilitation could significantly reduce postoperative complications, improve quality of life, and accelerate recovery. Current knowledge shows that microbiota supplement therapy in the perioperative period is mostly safe and beneficial. Tailoring interventions to individual patients requires further research considering specific procedures, intervention durations, and underlying diseases.

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Conflict of interest

The authors declare no conflict of interest.

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