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Low-residue diet with oral nutritional supplements prior to colonoscopy improves the quality of bowel preparation: an endoscopist-blinded, randomized controlled trial

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Abstract

Background Poor bowel preparation has been a great problem of endoscopists for a long time. Low-residue diet (LRD) is often recommended on the day before colonoscopy. However, the quality of bowel preparation with LRD alone is suboptimal. The aim of our study was to examine whether patients who consumed LRD with oral nutritional supplements (ONSs) had higher quality of bowel preparation than patients who consumed LRD alone before colonoscopy.

Methods An endoscopist-blinded, randomized controlled trial was conducted in inpatients who scheduled for colonoscopy with sedation. Patients were randomized to the non-ONS group and the ONS group. The primary outcomes were the rates of adequate bowel preparation measured by the Boston Bowel Preparation Scale (BBPS), the Ottawa Bowel Preparation Scale (OBPS) and the Colon Endoscopic Bubble Scale (CEBuS). The secondary outcomes were the adenoma detection rate (ADR), polyp detection rate (PDR), intubation time, withdrawal time and rates of adverse events.

Results In both groups, 100 patients were analyzed. The rates of adequate bowel preparation measured by the BBPS and OBPS and PDR were significantly higher in the ONS group than in the non-ONS group (all $P < 0.05$). However, no significant differences were observed in the CEBuS scores, ADR, intubation time and rates of adverse events between the two groups (all $P > 0.05$). The withdrawal time was longer in the non-ONS group than the in the ONS group ($P < 0.05$).

Conclusions LRD with ONSs helps increase the quality of bowel preparation. To help with colorectal cancer (CRC) screening, further studies are warrant.

Trial registration [Chinese Clinical Trial Registry], [ChiCTR2400091660], [31/10/2024], [Retrospectively registered]

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Keywords Low-residue diet, Oral nutritional supplements, Bowel preparation

Introduction

Colorectal cancer (CRC) has been considered a public health problem because of its high incidence and mortality. According to the GLOBOCAN 2022 estimates, CRC accounts for approximately 9.6% of all new cancer cases and 9.3% of cancer-related mortality worldwide [1]. By 2040, it is predicted that the number of cases of CRC will increase to 3.2 million new cases and 1.6 million deaths [2].

Colonoscopy screening and resection of precancerous lesions such as adenomas have reduced the risk of CRC incidence and death [3–5]. As an essential part of high-quality colonoscopy, adequate bowel preparation is critical for sufficient visualization of the colorectal mucosa [6]. One of the main causes of interval colorectal cancer which often occurs in the interval between scheduled colonoscopy is missed colorectal neoplasia at screening colonoscopy [7]. Low-quality bowel preparation can affect diagnostic accuracy and even lead to miss lesions [8, 9]. It also has a negative impact on the speed and completeness of colonoscopy [10].

The residue of digestion consists mainly of dietary fiber, micro-organisms, secretions and cells shed from the digestive tract [11, 12]. Until now, there has been no scientifically acceptable quantitative definition of residue. European Society of Gastrointestinal Endoscopy (ESGE) recommends a low-fiber diet on the day preceding colonoscopy [13]. In practice, the terms ‘low-residue diet (LRD)’ and ‘low-fiber diet’ are used interchangeably [11, 12]. A meta-analysis of 8 trials showed that 87% (629/723) of patients who underwent bowel preparation with LRD had adequate bowel preparation [14]. Similarly, Chen et al. [15] conducted a meta-analysis of 13 trials and found that the adequacy of bowel preparation in the LRD group was 73.2% (1034/1413). It is confirmed that the quality of bowel preparation with LRD alone is still suboptimal.

Enteral nutrition (EN) is the most natural means of nutrition and allows the intestines to absorb nutrients [16]. It provides patients who cannot maintain sufficient oral intake to meet their nutritional needs critical macro and micronutrients [17]. According to the nutritional needs of patients, EN can be long or short term. Patients with oral feeding could combine partial enteral nutrition (PEN) with another diet, depending on their diagnosis and condition.

In our study, we aimed to assess whether consuming LRD in combination with ONS was better than consuming LRD alone for the quality of bowel preparation before colonoscopy.

Methods

Study design

This prospective, single-blind, randomized controlled trial was conducted at the Endoscopy Center, the Affiliated Hospital of Hangzhou Normal University, China. Trial recruitment occurred between February 1, 2023, and April 30, 2024. The study was approved by the institutional review board of the Affiliated Hospital of Hangzhou Normal University (2022(E2)-HS-126).

Participant recruitment

Inclusion criteria were as follows: (1) adults aged 18–75 years; (2) the American Society of Anesthesiologists (ASA) I–II; (3) scheduled to undergo colonoscopy with sedation. The exclusion criteria were: (1) inflammatory bowel disease (IBD); (2) gastrointestinal obstruction or perforation; (3) toxic megacolon; (4) a history of CRC; (5) allergy or intolerance to polyethylene glycol (PEG), dimethyl silicone oil (DSO) or semi-solid enteral nutrients (the ONS used in our study); (6) pregnant or breastfeeding women; (7) hemodynamic instability; (8) previous bowel resection; (9) uncontrolled hypertension and diabetes; (10) heart or kidney failure.

Sample size

We estimated the sample size based on previous research, which indicated the rates of adequate bowel preparation by the isosmotic PEG containing electrolyte preparations were achieved in 81% with a standard deviation of 11 [18]. To achieve a power of 95% and a significance level of 0.05, we calculated that we would need approximately 81 participants per group to detect a meaningful difference in cleanliness. To account for potential dropout and non-compliance, we increased the sample size by 20%, resulting in a final target sample size of 100 participants. This calculation ensures that our study is adequately powered to provide reliable results.

Randomization and blinding

With the use of a computer-generated randomization table, patients were screened and randomly assigned to receive LRD alone (the non-ONS group) or LRD combined with ONSs (the ONS group) prior to colonoscopy. As a result of the dietary intervention that was prescribed, the participants could not be blinded. But the endoscopists and endoscopy staff were blinded to the randomization process and dietary intervention.

Diet intervention

Diets of approximately 1800 to 2500 calories per day were prescribed for the two groups on the day before

Table 1 Nutrient composition of a bag of semi-solid enteral nutrients

Dietary Component	Per 100 g	NRV (%)
Energy, KJ	427	5%
Protein, g	5.0	8%
Fat, g	2.3	4%
Saturated fatty acid, g	0.9	5%
Carbohydrates, g	15.7	5%
Dietary fiber, g	1.2	5%
Sodium, mg	177	9%
Vitamin A, μ g	82	10%
Vitamin D, μ g	2	40%
Vitamin E, μ g	3500	25%
Vitamin B1, μ g	320	23%
Vitamin B2, μ g	350	25%
Vitamin B6, μ g	450	32%
Vitamin B12, μ g	0.45	19%
Iron, mg	1.1	7%
Zinc, mg	1.8	12%

Nutrient Reference Values, NRV

Net weight: 300 g

Glycemic Index (GI): 53

colonoscopy. Patients in the non-ONS group were instructed to consume a 1-day LRD. In accordance with the eating habits of Chinese adults, advising dietary was as follows. Permitted staple foods include white bread, noodles and rice. Permitted meats include chicken, fish and eggs. Permitted vegetables include potatoes and carrots. They were also allowed to eat other low-residue foods such as crackers, yogurts, apples and clear liquids.

In the ONS group, the patients were instructed to consume a bag of semi-solid enteral nutrients (Aohaien, China Otsuka Pharmaceutical Co., Ltd., China) at dinner before colonoscopy. Nutrient composition of a bag of semi-solid enteral nutrients is shown in Table 1. Patients were also required to eat LRD for breakfast and lunch on the day prior to colonoscopy, as described above.

Bowel Preparation regimens

Patients were not allowed to eat or drink anything (except water containing PEG or DSO) after dinner on the day prior to colonoscopy. Patients in both groups received two boxes of PEG (Hengkangzhengqing, Jiangxi Hengkang Pharmaceutical Co., Ltd., China) and a bottle of DSO (Jianheng, Sichuan Jianeng Pharmaceutical Co., Ltd., China) to complete bowel preparation.

The split-dose bowel preparation regimen was as follows: patients were advised to take the first box of PEG dissolved and mixed in 2,000 ml of warm water at 7 pm on the day prior to colonoscopy and to complete the 2,000 ml PEG within 2 h. The second box of PEG dissolved and mixed in 1,000 ml of warm water and a 20-ml bottle of DSO should be taken at least 6 h before colonoscopy on the appointment day and completed within 1 h.

Table 2 The four BBPS grades

Score	Description
0	Unprepared colon segment with mucosa not seen because of solid stool that cannot be cleared.
1	Portion of mucosa of the colon segment seen, but other areas of the colon segment are not well seen because of staining, residual stool, and/or opaque liquid.
2	Minor amount of residual staining, small fragments of stool, and/or opaque liquid, but mucosa of colon segment is seen well.
3	Entire mucosa of colon segment seen well, with no residual staining, small fragments of stool, or opaque liquid.

The fasting time from completing the last dose of PEG to undergo colonoscopy was controlled within 5–6 h. Dietary intervention and bowel preparation were carried out at the general ward under the guidance of nurses.

Colonoscopy

In our study, the single-patient colonoscopy was performed with the Olympus 290 colonoscope. 10 endoscopists who performed more than 500 colonoscopy per year (over 5 years of endoscopic experience) were assigned to complete colonoscopy. After the endoscopists performed cleansing maneuvers (washing and suctioning of fluid), they would take images of all segments of colons. 2 endoscopists who had been trained to assess bowel cleansing using the Boston Bowel Preparation Scale (BBPS), the Ottawa Bowel Preparation Scale (OBPS) and the Colon Endoscopic Bubble Scale (CEBuS) were instructed to evaluate and record the outcome-related indicators. These results would be assessed during the withdrawal time and would be confirmed by recorded images of each segment of colons.

Outcomes

The primary outcomes were the rates of adequate bowel preparation, which were measured using the BBPS, OBPS and CEBuS. The BBPS is a widely accepted tool which reflects bowel cleanliness. It is a four-grade scale, to assess three segments of the colon: right segment (cecum and ascending colons), transverse segment (hepatic and splenic flexures), and left segment (descending and sigmoid colons, rectum) [19]. The scores ranged from 0 to 3, as shown in Table 2. Adequate bowel preparation was defined as a score ≥ 2 of any segment and the total score ≥ 6 .

Another scale for assessing the quality of bowel preparation is the OBPS. The OBPS consists of two parts: the cleanliness of each colon segment (right colon: cecum and ascending; mid colon: transverse and descending; rectosigmoid) between 0 and 4 and overall fluid quantity between 0 and 2 (Table 3). The total score, which is calculated by adding cleanliness of each segment and overall fluid quantity scores, has a range from 0 (perfect) to 14

Table 3 The two parts of OBPS grades

Score	Cleanliness of each segment	Overall fluid quantity
0	No fluid in the segment.	Small
1	Minimal fluid in the segment.	Moderate
2	Suction required to view the segment adequately.	Large
3	Washing and suction required to view the segment.	
4	Solid stool, not washable.	

Table 4 The three CEBuS grades

Score	Description
0	No or minimal bubbles, covering less than 5% of the surface, not hampering mucosa visibility.
1	Moderate number of bubbles, covering between 5% and 50% of the surface, affecting mucosa visibility and requiring additional time for removal.
2	Severe bubbling, covering more than 50% of the surface, obscuring mucosa visibility and requiring additional time for removal.

(a completely unprepared colon) [20]. A total score ≤ 5 is defined as adequate bowel preparation [21].

The level of colonic bubbles was measured according to the CEBuS (Table 4). It is a three-grade scale developed by Taveira et al. [22] to standardize the evaluation of colonic bubbles during colonoscopy. A CEBuS score of 0 for the whole bowel is considered as adequate bowel preparation.

The secondary outcomes were the adenoma detection rate (ADR), polyp detection rate (PDR), intubation time, withdrawal time and rates of adverse events. The ADR is the most important indicator for the quality of colonoscopy, defined as the proportion of people undergoing a complete colonoscopy with at least one adenoma detected. The PDR is defined as the proportion of people undergoing a complete colonoscopy with at least one polyp detected [7]. Better bowel preparation makes it possible to detect increased colorectal lesions [23]. Therefore, our study investigated the ability of the two dietary strategies to detect adenomas and polyps. After patients were enrolled in the trial, nurses called patients at night before the day of undergoing colonoscopy to record any adverse events during bowel preparation.

Statistical analysis

Statistical analysis was performed using SPSS 27.0 statistical software package (SPSS Inc., Armonk, NY, United States). Continuous data were presented as mean \pm standard deviation (mean \pm SD) or median (Interquartile Range, IQR). Qualitative data were presented as percentages. The Mann-Whitney U test and Pearson's chi-squared test with Yates' continuity correction and Fisher's exact test were used to compare the two groups.

A P -value < 0.05 was considered a statistically significant difference between the two groups.

Results

A total of 221 patients were eligible for inclusion. 10 of them were excluded as intolerance to PEG. 105 were randomized to the non-ONS group while 106 were randomized to the ONS group. 5 and 6 patients in the two groups, respectively did not undergo colonoscopy as scheduled. Finally, both groups have 100 patients in the analysis. The flowchart of the study is shown in Fig. 1. There were no significant differences in the distributions of basic characteristics and indication for colonoscopy between the two groups ($P > 0.05$). The details are listed in Table 5.

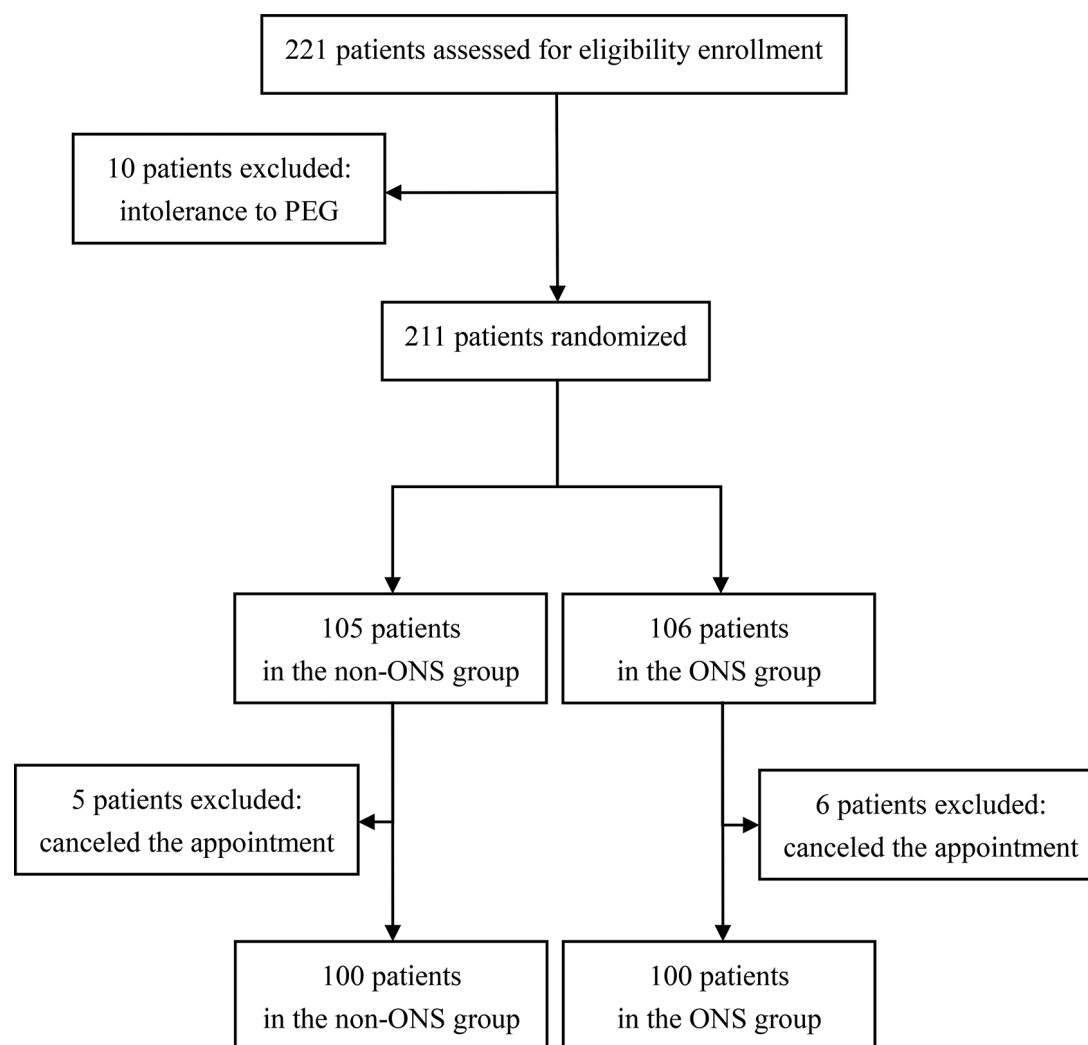
Patients in both groups followed a 1-day LRD and completed 3,000 ml of PEG and a 20-ml bottle of DSO for bowel preparation. Moreover, all patients in the ONS group consumed a bag of semi-solid enteral nutrients.

As is shown in Table 6, the rates of adequate bowel preparation measured by the BBPS were 87% and 96% in the non-ONS group and the ONS group, respectively. The rates of adequate bowel preparation measured by the OBPS were achieved in 89% of the non-ONS group and 97% of the ONS group. The proportion of patients who underwent adequate bowel preparation according to the BBPS and OBPS was higher in the ONS group than in the non-ONS group, with significant differences between the two groups (all $P < 0.05$). 100% of patients in both groups achieved the most minimal amounts of bubbles. Although the ADR and intubation time in the non-ONS group were similar with the ONS group (all $P > 0.05$), the non-ONS group had significantly lower PDR and longer withdrawal time than the ONS group (all $P < 0.05$).

The adverse events are presented in Table 7. There were no significant differences in the rates of any of the seven adverse events between the two groups (all $P > 0.05$).

Discussion

In clinical practice, ONSs have been used in the peri-operative period. A study by Liang et al. [24] demonstrated that the use of a semi-solid, low-residue enteral nutrient (such as ONSs) during bowel preparation not only reduced the incidence of hypoglycemia but also improved patient satisfaction and compliance. A randomized controlled study compared the ONS group (eating only ONSs and clear fluids for 5 days) to the PEG group (eating a light diet on the day before colonoscopy), with rectal enema and received PEG for bowel preparation, respectively [25]. The results showed that 6 of 27 (22%) in the ONS group and 1 of 23 (4%) in the PEG group could not achieve cecal intubation due to stools. However, the ONS group had a higher mean total OBPS scores than the PEG group. A sub-analysis of 8 patients

**Fig. 1** Flowchart

in the ONS group who received additional bowel preparation with PEG suggested that ONS in combination with PEG improved bowel cleansing compared with PEG alone. The study indicated that the utilization of ONSs may facilitate bowel cleansing. LRD is often recommended before colonoscopy because of its effect on reducing the formation of bowel contents. Our dietary strategy focuses on the benefits of both LRD and ONSs to improve the quality of bowel preparation.

The ONS used in our study has the following advantages. Firstly, it has both solid and liquid features with viscosity and elasticity which make it easier to digest and absorb than common foods. Secondly, it contains only 3.6 g of fiber per 300 g, allowing patients in both groups to follow a 1-day LRD. Thirdly, the glycemic index (GI) of the ONS is 53, which is categorized as a low-GI food ($GI \leq 55$). Therefore, it can be a choice of foods for patients with diabetes before colonoscopy. Fourthly, medium chain triglycerides (MCTs) are 20% of total fats

in the ONS. They are beneficial for absorption of nutrients and decrease intestinal inflammation. Moreover, MCTs can serve as a source of calories with minimal need of digestion [26].

In our study, the balanced distribution of basic characteristics between the two groups ($P > 0.05$) enhanced the reliability of the results. In terms of bowel preparation, the ONS group had significantly higher adequate bowel preparation rates according to both BBPS (96% vs. 87%) and OBPS (97% vs. 89%, $P < 0.05$), which is beneficial for clear mucosal observation during colonoscopy. Although the ADR rates were similar (30% vs. 34%, $P > 0.05$), the ONS group had a notably higher PDR (57% vs. 39%, $P < 0.05$), crucial for early colonic adenoma detection and colorectal cancer prevention. Writing in the journal JAMA, Nastazja D. Pilonis' team at the National Cancer Institute in Warsaw, Poland, analyzed data from 735,396 patients aged 50–75 who had a non - cancer - detecting colonoscopy between 2011 and 2017 [27]. Results

Table 5 Baseline characteristics and indication for colonoscopy of participants

Characteristics: study variables	Non-ONS group (N=100)	ONS group (N=100)	P value
Age, n (%)			0.558
< 50 years	35	39	
≥ 50 years	65	61	
Sex, n (%)			0.777
Male	54	52	
Female	46	48	
BMI, n (%)			0.061
< 24 kg/m ²	66	53	
≥ 24 kg/m ²	34	47	
History of colonoscopy, n (%)	75	83	0.951
Indication for colonoscopy, n (%)			0.578
Abdominal pain	19	14	
Screening	44	50	
Polyp surveillance	18	23	
Change in bowel habit	10	7	
Others	9	6	
History of abdominal surgery, n (%)	18	18	1
History of chronic constipation, n (%)	4	1	0.365
Cigarette smoking, n (%)	17	14	0.558
Alcohol drinking, n (%)	17	16	0.849
Medical comorbidities, n (%)			0.569
Hypertension	16	10	
Diabetes	4	5	
Coronary Artery Disease (CAD)	2	1	
No	80	86	

P values were calculated using Pearson's chi-squared test with Yates' continuity correction and Fisher's exact test

showed that patients of physicians with higher ADR had significantly lower risks of post-colonoscopy colorectal cancer and related deaths. ADR at or above the median (28.3%) were associated with a lower risk compared to rates below the median. Moreover, there were no significant differences in the rates of the seven adverse events between the two groups ($P>0.05$), indicating ONS's safety. Overall, ONS, without increasing adverse events, improves bowel preparation and PDR, offering a superior pre-colonoscopy option, and future research should focus on optimizing its usage.

Several limitations of this study should be mentioned. Firstly, the effects of different ONSs on the quality of bowel preparation are uncertain. Secondly, all patients were instructed to take 300 g of the ONS used in our study at dinner on the day before colonoscopy, further studies are required to ascertain the optimal time and volume of intake. Thirdly, no significant differences were observed in the ADR and the rates of adverse events between the two groups, which may be attributed to the insufficient sample size of the study.

Table 6 The BBPS and OBPS scores and quality indicators for colonoscopy between the two groups

	Non-ONS group (N=100)	ONS group (N=100)	P value
BBPS scores, mean ± SD			
Right segment	2.35 ± 0.575	2.50 ± 0.503	0.081
Transverse segment	2.21 ± 0.498	2.41 ± 0.494	0.007
Left segment	1.96 ± 0.425	2.28 ± 0.570	< 0.001
OBPS scores, mean ± SD			
Right colon	0.65 ± 0.575	0.50 ± 0.503	0.081
Mid colon	0.79 ± 0.498	0.59 ± 0.494	0.007
Rectosigmoid	1.03 ± 0.437	0.73 ± 0.617	< 0.001
Rate of adequate bowel preparation, n (%)			
BBPS	87	96	0.022
OBPS	89	97	0.027
CEBuS	100	100	
ADR, n (%)	30	34	0.544
PDR, n (%)	39	57	0.011
Intubation time, min, median (IQR)	4 (3.58,4.75)	4 (3.01,5)	0.903
Withdrawal time, min, median (IQR)	8 (7.34,10)	8 (7,9)	0.024

P values were calculated using Mann-Whitney U-test or Pearson's chi-squared test

For future research, we suggest recruiting a more diverse sample from multiple regions and ethnic groups to enhance generalizability. Increasing the sample size and prolonging the study period would improve the power to detect ADR differences. Additionally, it is advisable to add multiple categories, including those with constipation, elderly patients, and patients who have undergone abdominal surgery, etc., and compare the effectiveness and safety after the intervention. Moreover, exploring genetic factors related to ADR and new intervention strategies could offer fresh insights in this research area.

Table 7 The rates of adverse events between the two groups

Rates of adverse events, n (%)	Non-ONS group (N=100)	ONS group (N=100)	P value
Nausea	19	15	0.451
Vomiting	8	6	0.579
Abdominal pain	7	5	0.552
Abdominal bloating	10	6	0.297
Dizziness	6	4	0.516
Headache	4	2	0.678
Hypoglycemia	11	10	0.818

P values were calculated using Pearson's chi-squared test with Yates' continuity correction

Conclusions

Our study is the first trial to demonstrate that LRD with ONSs improves the quality of bowel preparation. Further studies are required before this new dietary strategy can be widely used for screening and polypectomy of precancerous lesions.

Abbreviations

LRD	Low-residue diet
ONSs	Oral nutritional supplements
BBPS	Boston Bowel Preparation Scale
OBPS	Ottawa Bowel Preparation Scale
CEBuS	Colon Endoscopic Bubble Scale
ADR	Adenoma detection rate
PDR	Polyp detection rate
CRC	Colorectal cancer
EN	Enteral nutrition
PEN	Partial enteral nutrition
ASA	American Society of Anesthesiologists
IBD	Inflammatory bowel disease
PEG	Polyethylene glycol
DSO	Dimethyl silicone oil
SD	Standard Deviation
IQR	Interquartile Range
GI	Glycemic index
MCTs	Medium chain triglycerides

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Author contributions

H.L.S & Y.J.S: conceptualization; data curation; formal analysis; writing—original draft; writing—review and editing. J.Q.W, X.Q.Z & G.D.L: data curation; formal analysis. W.M.L & J.Q: conceptualization; formal analysis; methodology; supervision; writing—original draft; writing—review and editing.

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Data availability

The data used in this paper will be provided by the corresponding author upon reasonable request.

Declaration

Ethics approval and consent to participate

The study was conducted in strict adherence to the principles of the Declaration of Helsinki. The study was approved by the institutional review board of the Affiliated Hospital of Hangzhou Normal University (2022(E2)-HS-126). Written informed consent was obtained from all participants.

Consent for publication

This is not applicable for this study.

Competing interests

The authors declare no competing interests.

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