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Retrospective Study

Factors influencing analysis of the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer

Probiotics and Nutrition in CRC Recovery

Abstract

BACKGROUND

Colorectal cancer is a prevalent malignancy with suboptimal postoperative recovery outcomes. Enhancing recovery and prolonging disease-free survival remains a critical challenge. This study investigates factors influencing the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer.

AIM

This study aims to identify predictors of therapeutic efficacy for probiotics combined with enteral nutrition in postoperative patients with colorectal cancer.

METHODS

A retrospective study was conducted with 511 patients with colorectal cancer who underwent surgery and received probiotics and enteral nutrition from January 2022 to March 2025. Patients were categorized into the "good efficacy group" (n = 279) and "poor efficacy group" (n = 232) based on outcomes observed 3 months post-surgery. Variables assessed included gut microbiota composition, nutritional intake, immune and inflammatory markers, and demographic characteristics.

RESULTS

Patients with favorable outcomes were typically younger, had higher caloric, protein, and fiber intake, and displayed enhanced intestinal mucosal barrier function with elevated levels of *Bifidobacterium* and *Lactobacillus*. Immune markers such as immunoglobulin A, immunoglobulin M, immunoglobulin G, and CD4+/CD8+ T-cell ratios were significantly higher in the good efficacy group. High numbers of *Fusobacterium nucleatum* and *Bacteroides fragilis* and levels of tumor necrosis factor-alpha and interleukin-6 were associated with poor efficacy. Multivariate analysis identified age, tumor node metastasis stage, protein intake, and gut microbiota composition as significant predictors of therapeutic success.

CONCLUSION

The efficacy of combining probiotics with enteral nutrition in postoperative patients with colorectal cancer was influenced by age, nutritional intake, microbiota balance, immune status, and inflammatory markers.

Key Words: Colorectal cancer; Probiotics; Enteral nutrition; Postoperative recovery; Gut microbiota; Immune markers

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Core Tip: This retrospective study identifies key predictors influencing the efficacy of probiotics combined with enteral nutrition in 511 postoperative colorectal cancer patients. Younger age, higher protein intake, balanced gut microbiota (elevated Bifidobacterium, reduced Fusobacterium nucleatum), and improved immune markers independently correlated with better outcomes. These findings highlight modifiable factors—nutritional optimization and microbiota modulation—for enhancing recovery.

Multivariate analysis confirmed age, Tumor Node Metastasis stage, protein intake, and microbial composition as significant prognostic indicators.

INTRODUCTION

Colorectal cancer, which remains one of the most prevalent malignancies globally, poses significant challenges to healthcare systems and affects a considerable proportion of the adult population. Despite advancements in surgical techniques and adjuvant therapies, postoperative recovery in patients with colorectal cancer remains suboptimal and is often complicated by recurrence, metastasis, and impaired quality of life. The demand for innovative therapeutic strategies that enhance recovery and prolong disease-free survival has fueled interest in adjunctive treatments, particularly those that can modulate gut microbiota and nutritional absorption [1–3].

In recent years, the integration of probiotics with enteral nutrition has garnered attention as a promising intervention to enhance postoperative outcomes in patients with colorectal cancer. Probiotics, defined as live microorganisms that confer health benefits to the host when administered in adequate amounts, play an integral role in maintaining gut homeostasis[4]. They have been shown to influence immune responses, compete against pathogenic bacteria, and reinforce the gut mucosal barrier. Enteral nutrition is critical in supplying necessary macronutrients and micronutrients that support tissue repair, immune function, and overall metabolic stability to facilitate a favorable surgical recovery. The synergistic potential of combining probiotics with enteral nutrition offers a multifaceted approach to addressing the complex needs of postoperative patients with colorectal cancer[5,6].

The gut microbiota, a dynamic community of microorganisms residing in the gastrointestinal tract, significantly influences local and systemic health processes. Numerous studies have illuminated the impact of the gut microbiome on cancer progression, immune modulation, and inflammatory processes[7,8]. Specifically, the presence and balance of beneficial bacteria such as *Bifidobacterium* and *Lactobacillus*, contrasted with pathogenic species, such as *Fusobacterium nucleatum* and *Bacteroides* *fragilis*, appear to be key determinants in the therapeutic efficacy of probiotics[9]. Alterations in microbial composition can affect mucosal immunity and the gut barrier, both of which are crucial in the host's ability to recover from surgical interventions and resist tumor recurrence[10].

Nutritional intake is a cornerstone of postoperative care and influences recovery through wound healing, muscle maintenance, and overall homeostasis. Enteral nutrition not only ensures continuous supply of vital nutrients but also preserves the functionality of the gastrointestinal tract to provide an environment conducive to probiotic activity and microbial balance[11,12]. High caloric, protein, and fiber intake has been linked with improved gut health and enhanced immune responses, suggesting that targeted nutritional strategies can optimize therapeutic outcomes in cancer patients[13].

Despite the theoretical and preliminary clinical underpinnings supporting the combination of probiotics and enteral nutrition, precise factors influencing their efficacy have not been comprehensively elucidated. This is particularly relevant for understanding why certain patients derive significant benefit while others do not. The interplay between these factors and their collective impact on postoperative recovery remains an area of active investigation and clinical importance[9].

Inflammatory responses play a crucial role in the healing process and are influenced by nutritional and microbial factors[14,15]. 3 Elevated levels of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), are often markers of suboptimal recovery and poor prognosis in patients with colorectal cancer. Probiotics have been proposed to mitigate inflammation, enhance mucosal barrier integrity, and thus indirectly improve the postoperative course[16,17].

MATERIALS AND METHODS

2.1 Study Design

A retrospective study was performed involving 511 patients with colorectal cancer who underwent surgical procedures and subsequently received a combination of probiotics and enteral nutrition treatment at the First People's Hospital of Zunyi between January 2022 to March 2025. Patients were divided into two groups based on their therapeutic outcomes observed 3 months post-surgery: The "good efficacy group" (n = 279) and the "poor efficacy group" (n = 232). Patients were classified as belonging to the "poor efficacy group" if they experienced any of the following within 3 months after surgery: Imaging-confirmed tumor recurrence or metastasis; occurrence of a serious post-operative complication requiring significant intervention; and elevated serum tumor marker levels exceeding established normal ranges. Patients who did not experience any of these adverse events and showed stable or improved clinical parameters, including no evidence of tumor recurrence or metastasis, absence of significant postoperative complications, and normal serum tumor marker levels, were classified into the "good efficacy group.

2.2 Ethical Statement

The study received approval from the institutional review board and ethics committee of the First People's Hospital of Zunyi. The need for informed consent was waived because of the retrospective nature of the study and the use of anonymized patient data. This exemption was granted in alignment with established regulatory and ethical guidelines for conducting retrospective analyses to ensure that no potential risks or adverse consequences affect the patients.

2.3 Inclusion and Exclusion Criteria

The inclusion criteria for the study were as follows: (1) a confirmed diagnosis of colorectal cancer through pathological examination, without invasion of adjacent tissues or organs and no distant metastasis; (2) first-time diagnosis of colorectal cancer; (3) aged 18 years or older; (4) underwent colorectal cancer surgery at the First People's Hospital of Zunyi; (5) Eastern Cooperative Oncology Group performance status (ECOG) score of 0–2 points The ECOG score is a scale used to assess the general health and functional status of cancer patients. This scale classifies patients' activity levels from 0 (fully active, symptomatic but without restricted activity) to 5 (death)[18]; and (6) availability of complete clinical data.

The exclusion criteria were as follows: (1) the presence of concurrent malignant tumors; (2) severe infections or immunological diseases; (3) significant lesions in vital organs such as the heart, liver, or kidneys; (4) conditions such as intestinal obstruction or perforation prior to treatment; (5) use of probiotic preparations or antibiotics within 3 weeks before treatment; (6) receipt of neoadjuvant therapy, including radiotherapy, chemotherapy, targeted therapy, or immunotherapy, prior to surgery; and (7) severe malnutrition or obesity.

2.4 Treatment Methods

The enteral nutrition formula used was Youkangli (National Food Registration No. TY20200002), containing 15.8 g protein, 1600 kJ, energy, and 3.5 g dietary fiber per 500 mL. The enteral nutrition protocol was as follows: Postoperative day 1: 100 mL of Youkangli (diluted concentration), with 50 mL per dose at ≥ 2-hour intervals; postoperative day 2: 250 mL of Youkangli at 50 mL per dose at ≥ 2-hour intervals; postoperative day 3: 500 mL of Youkangli at 50 mL per dose at ≥ 2-hour intervals; postoperative day 4: 1000 mL of Youkangli self-administered orally; postoperative day 5: Full enteral nutrition volume (1 g protein/kg/day, 83.7–104.6 kJ energy/kg/day), with any deficit supplemented by parenteral nutrition. The intervention continued until postoperative day 7. Hospital dietitians were responsible for preparing and delivering the formulas to patients. After surgery, the patients commenced a regimen of probiotic granules (containing *Lactobacillus acidophilus*, *Bifidobacterium longum*, *Lactobacillus paracasei*, *Lactobacillus rhamnosus*, *Lactobacillus fermentum*, *Lactobacillus helveticus*, and *Streptococcus thermophilus)*, which were produced by Synbio Tech (Nanjing) Co., Ltd. and commissioned by Shanghai Licheng Nutrition Products Technology Co., Ltd. (Product standard: Q/SHKJ00035, Production license: SC10632012400092). The probiotics were administered at a dosage of two sachets daily (live bacteria count > 10^{10}

CFU/sachet), taken orally with warm water below 40 °C 30 minutes after breakfast, for 12 weeks.

2.5 Detection Methods

2.5.1 Gut Microbiota Detection

The primary objective was to assess changes in the quantities of four bacterial groups: *Bifidobacterium*, *F. nucleatum*, *Lactobacillus*, and *B. fragilis* across three time points, namely, before treatment, on day 1, and on day 7 after treatment[19]. The detection method involved collecting fresh fecal samples from patients before starting chemotherapy and on the morning of the fifth day of chemotherapy. A 0.1 g sample of fresh feces was placed in a sterile centrifuge tube and diluted tenfold with 0.9 mL of sterile saline. A 10 μL aliquot of this suspension was serially diluted and inoculated onto selective media. The media used included BBL for *Bifidobacterium* (Beijing Luqiao Technology Co., Ltd.), CDC anaerobic blood agar for *F. nucleatum* and *B. fragilis* (Tianjin Jinzhang Science and Technology Development Co., Ltd.), and MRS agar for *Lactobacillus* (Hangzhou Baishi Biotechnology Co., Ltd.). *Bifidobacterium* and *Lactobacillus* were cultured using an anaerobic jar at 35 °C for 48 hours, whereas *F. nucleatum* and *B. fragilis* were cultured in an anaerobic chamber at 35 °C for 72 hours. The VITEK 2 COMPACT automated microbial identification system was used for bacterial identification, and results were expressed as the logarithm of colony-forming units per gram of wet feces (lgCFU/g).

2.5.2 Nutritional Intake Assessment

Postoperative nutritional intake was assessed by calculating the patient's meal consumption. Prior to each meal, food was weighed using a kitchen scale, and its energy content was calculated using the United States Department of Agriculture National Nutrient Database[20]. The total daily intake of calories, protein, carbohydrates, and fats was then summed to determine the patient's postoperative nutritional intake status.

2.5.3 Hematological Testing

Peripheral venous blood samples were collected from fasting patients at three time points: Before treatment and on days 1 and 7 post-treatment. Diamine oxidase (DAO) levels and endotoxin concentrations were measured using enzyme-linked immunosorbent assay (ELISA) kits [DAO kit: Cusabio Technology LLC, catalog number: CSB-E12759h; endotoxin kit: Danaher (Tianjin) Biotech Co., Ltd.], with a microplate reader [TECAN Sunrise, Danaher (Tianjin) Biotech Co., Ltd.][21]. Intestinal fatty acid-binding protein (I-FABP) levels were assessed using an I-FABP ELISA kit (Shanghai Boyan Biotechnology Co., Ltd., catalog number: BY-B0034) and a multifunctional microplate reader [MULTISKAN FC, Thermo Fisher Scientific (China) Co., Ltd.][22]. 7 Immunoglobulin A (IgA), immunoglobulin M (IgM), immunoglobulin G (IgG), and C-reactive protein (CRP) levels were determined using an automatic biochemical analyzer (Hitachi 7180, Hitachi High-Technologies Corporation) through immunonephelometry. TNF-α and IL-6 concentrations were measured using ELISA kits (DTH100 for TNF-α, D6050 for IL-6, R&D Systems, Inc.). 8 Cluster of differentiation 4 positive (CD4+) and cluster of differentiation 8 positive (CD8+) cell ratios were determined using flow cytometry [FACSCanto II, BD Medical Device (Shanghai) Co., Ltd.]. The CD4+/CD8+ ratio was calculated. All procedures were conducted according to the manufacturers' instructions[23].

2.6 10 Statistical Analysis

The statistical analysis was conducted using SPSS software version 29.0. Continuous variables were presented 1 as means and standard deviations (mean ± SD), and group comparisons were performed using independent samples t-tests. Categorical variables were expressed as percentages, with group differences analyzed *via* χ^2 5 tests. Statistical significance was defined by a p-value of less than 0.05. Spearman rank correlation analysis was employed for non-parametric or categorical data. Additionally, factors influencing the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer were examined through univariate and multivariate analyses.

RESULTS

3.1 Baseline Data

Patients in the good efficacy group were significantly younger, with a mean age of 49.63 ± 8.54 years compared with 52.66 ± 7.57 years in the poor efficacy group (t = 4.207, $P < 0.001$, Table 1). The distribution of sex, ethnicity, body mass index (BMI), smoking and drinking history, hypertension, diabetes, educational level, and marital status showed no significant differences between groups, highlighting their comparable baseline characteristics. Additionally, a higher prevalence of patients had an ECOG status of 0 in the good efficacy group (87.1%) than in the poor efficacy group (79.74%; $\chi^2 = 5.037$, $P = 0.025$). This finding suggests that better functional status may contribute to improved therapeutic outcome. Furthermore, a significantly higher proportion of patients in the good efficacy group had tumor node metastasis (TNM) stage ≤ II (49.1% vs. 39.22%; $\chi^2 = 5.004$, $P = 0.025$), while advanced stages (> II) were more frequent in the poor efficacy group (60.78% vs. 50.9%). Despite the trend toward a difference in the ratio of family income to poverty (RIP) ($\chi^2 = 5.313$, $P = 0.070$) and tumor size (t = 1.478, $P = 0.140$), these differences did not reach statistical significance. These findings indicate that age, ECOG performance status, and TNM stage may play influential roles in the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer.

3.2 Surgical Factors

The average surgery duration was 189.15 ± 25.11 minutes for the good efficacy group compared with 192.35 ± 27.04 minutes for the poor efficacy group (t = 1.387, $P = 0.166$; Table 2). Blood loss was similar between groups, with averages of 153.9 ± 30.75 and 158.45 ± 50.03 mL for the good and poor efficacy groups, respectively (t = 1.208, $P = 0.228$). The number of lymph nodes removed also showed no significant difference, with a mean of 17.32 ± 4.54 nodes in the good efficacy group *vs* 16.87 ± 3.78 nodes in the poor efficacy group (t = 1.212, *P* = 0.226). The occurrence of immediate postoperative complications was comparable, affecting 8.24% of patients in the good efficacy group and 9.91% in the poor efficacy group (χ^2 = 0.431, *P* = 0.511). These findings suggest that the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer was not markedly influenced by these surgical-related factors.

3.3 Nutritional Intake

The good efficacy group had a higher mean caloric intake, consuming 2029.48 ± 180.64 kcal/day compared with 1991.33 ± 165.72 kcal/day in the poor efficacy group (t = 2.468, *P* = 0.014; Figure 1). Protein intake was also significantly higher in the good efficacy group, with an average of 82.56 ± 11.92 g/day *vs* 79.87 ± 12.61 g/day in the poor efficacy group (t = 2.48, *P* = 0.013). Additionally, fiber intake was higher in the good efficacy group, measuring 23.69 ± 5.38 g/day compared with 22.68 ± 4.64 g/day in the poor efficacy group (t = 2.291, *P* = 0.022). Conversely, no significant differences were observed in carbohydrate intake, with means of 253.24 ± 29.28 g/day and 254.31 ± 25.05 g/day (t = 0.444, *P* = 0.658), and fat intake, with means of 86.63 ± 12.51 g/day and 85.67 ± 15.22 g/day (t = 0.77, *P* = 0.442) between the two groups. These findings suggest that higher caloric, protein, and fiber intakes were associated with improved efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer.

3.4. Intestinal Mucosal Barrier Function Indicators

Preoperative values for DAO, intestinal fatty acid binding protein (I-FABP), lipopolysaccharide (LPS), and D-lactate (D-Lac) levels showed no significant differences, with t-values ranging from 0.066 to 0.876 and p-values > 0.382, indicating comparable baseline levels (Table 3). By postoperative day 7, the good efficacy group exhibited significantly lower averages for DAO (3.98 ± 0.62 U/L vs. 4.11 ± 0.58 U/L; t = 2.493, *P* = 0.013), I-FABP (47.54 ± 10.27 μg/L vs. 50.21 ± 12.83 μg/L; t = 2.564, *P* = 0.011), LPS (4.59 ± 1.32 U/L vs. 4.87 ± 1.55 U/L; t = 2.218, *P* = 0.027), and D-Lac (6.63 ± 1.22 mg/L vs. 7.02 ± 2.37 mg/L; t = 2.243, *P* = 0.026) compared with the poor efficacy group. These data suggest improved intestinal mucosal barrier function in patients who achieved better efficacy from the combination of probiotics with enteral nutrition, particularly apparent by the first postoperative week. These indicators may thus serve as important biomarkers for assessing the treatment efficacy in postoperative patients with colorectal cancer.

3.5 Gut Microbiota Indicators

Preoperative values did not differ significantly between the groups, with t-values ranging from 0.445 to 1.642 and p-values > 0.101, indicating comparable baseline microbiota profiles (Table 4). However, by postoperative day 7, the good efficacy group showed significantly higher levels of *Bifidobacterium* (9.01 ± 0.53 IgCFU/g vs. 8.87 ± 0.68 IgCFU/g; t = 2.492, *P* = 0.013) and *Lactobacillus* (8.75 ± 0.75 IgCFU/g vs. 8.62 ± 0.53 IgCFU/g; t = 2.145, *P* = 0.032) and lower levels of *F. nucleatum* (5.94 ± 0.45 IgCFU/g vs. 6.03 ± 0.20 IgCFU/g; t = 3.014, *P* = 0.003) and *B. fragilis* (5.68 ± 0.29 IgCFU/g vs. 5.74 ± 0.27 IgCFU/g; t = 2.75, *P* = 0.006). These findings suggest that the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer was associated with the modulation of gut microbiota, potentially contributing to the improved postoperative outcomes observed in the Good Efficacy Group.

3.6 Immune Indicators

Preoperative levels of immunoglobulins (IgA, IgM, IgG) and CD4+/CD8+ ratios were similar between the two groups, and the differences were not significant (t-values ranging from 0.073 to 1.312; p-values > 0.19; Table 5). However, by postoperative day 7, the good efficacy group exhibited significantly higher levels of IgA (2.46 ± 0.48 g/L vs. 2.34 ± 0.63 g/L; t = 2.472, *P* = 0.014), IgM (1.31 ± 0.22 g/L vs. 1.25 ± 0.31 g/L; t = 2.553, *P* = 0.011), and IgG (11.23 ± 1.89 g/L vs. 10.71 ± 1.73 g/L; t = 3.216, *P* = 0.001) than the poor efficacy group. Additionally, the CD4+/CD8+ ratio was significantly higher in the good efficacy group (1.65 ± 0.35 vs. 1.57 ± 0.33; t = 2.521, P = 0.012) by day 7. These findings suggest that enhanced immune function, as indicated by elevated immunoglobulin levels and improved CD4+/CD8+ ratios, may be associated with the improved outcomes of combining probiotics with enteral nutrition in postoperative patients with colorectal cancer.

3.7 Inflammatory Indicators

Preoperative levels of CRP, TNF-α, and IL-6 were comparable between the groups, and the differences were not significant (t-values ranging from 0.193 to 0.604; p-values > 0.546; Figure 2). By postoperative day 7, the good efficacy group showed significantly lower levels of CRP (17.86 ± 2.19 mg/L vs. 18.37 ± 3.04 mg/L; t = 2.136, P = 0.033), TNF-α (36.58 ± 10.46 ng/L vs. 39.27 ± 11.53 ng/L; t = 2.761, P = 0.006), and IL-6 (28.14 ± 6.23 pg/mL vs. 29.27 ± 6.07 pg/mL; t = 2.062, P = 0.04) than the poor efficacy group. These findings suggest that the observed clinical benefits in the good efficacy group may be mediated by reduced systemic inflammation, potentially contributing to improved postoperative recovery in patients with colorectal cancer receiving probiotics and enteral nutrition.

3.8 Correlation Analysis

Age showed a modest positive correlation with therapeutic efficacy (rho = 0.187, P < 0.001), suggesting potential age-related differences in treatment response (Figure 3). Negative correlations were observed in ECOG performance status (rho = -0.099, P = 0.025) and TNM stage (rho = -0.099, P = 0.025), indicating that worse baseline functional status and more advanced disease stage may slightly undermine therapeutic outcomes. Nutritional factors such as caloric intake (rho = -0.088, P = 0.047) and protein intake (rho = -0.108, P = 0.014) were inversely related to efficacy, potentially highlighting the importance of optimizing nutritional strategies after surgery. Significant biomarkers on postoperative day 7, including DAO (rho = 0.102, P = 0.021) and I-FABP (rho = 0.107, P = 0.015) were correlated positively with efficacy. Meanwhile, elevated levels of *F.*

nucleatum (rho = 0.124, *P* = 0.005) and TNF-α (rho = 0.130, *P* = 0.003) were associated with poor outcomes. Conversely, higher levels of *Bifidobacterium* (rho = –0.113, *P* = 0.010) and IgG (rho = -0.138, *P* = 0.002) demonstrated a protective effect, that is, they were correlated negatively with treatment efficacy. These findings underscore the multifactorial nature of therapeutic responses in postoperative settings and emphasize the potential for targeted interventions to enhance treatment outcomes.

3.9 Univariate Logistic Regression Analysis

Increasing age was a positive predictor of efficacy (Coefficient = 0.046, SE = 0.011, *P* < 0.001, OR = 1.047, 95%CI: 1.025–1.071; Table 6). Conversely, a poor ECOG performance status and advanced TNM stage were associated with decreased efficacy, with coefficients of -0.539 (*P* = 0.026, OR = 0.583, 95%CI: 0.361–0.935) and –0.402 (*P* = 0.026, OR = 0.669, 95%CI: 0.469–0.951), respectively. Nutritional factors including lower caloric (Coefficient = -0.001, *P* = 0.015, OR = 0.999) and protein intake (Coefficient = -0.018, *P* = 0.014, OR = 0.982) and reduced fiber intake (Coefficient = -0.040, *P* = 0.025, OR = 0.961) were inversely related to efficacy. Inflammatory and microbial markers, such as higher postoperative day 7 Levels of DAO (Coefficient = 0.371, *P* = 0.014, OR = 1.448), I-FABP (Coefficient = 0.020, *P* = 0.010, OR = 1.020), LPS (Coefficient = 0.141, *P* = 0.026, OR = 1.151), and D-Lac (Coefficient = 0.115, *P* = 0.019, OR = 1.122), were positively associated with therapeutic efficacy. *Bifidobacterium* and *Lactobacillus* levels on postoperative day 7 exhibited protective effects (Coefficients = –0.376 and –0.282, *P* = 0.012 and *P* = 0.039, ORs = 0.687 and 0.754, respectively). Higher numbers of *F. nucleatum* and *B. fragilis* were associated with reduced efficacy (Coefficients = 0.705 and 0.876, *P* = 0.005 and 0.007, ORs = 2.023 and 2.401, respectively). Immune markers such as IgA, IgM, IgG, and CD4+/CD8+ ratios were negatively correlated with efficacy, indicating a complex relationship between immune modulation and therapeutic success. Elevated CRP, TNF-α, and IL-6 Levels were also significantly associated with efficacy, suggesting that inflammation plays a critical role in patient outcomes. These insights highlight the multifaceted nature of factors influencing treatment efficacy in this patient cohort.

3.10 Multivariate Logistic Regression Analysis

The multivariate logistic regression analysis identified several independent factors that were significantly associated with therapeutic efficacy in postoperative patients with colorectal cancer receiving probiotics combined with enteral nutrition (Table 7). Age was a strong positive predictor of efficacy, with each additional year increasing the odds of a positive therapeutic outcome (Coefficient = 0.049, $P < 0.001$, OR = 1.050, 95%CI: 1.023–1.078). Conversely, more advanced TNM stage was associated with reduced efficacy (Coefficient = –0.427, $P = 0.041$, OR = 0.653, 95%CI: 0.434–0.982). Nutritional components such as protein intake also showed an inverse relationship with efficacy (Coefficient = –0.018, $P = 0.028$, OR = 0.982, 95%CI: 0.966–0.998), whereas caloric and fiber intake did not reach conventional levels of statistical significance. Among inflammatory and mucosal markers, higher DAO levels on postoperative day 7 were associated with increased efficacy (Coefficient = 0.408, $P = 0.020$, OR = 1.504, 95%CI: 1.065–2.125), while LPS levels (Coefficient = 0.204, $P = 0.005$, OR = 1.226) were also positively correlated with treatment success.

Microbiota composition postoperatively had significant effects. High numbers of *F. nucleatum* predicted reduced efficacy (Coefficient = 0.808, $P = 0.005$, OR = 2.244, 95%CI: 1.278–3.941), and high numbers of *Bifidobacterium* indicated protective effects (Coefficient = -0.451, $P = 0.010$, OR = 0.637, 95%CI: 0.453–0.896). In terms of immune markers, decreased IgM and IgG levels were associated with improved efficacy (IgM Coefficient = -0.926, $P = 0.017$, OR = 0.396; IgG Coefficient = –0.183, $P = 0.002$, OR = 0.832), suggesting potential immunomodulatory benefits. Elevated CRP levels postoperatively were positively associated with treatment efficacy (Coefficient = 0.094, $P = 0.020$, OR = 1.098). These findings highlight the complex interplay of demographic, nutritional, microbiological, and immunological factors in determining the efficacy of probiotic and enteral nutrition therapy in enhancing recovery and outcomes in patients with colorectal cancer.

DISCUSSION

9
In this study, we aimed to investigate factors influencing the efficacy of probiotics combined with enteral nutrition in postoperative patients with colorectal cancer.

An interesting observation from our study is the correlation between younger age and better therapeutic outcomes. The finding that younger age correlated with better outcomes aligns with emerging evidence on immunosenescence. A 2022 trial by Essink *et al*.[24] demonstrated that age influences immune function, with younger patients typically having a more robust immune response. The aging immune system, known as immunosenescence, may impair the ability to benefit from treatments intended to modulate gut microbiota and systemic immunity. Additionally, Li *et al*.[25] demonstrated that probiotics enhance immunity by increasing the production of immunoglobulins and cytokines. In younger patients, these probiotics may induce a significant immune response, thereby accelerating their post-surgical recovery.

The role of nutritional intake is another significant finding, particularly the higher caloric, protein, and fiber intake associated with improved outcomes. These nutrients are fundamental components that influence gut health and modulate immune responses. Postoperative nutrition is crucial for recovery; it supports not only wound healing and muscle maintenance but also the overall functional integrity of the gut[26, 27]. The 2022 study by Najme *et al*.[28] corroborates our findings. Their research indicates that enteral nutrition is superior to parenteral nutrition in maintaining the integrity of the intestinal mucosa, thereby supporting an effective intestinal barrier. This enhanced barrier function can boost the efficacy of probiotics. Conversely, inadequate nutrient intake, especially deficiencies in protein and fiber, can hinder mucosal recovery and diminish the efficiency of probiotic colonization in the gut, ultimately resulting in suboptimal outcomes. Fibers are known to ferment into short-chain fatty acids, which are pivotal in maintaining colonic health and providing an energy source for colonocytes to support recovery[29,30].

Our study also highlights the significant impact of gut microbiota modulation on treatment outcomes. An intriguing observation is the elevation of intestinal mucosal barrier function indicators such as DAO and I-FABP on postoperative day 1 compared with preoperative levels and those observed on postoperative day 7. This initial increase likely reflects acute surgical stress and the resultant disruption of the intestinal barrier, leading to increased permeability and systemic absorption of bacterial products and endotoxins[29, 31]. By postoperative day 7, the gradual recovery of the intestinal barrier function is indicated by the reduction in these markers, suggesting the beneficial effects of probiotics combined with enteral nutrition in restoring gut integrity. Conversely, low numbers of *F. nucleatum* and *B. fragilis* were associated with poor outcomes, suggesting that these bacteria might impede recovery possibly through inflammatory processes. *F. nucleatum*, in particular, has been associated with increased inflammation and cancer progression, which may undermine therapeutic efficacy[32]. Future research should focus on comparing these temporal changes statistically among groups and elucidating the underlying mechanisms, including potential immunomodulatory and anti-inflammatory roles played by probiotics during the early postoperative period.

Immune function was enhanced in patients with improved therapeutic outcomes, as evidenced by high levels of immunoglobulins (IgA, IgM, IgG) and an increased CD4+/CD8+ ratio. Probiotics may enhance mucosal immunity, a crucial aspect of the body's defense against tumor recurrence and infections, by upregulating these immunoglobulins. Probiotics and enteral nutrition may synergistically protect against postoperative immunosuppression to maintain a balanced immune environment that favors recovery. Furthermore, the observed correlation between high levels of inflammatory markers and poor outcomes underscores the notion that probiotics might mitigate this response, contributing to a favorable pro-healing environment. Elevated inflammatory markers such as TNF-α and IL-6 in the poor efficacy group suggest a state of chronic inflammation that might precipitate complications or slow recovery. Thus, the modulation of inflammation *via* probiotics could be a key mechanism for improved outcomes[33].

The multivariate analysis illuminated the independent factors significant to therapeutic efficacy, thereby reinforcing the interplay of bacterial colonization, inflammation, and immune modulation. The association between high levels of DAO and LPS on postoperative day 7 with good efficacy suggest that these parameters are markers of improved gut barrier function, possibly reflecting successful probiotic and nutritional therapy in strengthening intestinal health. These results indicate that the integrity of the intestinal mucosal barrier plays a crucial role in therapeutic outcomes for postoperative patients with colorectal cancer.

This study provides valuable insights, but it also has limitations. The retrospective design limits causative conclusions and may involve inherent biases. Future prospective investigations are warranted to confirm these findings and further explore the mechanistic pathways involved. Incorporating multi-omics technologies could also elucidate the interaction between the microbiome and the immune system clearly, potentially tailoring personalized therapeutic strategies for postoperative patients with colorectal cancer based on their microbiome signatures and immune profiles. Specifically, the exploration of microbiome genomics to identify strains with optimal probiotic potential could further refine and improve treatment efficacy.

CONCLUSION

Probiotics combined with enteral nutrition can significantly promote gastrointestinal function recovery in postoperative patients with colorectal cancer. The therapeutic effect is influenced by multiple complex factors, including age, nutritional intake, gut microbiota balance, immune status, and inflammation. These findings highlight the importance of comprehensive patient management strategies that integrate nutritional optimization and microbiota modulation to improve postoperative recovery and outcomes. Advancement of such strategies may benefit not only patients with colorectal cancer but also broader surgical and oncological populations, underscoring the value of personalized care in cancer treatment.

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