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Review

Achalasia and Gut Microbiota: Is Dysbiosis an Overlooked Factor in Postoperative Surgical Outcomes?

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Abstract

Background: Esophageal achalasia is a rare motility disorder characterized by impaired lower esophageal sphincter (LES) relaxation and food stasis. Surgical interventions, including Heller myotomy with fundoplication or peroral endoscopic myotomy (POEM), effectively alleviate symptoms but induce significant anatomical and functional alterations. In various gastrointestinal surgeries, microbiota have been implicated in modulating clinical outcomes; however, their role in achalasia surgery remains unexplored. **Methods**: We performed a narrative literature search of various databases to identify studies exploring potential interactions between the gastroesophageal microbiota, achalasia pathophysiology, and surgical treatment, proposing clinical implications and future research avenues. **Results**: Chronic esophageal stasis in achalasia promotes local dysbiosis by facilitating aberrant bacterial colonization. Surgical restoration of esophageal motility and gastroesophageal transit induces substantial shifts in the microbial ecosystem. Analogous microbiota alterations following procedures such as fundoplication, gastrectomy, and bariatric surgery underscore the significant impact of mechanical modifications on microbial composition. Comprehensive microbiota profiling in patients with achalasia may enable the identification of dysbiotic phenotypes predisposed to complications, thereby providing personalized therapeutic interventions including probiotics, prebiotics, dietary modulation, or targeted antibiotic therapy. These insights hold promise for clinical benefits, including the mitigation of inflammation and infection, monitoring of surgical efficacy through microbial biomarkers, and optimization of postoperative nutritional strategies to reestablish microbial homeostasis, ultimately enhancing patient outcomes beyond conventional treatment paradigms. **Conclusions**: The gastroesophageal microbiota is a compelling mediator of surgical outcomes in achalasia. Future investigations integrating microbiological and inflammatory profiling are warranted to elucidate the functional role of the gastroesophageal microbiota and assess its potential as a biomarker and therapeutic target.

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1. Introduction

In recent decades, the gut microbiota (GM) has emerged as a pivotal factor in the pathophysiology of numerous gastrointestinal and systemic diseases, influencing immune modulation, inflammation, and tissue repair [1–5]. Dysbiosis, defined as an alteration in the composition and function of the GM, can contribute substantially to postoperative complications [6]. Consequently, there has been growing interest in strategies to modulate the GM (such as the use of probiotics, prebiotics, and fecal microbiota transplantation) to improve clinical outcomes and reduce surgical site infections, as well as other short- and long-term sequelae [6–10].

Despite this, the role of GM in patients with esophageal achalasia, a rare motility disorder characterized by loss of peristalsis and impaired relaxation of the lower esophageal sphincter (LES), remains unclear [1,11–13]. This dysfunction leads to stasis of ingested food within the esophagus, progressive esophageal dilation, and LES hypertrophy, which collectively predispose patients to dysbiosis and alterations in the esophageal mucosal microenvironment [14]. Patients with achalasia present with typical symptoms, including dysphagia, regurgitation, chest pain, and weight loss, and atypical manifestations, such as nocturnal cough, heartburn, and an increased risk of esophageal carcinoma [14].

Surgical and endoscopic interventions for achalasia, including Heller's myotomy (HM) with fundoplication and peroral endoscopic myotomy (POEM), significantly alter esophageal transit physiology and may affect local and systemic microbial environments, potentially influencing postoperative outcomes [14].

This narrative review aimed to synthesize current evidence on the role of GM in postoperative complications during general surgery, critically examine the mechanisms through which dysbiosis might affect outcomes after achalasia surgery, and propose directions for future clinical and translational studies.

Given the paucity of specific studies addressing microbiota in patients with achalasia, this review aims to provide a conceptual framework and rationale for guiding future investigations in this emerging yet understudied field.

2. Materials and Methods

This narrative review summarizes the current literature on the possible implications of the microbiota and postoperative surgical outcomes in achalasia patients.

We conducted a comprehensive literature search on PubMed, Cochrane Library, Embase, Scopus, and Google Scholar databases. The search strategy used Boolean operators to combine keywords and MeSH terms such as "microbiota", "post-achalasia surgery", "achalasia", "Heller Myotomy", "Peroral Endoscopic Myotomy", and "probiotics". Based on these combinations, we included articles from January, 2011 to May, 2025. Only English-language studies were included. We excluded incomplete, duplicate, and non-peer-reviewed preprint articles. We focused our attention on randomized controlled trials (RCTs), meta-analyses, systematic reviews, and observational studies on cohorts of patients. Our aim was to explore potential interactions between the gastroesophageal microbiota, achalasia pathophysiology, and surgical treatment, proposing clinical implications and future research avenues.

3. Esophageal Microbiota, Immune Response, and Surgical Implications

The GM is a complex ecosystem colonized by over 100 trillion microorganisms [1,2,15–17]. In addition to its digestive functions, the GM acts as a metabolic and immunological organ [18,19]. Immune homeostasis and intestinal barrier integrity depend on a balanced interaction among symbiotic, commensal, and potentially pathogenic microorganisms [15–17]. Under eubiotic conditions, the GM contributes to host protection by producing metabolites such as short-chain fatty acids (SCFAs), including butyrate, propionate, and acetate [20]. These metabolites exert anti-inflammatory effects, enhance intestinal epithelial barrier function, and modulate regulatory T cell activation, thereby maintaining immunological tolerance [18,19,21–23].

However, perioperative factors, including metabolic stress, systemic inflammatory response, fasting, and broad-spectrum antibiotic use, can profoundly disrupt GM composition, resulting in dysbiosis [24]. Dysbiosis is characterized by reduced microbial diversity (α-diversity), depletion of beneficial species, such as *Faecalibacterium prausnitzii* and *Bifidobacteria*, and expansion of pro-inflammatory pathobionts, notably members of the *Enterobacteriaceae* family, pathogenic *Clostridia*, and *Fusobacteria* [25–27]. This imbalance promotes the production of lipopolysaccharides (LPS) and other pro-inflammatory molecules that activate the toll-like receptor 4 (TLR4)/nuclear factor kappa B signaling pathway in innate immune cells. Moreover, dysbiosis facilitates translocation of bacteria and bacterial products into the bloodstream, contributing to sepsis, infectious complications, and delayed wound healing, as certain microbes interfere with neoangiogenesis and extracellular matrix remodeling [22,24–29].

Multiple studies on colorectal and gastric surgeries have demonstrated that pre- or postoperative dysbiosis correlates with increased complications such as postoperative ileus, surgical site infections, fistulas, and anastomotic leakage [30–36]. Specifically, decreased intestinal microbial diversity and dominance of pro-inflammatory bacteria are associated with a more complicated postoperative course [36–40]. Notably, predominance of *Enterococcus faecalis* and *Escherichia coli* in postoperative stool samples correlates with a higher risk of anastomotic leakage [37,38,41–44], whereas the *Lactobacillus* spp. and *Akkermansia muciniphila* are linked to improved recovery of intestinal function (Table 1) [45–51]. Furthermore, clinical trials have shown that perioperative administration of probiotics or symbiotics significantly reduces the incidence of postsurgical infections and shortens hospital stay [52,53].

Table 1. Key Pathogens of the Microbiota Relevant to Achalasia and Surgical Outcomes.

Microorganism	Role in Microbiota/Dysbiosis	Clinical Implications	Notes in Achalasia/Postoperative Context
PREVOTELLA SPP.	Increased in esophageal stasis and inflammation	Potential pro-inflammatory role	High abundance in dilated esophagus
FUSOBACTERIUM SPP.	Associated with mucosal inflammatory processes	Potential promotion of chronic inflammation	Elevated in reflux and stasis
ENTEROBACTERIACEAE	Proliferation in bile reflux-altered environment	Associated with mucosal damage and potential infection	Increased post-POEM or biliary reflux
***FIRMICUTES* (REDUCTION)**	Reduction in beneficial species	Loss of barrier and immune control	Reduced microbial diversity in achalasia
LACTOBACILLUS SPP.	Protective fermentative bacteria	Potential role in maintaining equilibrium	Decreased after reflux-inducing procedures
CANDIDA SPP.	Opportunistic fungi proliferating in dysbiosis	Risk of opportunistic infections in compromised esophagus	Reported in patients with stasis and esophageal dysfunction

Although direct evidence in patients with achalasia is currently lacking, it is plausible to hypothesize that microbiota modulation similarly affects postoperative outcomes in this setting (Table 2). Impaired esophageal motility in achalasia, exacerbated by chronic food stasis, may induce significant alterations in local pH and microbial colonization [54]. Such changes can affect both esophageal and gastric microbiota, potentially fostering a pro-inflammatory environment or enabling colonization by opportunistic pathogens—

especially following interventions like HM or POEM [54–57]. Unlike the extensively studied intestinal microbiota, the esophageal microbiota has only recently gained attention. Under normal conditions, the lower esophagus harbors a relatively low-diversity microbiota, predominantly composed of *Firmicutes* (e.g., *Streptococcus* spp.), *Proteobacteria* (e.g., *Neisseria*), and *Bacteroidetes* [58–60]. Its composition is shaped by saliva, swallowing, retrograde reflux, and esophageal motility [58,61,62]. In disorders such as achalasia or GERD, esophageal dysbiosis has been associated with increased abundance of *Fusobacterium*, *Prevotella*, and *Candida*, which may contribute to mucosal inflammation, metaplasia, and carcinogenesis [62].

Table 2. Alterations of Microbiota in Esophageal Stasis and Reflux Conditions: Potential Correlations with Achalasia.

Condition	Type of Dysbiosis Reported	Pathogenetic Mechanism	Relevance for Achalasia
CHRONIC ESOPHAGEAL STASIS	Increase in oral bacteria (Prevotella, Fusobacterium)	Slowed transit → retrograde bacterial growth	Typical scenario in untreated achalasia
GASTROESOPHAGEAL REFLUX	Reduced diversity, increase in pro-inflammatory microbes	Acid/bile reflux → hostile microenvironment	Possible after myotomy without fundoplication
EXPOSURE TO BILIARY SECRETIONS	Increase in Enterobacteriaceae, reduction in Firmicutes	Duodenal reflux → mucosal damage and microbial selection	Risk after POEM procedure
ADVANCED ACHALASIA	Scarce data (hypothetical increase in anaerobic microorganisms)	Stasis and esophageal dilation → fermentative environment	Central hypothesis to be tested in future studies

4. Post-Operative Complications and Dysbiosis: Evidence in General Surgery

In recent years, interest in the role of GM in postoperative processes has grown substantially, with an increasing number of clinical and preclinical studies demonstrating correlations between intestinal dysbiosis and postsurgical complications in patients undergoing major abdominal surgery [34,36–39,42,43,58]. These complications include surgical site infections (SSI), postoperative ileus, anastomotic leakage, systemic inflammatory response syndrome (SIRS), and impaired wound healing.

4.1. Surgical Site Infections (SSI)

Patients undergoing colorectal resection often exhibit an unfavorable intestinal microbial profile characterized by predominance of proteobacteria and reduction in *Firmicutes* and *Bacteroidetes*. These dysbiotic profiles are associated with increased rates of postoperative infections [41,44,53]. Ohigashi et al. reported that patients who developed SSI after colorectal surgery had significantly lower concentrations of *Bifidobacteria* and *Lactobacillus* spp., which are known for their immunomodulatory effects and competitive inhibition of opportunistic pathogens [63]. The prevailing hypothesis suggests that dysbiosis impairs intestinal dendritic cell maturation, leading to an exaggerated systemic inflammatory response and heightened susceptibility to infections by opportunistic bacteria, such as *Enterococcus faecalis* and *Pseudomonas aeruginosa*, including at surgical sites [60–62].

4.2. Postoperative Ileus and Neuroimmune Dysbiosis

Postoperative ileus is one of the most common and debilitating complications of abdominal surgery [63]. Emerging evidence indicates that surgery- or antibiotic-induced dysbiosis disrupts bidirectional communication between the microbiota and enteric nervous system (gut–brain axis) [64]. In murine models, antibiotic-driven dysbiosis prolongs postsurgical ileus duration, whereas restoration of the microbiota via conventional means or probiotics accelerates the recovery of intestinal motility [65,66]. This beneficial effect is likely mediated by the reduced activation of pro-inflammatory intestinal macrophages and enhanced production of neuroprotective SCFAs [67].

4.3. Anastomotic Leakage

Anastomotic leakage is a severe complication of gastrointestinal surgery with potential progression to peritonitis and sepsis [44,68]. Shogan et al. demonstrated that certain intestinal pathogens secrete bacterial metalloproteinases that degrade collagen in the extracellular matrix, thereby compromising anastomotic integrity [69]. Specifically, *Enterococcus faecalis* enzymatically digests hydroxylated lysine, a critical component of type I collagen, thereby undermining wound strength [69]. Furthermore, empirical perioperative antibiotic use can disrupt protective microbial populations and favor the proliferation of pathogenic bacteria, thereby increasing the risk of anastomotic failure [44].

4.4. Systemic Dysbiosis and Aberrant Inflammatory Response

Dysbiosis also affects postoperative systemic inflammation through microbial translocation [70]. Bacteria and bacterial components, such as LPS and peptidoglycans, can traverse a compromised intestinal barrier, enter systemic circulation, and activate TLRs on innate immune cells [71]. This process can trigger non-infectious systemic inflammatory responses, such as fever, leukocytosis, and SIRS, even in the absence of detectable bacteremia [72].

4.5. Relevance to Esophageal Achalasia

Although most studies have focused on colorectal, hepatobiliary, pancreatic, and bariatric surgeries, these findings are relevant to achalasia surgery. Persistent preoperative food stasis in achalasia may create a microenvironment conducive for anaerobic bacterial proliferation, potentially impacting postoperative outcomes [11,14]. Additionally, achalasia surgery procedures (including laparoscopic or robotic HM and POEM) alter gastroesophageal physiology (Figure 1) [14,54]. These interventions affect food transit, acid exposure, the esophageal microbial environment, and gastroesophageal valve function, potentially promoting retrograde migration of gastric and intestinal microbiota (Table 3) [54,73]. Such alterations may facilitate esophageal colonization by bacteria that are not normally present, as observed in conditions such as reflux esophagitis, esophageal dysmotility, and stasis [11,54,74–80].

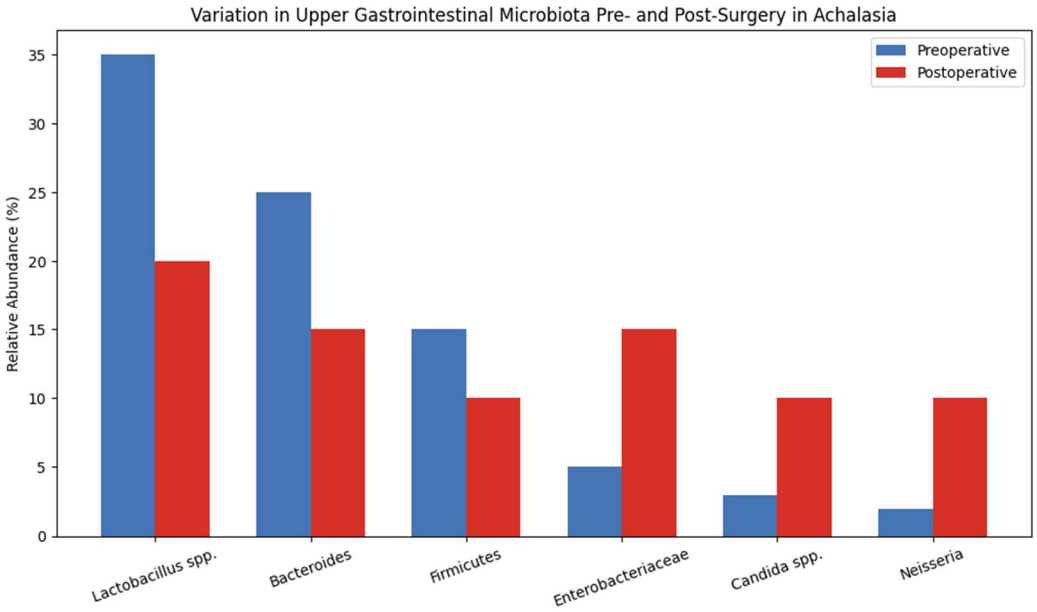

Figure 1. Relative abundance of selected gut microbial taxa before and after surgical treatment for achalasia. Changes in the esophageal microbiota composition in patients with achalasia undergoing

surgical treatment (POEM). The chart illustrates a reduction in beneficial strains such as *Lactobacillus* spp. and *Bacteroides*, and a postoperative increase in potentially pathogenic taxa such as *Neisseria*. These changes may be associated with surgical manipulation, perioperative antibiotic use, and altered esophageal pH post-treatment. The observed dysbiosis suggests a possible role in the development or exacerbation of postoperative complications [54].

Table 3. Surgical Interventions for Achalasia and Potential Effects on Gastroesophageal Microbiota.

Surgical Technique	Anatomical–Functional Modifications	Potential Impact on Microbiota	Clinical Notes
HELLER MYOTOMY + FUNDOPLICATION	LES release + partial antireflux barrier	Minimal reflux, lower risk of dysbiosis	Protective standard against dysbiosis
POEM	LES release without antireflux protection	Increased acid/bile reflux → possible dysbiosis	May alter microbial environment long-term
LAPAROSCOPIC MYOTOMY	Like Heller but sometimes without fundoplication	Depends on presence of antireflux barrier	Postoperative microbiological studies lacking

5. Esophageal Achalasia, Surgery, and Microbiota: A Theoretical but Plausible Interaction

Laparoscopic and robotic HM combined with Dor or Toupet fundoplication are recommended for achalasia types I and II (according to the Chicago classification), whereas POEM is generally preferred for type III achalasia [78]. Most patients experience significant and sustained symptom relief after surgical or endoscopic intervention [54]. Nonetheless, a subset of patients continue to report persistent symptoms despite negative findings on follow-up evaluations [54,80–82]. In these cases, the potential contribution of the esophageal microbiota to symptom persistence deserves investigation [54,83–85]. Dysbiosis and mucosal microenvironment alterations may underlie residual esophageal motility dysfunction, local inflammation, or mucosal hypersensitivity, opening new avenues for studies and adjunctive therapeutic strategies [54,86–90].

5.1. Esophageal Microbial Environment in Achalasia: Stasis and Abnormal Bacterial Colonization

Recent clinical studies have demonstrated that patients with untreated achalasia exhibit significant alterations in the esophageal microbiota [81–83]. Specifically, increased relative abundance of anaerobic and microaerophilic taxa such as *Prevotella*, *Fusobacterium*, and *Neisseria* has been reported, likely due to chronic esophageal stasis and altered luminal pH [83]. These microbial communities may contribute to mucosal inflammation and could be involved in the pathogenesis of esophagitis and metaplastic transformation [81–83]. Following surgical treatment, particularly with POEM, further microbiota shifts have been observed. Yeh et al. (2023) and Takahashi et al. (2021) documented postoperative reductions in beneficial commensals like *Lactobacillus* spp. and *Bacteroides*, alongside increases in potentially pro-inflammatory taxa [14,54]. These changes are likely influenced by surgical disruption, increased exposure to acid and bile, and perioperative antibiotic use [81,84]. Collectively, these findings support the hypothesis that esophageal dysbiosis may influence healing processes and the persistence of postoperative symptoms.

Under normal conditions, the esophagus is primarily colonized by *Firmicutes* and *Proteobacteria*, with peristalsis, antibacterial saliva, and retrograde gastric acidity acting as protective factors [54,75]. In achalasia, chronic stasis of food and saliva alters the esophageal milieu by changing pH and reducing oxygen availability, thereby creating a niche conducive to bacterial overgrowth [54,73]. Although direct data on esophageal microbiota in achalasia remain limited, it is plausible that aberrant bacterial proliferation occurs, particularly in anaerobic and microaerophilic species [75,76]. This pattern parallels observations in other stasis-related conditions such as esophageal diverticula and intestinal pseudo-

obstruction [12,76]. The frequent occurrence of fungal infections, chronic esophagitis, and Barrett's metaplasia in advanced achalasia further supports the notion of disrupted host microbiota equilibrium [12,75–77].

Long-standing achalasia fosters abnormal bacterial colonization and fermentation within the esophagus, thereby producing potentially harmful metabolites, such as SCFAs, aldehydes, and nitrosamines, which contribute to chronic mucosal inflammation [12]. This persistent inflammatory state has been implicated in esophageal carcinogenesis, particularly in the development of squamous cell carcinoma, positioning bacterial fermentation as a potential cofactor in neoplastic transformation in untreated chronic achalasia [12].

5.2. Effects of Surgery on the Gastroesophageal Microbiota

The principal surgical treatments for achalasia (HM with Dor or Toupet fundoplication and POEM) induce substantial anatomical and physiological changes [78–80]. HM is a surgical procedure performed via a laparoscopic or robotic approach that involves a longitudinal incision of the circular muscle fibers of the distal esophagus and proximal stomach to relieve the functional obstruction caused by non-relaxing lower esophageal sphincter (LES) [78].

The extent of the myotomy typically spans 6–8 cm in the esophagus and 2–3 cm into the gastric cardia [78]. Myotomy is associated with partial fundoplication to reduce gastroesophageal reflux [78]. Dor fundoplication, an anterior 180° wrap, is often preferred in cases with mucosal perforation risk or in patients with prior thoracic interventions due to its simplicity and reduced tension in the esophageal wall [90]. Conversely, Toupet fundoplication, a posterior 270° wrap, is favored when enhanced reflux control is needed, particularly in patients with pre-existing reflux or esophagitis [78]. Both approaches aim to preserve esophageal clearance while minimizing reflux, with selection based on surgeon experience, anatomical considerations, and individual patient physiology [78,91].

In contrast, POEM is a minimally invasive endoluminal technique that employs a flexible endoscope to access the esophageal submucosa [78]. After a mucosal incision is made 10–12 cm proximal to the gastroesophageal junction, a submucosal tunnel is created, allowing for targeted myotomy of the circular muscle layer extending 6–10 cm distally [78]. Unlike HM, POEM does not include an antireflux procedure, which accounts for its higher incidence of postoperative acid and bile reflux [78]. However, POEM offers superior flexibility in tailoring the length and location of the myotomy and is especially advantageous in type III achalasia or spastic esophageal disorders involving the mid or proximal esophagus [78]. It is also suitable for patients with prior failed interventions. The submucosal tunnel preserves mucosal integrity, while the deep muscle incision effectively disrupts hypercontractile or non-relaxing segments [78]. Despite its technical complexity, POEM has demonstrated excellent short- and long-term outcomes in symptom relief and is increasingly favored in specialized centers for complex motility disorders [78].

Notably, a sustained reduction in basal LES pressure promotes gastroesophageal reflux, facilitating the ascent of gastric and duodenal bacteria into the esophageal lumen. Increased acid and bile reflux may further affect the esophageal microbiota by selecting acidophilic or pathogenic species [79–81]. Post-POEM studies have reported the occurrence of alkaline reflux gastritis and gastric bacterial overgrowth, phenomena capable of altering the microbiota throughout the upper gastrointestinal tract [14,78,81]. Improved postoperative esophageal clearance might reduce bacterial stasis but also promote recolonization by gastric and oral microbiota, the clinical significance of which remains undetermined. Despite individual descriptions of these phenomena, no study has yet systematically characterized pre- and postoperative microbiota changes in patients with achalasia or correlated these

changes with clinical outcomes, such as persistent dysphagia, reflux, esophagitis, infections, or mucosal healing.

5.3. Analogous Findings from Related Surgeries: Fundoplication, Gastrectomy, Bariatric Surgery

In the absence of achalasia-specific data, evidence from gastric surgery, which alters sphincter pressure and digestive physiology, is informative. Following Nissen fundoplication, mucosal and salivary analyses reveal reduced esophageal microbial diversity and increased anaerobic bacteria, especially in cases of valve dysfunction or persistent reflux [79,80,82–84]. Patients undergoing total or sleeve gastrectomy exhibit enrichment of oral bacteria in the upper intestinal tract, linked to loss of gastric acidity and reduced peristalsis, with potential metabolic and inflammatory consequences [38,39,41,58,85]. Bariatric surgery induces marked changes in the intestinal microbiota, which correlate with improved insulin resistance and systemic inflammation, indicating that targeted anatomical alterations can therapeutically modulate host–microbiota interactions [38,39,41,58,86].

5.4. Hypotheses for Future Investigations

Based on these considerations, it is plausible that achalasia surgery significantly alters the esophageal and gastric microbiota, and that preoperative dysbiosis may impact long-term clinical outcomes such as refractory reflux, chronic mucosal inflammation, or bacterial overgrowth. Future studies should investigate whether perioperative microbiota monitoring (via salivary, esophageal, or gastric sampling) can serve as a predictive or therapeutic tool for achalasia treatment.

6. Future Perspectives and Clinical Implications: Microbiota as an Emerging Target in Achalasia Surgery

An analysis of the available evidence indicates that GM is a critical determinant of the inflammatory response and postoperative outcomes across multiple surgical domains. However, in the context of the surgical treatment of achalasia, the role of GM remains largely unexplored. This represents a significant gap in the current literature, particularly considering the anatomical and functional alterations induced by achalasia and its treatment, which likely affects esophageal and gastric microbial microenvironments (Table 4).

Table 4. Clinical Implications and Future Research Directions on Microbiota in Achalasia Surgery.

Field	Possible Clinical Applications	Open Research Questions
DIAGNOSTICS	Microbiota profiling pre- and post-intervention	Are there dysbiotic phenotypes predictive of poor surgical outcomes?
PREVENTION	Prebiotic/probiotic interventions in selected patients	Can microbiota modulation reduce postoperative complications?
PERSONALIZED TREATMENT	Surgical technique choice based on individual microbiota	Can microbiota guide choice between POEM and Heller + fundoplication?
POSTOPERATIVE SURVEILLANCE	Use of microbial markers for monitoring	Can dysbiosis predict recurrent symptoms or persistent reflux?

6.1. Research Perspectives: Directions for Future Studies

Achalasia refers to a chronic condition of esophageal stasis, which alters local protective mechanisms (peristalsis, retrograde acidity, salivary flow) and favors abnormal microbial colonization, presumably enriched with anaerobes and oral pathogens [12,87–92]. After HM with fundoplication or POEM, an abrupt change in pressure dynamics and esophago-gastric transit occurs [11,14,78,93–97]. This may promote improved mechanical clearance, limiting bacterial stasis and hypercolonization, and promote chronic gastroduodenal reflux, again altering the pH and esophageal bacterial populations [14,55,57,78,89].

These elements suggest that the interaction between GM, esophageal mucosa, and post-surgical inflammation may be relevant in the clinical evolution of patients operated on for achalasia, especially in relation to the appearance of refractory reflux, chronic esophagitis, metaplasia, atypical chest pain, and persistent functional disorders. Considering the theoretical framework presented, some priority lines of investigation can be outlined, with potential clinical implications.

6.1.1. Pre- and Postoperative Profiling of the Esophageal and Gastric Microbiota

The use of high-throughput sequencing technologies, such as 16S rRNA gene sequencing or shotgun metagenomics, allows for the comprehensive analysis of esophageal and gastric microbiota from preoperative endoscopic samples (e.g., mucosal biopsies, esophageal washings, or brushings) and their longitudinal monitoring following myotomy [76,87–97]. In the reviewed studies, microbiota composition was assessed using techniques such as 16S rRNA gene sequencing and, in some cases, shotgun metagenomics [90–95]. The sampling methods included esophageal mucosal biopsies, submucosal brushings, and lavage fluid obtained during endoscopy or POEM [95–97]. Analytical workflows quantified microbial diversity (e.g., α- and β-diversity), relative abundance, and taxonomic shifts [90–96]. These methods enabled the identification of dysbiotic patterns, such as loss of *Lactobacillus* and enrichment of *Prevotella* or *Fusobacterium*, correlated with esophageal stasis or reflux after myotomy [88].

Such profiling could help identify microbial signatures associated with specific postoperative phenotypes (e.g., reflux, residual dysphagia, and infection), clarify the dynamics of post-myotomy retrograde microbial colonization across the LES, assess the presence of SCFA-producing bacteria, and enrich pathobionts [76,88].

6.1.2. Correlation with Local and Systemic Inflammatory Markers

Integrating microbiota data with local and systemic inflammatory profiles (e.g., interleukin (IL)-6, IL-1β, tumor necrosis factor alpha, zonulin, and salivary or serum calprotectin) could elucidate shared pathophysiological mechanisms linking dysbiosis to mucosal inflammation and postoperative complications [87–89].

6.1.3. Predictive Role of the Microbiota in Postoperative Outcomes

As observed in colorectal and bariatric surgery, it is plausible that preoperative microbiota composition may affect the development of postoperative esophagitis or refractory reflux, the time course of functional recovery, and the need for long-term antisecretory therapy [13,39,58,81,83].

6.1.4. Microbiota Modulation Strategies

If significant associations are established, targeted interventions to modulate microbiota in the perioperative period may be considered. These could include the following: administration of oral probiotics or symbiotics to counteract dysbiosis and inflammation; prebiotic dietary strategies rich in fermentable fibers; rational, selective use of perioperative antibiotics to limit collateral damage to commensal flora; and experimental topical treatments (e.g., oroesophageal gargles, washes, or probiotic gels) designed to directly modulate the upper GI microbiome [90–95]. Although it is limited, evidence suggests that oral administration of probiotics such as *Lactobacillus reuteri* and *Bifidobacterium animalis* may reduce gastric inflammation and modulate upper GI microbiota [95]. For example, randomized controlled trials demonstrated that *L. reuteri* reduced *Helicobacter pylori* colonization and improved dyspeptic symptoms [94–96]. Other studies report decreased expression of esophageal proinflammatory cytokines and improved mucosal integrity in GERD patients treated with probiotics, suggesting a protective effect on the esophageal

microenvironment [94–96]. These findings, although preliminary, support the rationale for probiotic modulation in achalasia-related dysbiosis.

6.2. Translational Implications and Therapeutic Opportunities

The integration of advanced microbiological techniques, surgical practices, and immunological insights may revolutionize the management of post-surgical achalasia, transitioning toward a more personalized and predictive model of care. For example, the identification of pathogen-dominated microbiota profiles may help stratify patients at risk of post-POEM reflux, thereby influencing the choice between POEM and HM with fundoplication; the presence of dysbiosis-related biomarkers could guide personalized probiotic prophylaxis, and longitudinal microbiota surveillance could serve as a tool for monitoring disease progression, particularly toward chronic esophagitis or Barrett's metaplasia.

Although no direct clinical or experimental studies have yet investigated the microbiota–surgery interaction in the treatment of achalasia, evidence from related surgical and gastroenterological contexts supports the plausibility of a clinically meaningful link. From a translational medicine perspective, elucidating this axis offers a promising avenue to better understand postoperative complications, optimize therapeutic strategies, and prevent the progression of esophageal disease.

Comprehensive characterization of the microbiota before and after surgical intervention, supported by longitudinal cohort studies and interventional clinical trials, can establish a foundation for a microbiota-sensitive approach to achalasia surgery. Such a paradigm has the potential to enhance not only patient outcomes but also our broader understanding of the disease's pathogenesis.

7. Conclusions

The GM has emerged as a potential mediator in the pathophysiology and postoperative outcomes of achalasia. While this review incorporates insights from other gastrointestinal surgeries to support biological plausibility, its central focus remains on the microbiota-specific implications in achalasia. Despite limited direct evidence, available data suggest that disease- and surgery-induced microbial shifts may influence symptoms, reflux, and mucosal healing. Future studies integrating microbiota profiling, inflammatory markers, and clinical outcomes are needed to develop targeted modulation strategies. Such an approach may offer a new frontier in personalized care and translational research in achalasia management.

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Abbreviations

The following abbreviations are used in this manuscript:

LES	Lower esophageal sphincter
POEM	Peroral endoscopic myotomy
HM	Heller myotomy
EF	*Enterococcus faecalis*
EC	*Escherichia coli*
TLRs	Activating Toll-like receptors
AM	*Akkermansia muciniphila*
SSI	Surgical site infections
GM	Gut microbiota
LPS	Lipopolysaccharides

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