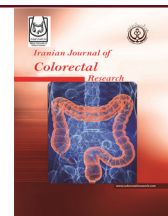


# Iranian Journal of Colorectal Research



## Potential Impact of Probiotics on Low Anterior Resection Syndrome: An Emerging Area of Research

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Received: 2023-09-01

Revised: 2023-09-15

Accept: 2023-09-15

Please cite this paper as:

Shojaei-Zarghani S, Safarpour AR, Bananzadeh AM. Potential Impact of Probiotics on Low Anterior Resection Syndrome: An Emerging Area of Research. *Iran J Colorectal Res.* 2023;11(1). doi: .

The worldwide age-standardized incidence and mortality rates of rectal cancer are estimated to be 7.6 and 3.3 per 100,000, respectively (1). Previous literature suggests that low anterior resection (LAR) may be superior to abdominoperineal resection (APR) for rectal cancer, with better 5-year survival, local recurrence rate, oncological outcomes, and prognosis (2). However, it is reported that around 41% of patients who underwent LAR experience major low anterior resection syndrome (LARS) one year after surgery. LARS is characterized by fecal and gas incontinence, diarrhea, urgency or frequency of stools, sensation of incomplete emptying, and clustering of bowel motions (3). These symptoms are reported to persist over time and influence health related quality of life (4), functional bowel symptoms may also occur after sigmoid resection (5). Despite assessing the effects of several therapeutic strategies in reducing the LARS symptoms, its treatment is still challenging (6).

Perturbation of the gut microbiome has been linked to numerous chronic diseases, such as obesity, endocrine disorders, gastrointestinal diseases, cancer, cardiovascular diseases, etc.(7). Therefore, several research studies have been conducted to assess the effects of modulating the gut microbiome using pre/probiotics. The potential effects of probiotics on colonic disorders complicated by incontinence and abnormal frequency have also been investigated (8, 9). The bidirectional relationship between the gut

microbiome and colonic motility (8) emphasizes the need to assess both the effects of probiotics on LARS and the impact of LARS on gut microbiota.

Few randomized controlled trials (RCT) have assessed the effects of probiotics on LARS score following rectal cancer surgeries with conflicting findings. *Lactobacillus plantarum* CJLP243 as well as VSL#3 (a combination of *Streptococcus thermophilus*, *Bifidobacterium breve*, *Bifidobacterium longum*, *Bifidobacterium infantis*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus delbrueckii* subsp. *bulgaricus* and *Lactobacillus plantarum*) supplementation had no effects on bowel motions and LARS score when administered in the perioperative period of ileostomy reversal or exactly following reversal of a temporary loop ileostomy (10, 11). However, in another RCT, probiotic administration (*Bifidobacterium animalis* subsp. *lactis* HY8002, *Lactobacillus casei* HY2782, and *Lactobacillus plantarum* HY7712), starting one week before surgery and continuing for 21 days after anterior sigmoid colon cancer resection, improved flatus control compared to the placebo. Nonetheless, it had no effect on the total LARS score (12). Differences in the site of cancer, type and dosage of probiotics, and timing following surgery or stoma reversal could explain this conflicting evidence.

A recent study evaluated gut microbiome 13.3 and 2.2 months after LAR and ileostomy closure, respectively. A decreased diversity of gut microbiome,

a higher level of *Bacteroidaceae* enterotype, and lower levels of *Prevotellaceae* enterotype and lactic acid-producing bacteria, including *Lactobacillus* and *Bifidobacterium*, were detected in patients with frequency-dominant LARS. The authors suggested that modulating gut microbiota could be a potential therapeutic option for patients experiencing symptoms related to frequency, including frequency, clustering, and urgency, but not for those with an incontinence-dominant pattern of LARS (13).

Based on the existing literature, it is recommended that the long-term effects of pre/probiotics be assessed after overcoming the acute phase of LARS, which typically occurs immediately following surgery and

stoma reversal. Research should also investigate the effects of probiotics on various symptoms of LARS and their impact on the gut microbiome.

### Authors' Contribution

Sara Shojaei-Zarghani, AliReza Safarpour, Alimohammad Bananzadeh: substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; all authors approved the final version.

**Conflict of interest:** None declared.

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