Comparable quality of bowel preparation with single-day versus three-day low-residue diet: Randomized controlled trial

One-day is non-inferior to three-days low-residue diet in achieving adequate colonoscopy preparation. Results of a non-inferiority randomised-controlled trial.

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COVER PAGE

Title: One-day is non-inferior to three-days low-residue diet in achieving adequate colonoscopy preparation. Results of a non-inferiority randomised-controlled trial.

Short Title: One-day low-residue diet before colonoscopy.

Updated Title
Comparable quality of bowel preparation with single-day versus three-day low-residue diet: Randomized controlled trial

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None of the Authors have competing interests regarding the subject of the study to disclosure.

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Abstract

Background and Aims: There is controversy about the length of low-residue diet (LRD) for colonoscopy preparation. The aim of the study was to compare one-day vs. three-day LRD associated to standard laxative treatment for achieving an adequate colonoscopy preparation in average risk patients undergoing screening colonoscopy.

Methods: A non-inferiority, randomised, controlled, parallel-group clinical trial was performed in the setting of average risk colorectal cancer screening program. Participants in the were randomised to receive 1-day vs. 3-day LRD in addition to standard polyethilenglicol treatment. Adequacy of preparation was evaluated by using the Boston Bowel Preparation Scale (BBPS). Primary outcome was achieving a BBPS ≥2 in all colon segments. Analysis was performed for a non-inferiority margin of 5%, a 95% statistical power and one-sided 0.05 significance level.

Results: A total of 855 patients were randomised. Adequate bowel preparation was similar between groups: 97.9% of patients in the 1-day LRD group vs 96.9% in the 3-day LRD group achieved the primary outcome (p-value for non-inferiority <0.001. The percentage of patients with BBPS scores ≥ 8 was superior in 1-day LRD group (254 vs 221 in the 3-day LRD group, p=0.032). The 1-day regimen was better tolerated than the 3-day diet. A 47.7% (vs, 28.7%, p<0.05) of patients rated the One-day LRD as very easy to follow.

Conclusion: One-day LRD is non-inferior to three-day LRD for achieving an adequate colon cleansing before colonoscopy. These results support the use of one-day LRD as the standard preparation for average risk screening colonoscopy. Clinicaltrials.gov (NCT03763266).

INTRODUCTION AND BACKGROUND

Colonoscopy is the most accurate method for the evaluation of the colorectal mucosa. It is the method of choice to diagnose colorectal cancer (CRC)[1,2] and for removing premalignant lesions. It has been estimated that in the US 15 million scheduled colonoscopies are performed each year [3,4].

The number of colonoscopies is currently increasing, due to the introduction of early detection screening programs around the world [5–8] and the resulting surveillance colonoscopies [5,6]. In this context, adequate bowel cleansing is of paramount importance for improving the efficiency of the examination [8,9].

Bowel preparation process is often considered burdensome and might have an impact in participation rates in populational screening programs and impact quality of life of subjects at increased risk of colorectal cancer that require periodic surveillance colonoscopies [10,11]. Therefore, improving the safety and tolerability of the bowel cleansing preparation may help to promote participation in the screening programs [9,12].

Some measures have been shown to improve bowel preparation. In this sense, consistent data support both the use of split dose regimens [13,14] and the reduction of the interval between bowel preparation and the start of colonoscopy [15]. In a recent systematic review, low-volume polyethylene glycol (PEG) split-dose regimens were as effective as high-volume regimens. Furthermore, low-volume preparations showed better tolerance and adherence[16].

Regarding diet before colonoscopy, low-residue diet (LRD) has been shown to be better tolerated than the traditionally endorsed clear liquid diet (CLD) [17–20].

Diet restriction may have a clear impact in patient satisfaction, quality of life and willingness to repeat the procedure [23,24]. For this reason, it is important to assess the most useful duration of LRD for colon preparation not only in terms of quality of bowel cleansing, but also regarding tolerability and patient' satisfaction [21,25,26].

The aim of the present study was to compare the efficacy and tolerability of a 1-day LRD versus a 3-day LRD colon cleansing by performing a non-inferiority randomised controlled clinical trial.

METHODS

Design and setting

Between December 2018 and January 2020, a randomised, controlled, parallel-group clinical trial was performed in the Endoscopy Unit of the Hospital Universitari Parc Taulí (Sabadell, Barcelona, Spain), in the context of early CRC screening program of the Vallès Occidental county (Barcelona, Spain).

The study protocol was approved by the Ethical Commission for Scientific Research of Fundació Parc Taulí (dated 25th July 2017) and procedures were in accordance with the ethical standards laid down in the Declaration of Helsinki, as revised in the year 2000. Written informed consent was obtained from all participants. The study was reported in accordance with the Consolidated Standards of Reporting Trials and registered in Clinicaltrials.gov (NCT03763266)

Subjects and procedures

Participants in the early CRC detection program aged between 50 and 69 years, who agreed to undergo colonoscopy after positive results on the immunological fecal occult blood test, were eligible to participate in the study. Potential participants were excluded in case of contraindication to colonoscopy, patient refusal to participate or inability to understand the risks or give informed consent. Subjects were randomly assigned to receive the 1-day or the 3-day LRD regimen at a ratio of 1:1, using random block sizes of 6. Random sequence was created by the principal investigator using the Sealed Envelope® program. Allocation concealment was performed using sequentially numbered, opaque envelopes. Participants were instructed about bowel cleansing and the study protocol. Low-volume PEG plus ascorbic acid in split-dose regimens (MoviPrep®, Norgine BV, Amsterdam, Netherlands), was prescribed. First dose was administered the evening of the day before at 20:00 h. The second dose was scheduled to finish 2-4 hours before the colonoscopy. Dietary instructions were designed by an endocrinologist specialized in nutrition. All the subjects received a logbook and were requested to register the diet taken during the 3 days before colonoscopy. Participants of both arms who reported being constipated recurrently received additional preparation with 5mg of bisacodyl every 12 hours during three days before the exploration.

All colonoscopies were performed by senior staff endoscopists, who were already routinely evaluating cleansing quality by using the Boston Bowel Preparation Scale (BBPS). Furthermore, all endoscopists repeated the BBPS Educational Program available at http://domweb.bumc.bu.edu/bowelprep/ before the first participant appointment [27].

Investigators involved in the study, including the endoscopy staff performing the BBPS were blinded to the study regimen received by the subjects. Only the researcher in charge of recruitment, group assignment and review of dietary logbooks was aware of the treatment arm.

Variables collected

Experimental variables

BBPS was registered by the endoscopists immediately after the exploration. The primary outcome of the study was adequate bowel cleansing. Bowel cleansing was considered adequate when each colon segment was scored ≥ 2 points.

Secondary outcomes were the rate of patients achieving an excellent preparation (arbitrarily defined as an overall score of ≥8 points), preparation and diet tolerability, proportion of patients with adequate cleansing in each segment, adenoma and polyp detection rate and colonoscopy exploration times (from anus to cecum and withdrawal times)

Before the colonoscopy, the participant answered a 5-point Likert scale survey *(Table S1)* designed to assess the diet and preparation tolerability. Adherence to diet, completeness of the laxative preparation and bisacodyl use when indicated were also recorded before entering the endoscopy room. Other variables registered during and after the colonoscopy where the endoscopist performing the study, colonoscopy findings and causes of incomplete exploration. Immediate or delayed -until 30 days- adverse events related to the procedure or the sedation were registered.

Basal variables

Variables potentially influencing the preparation quality were also recorded: days from bowel preparation instructions until colonoscopy, time lapse between the end of preparation and the beginning of the colonoscopy, age, gender, height and weight for BMI calculation, antidepressant or opioid treatment, reduced mobility, and hepatic cirrhosis.

Sample size calculation

For sample size calculation we assumed from previous data in our center that 3-day LRD protocol will achieve a 95% of adequate preparation[28]. We set power at 95% (1-β=0.95) with an α error of 0.05 and non-inferiority margin (δ) of -5%). Based on this we estimated a required sample size of 824 participants, 412 per group. Sample size calculation was done using the Sealed Envelope® (London, UK program) using the power calculator for binary outcome, non-inferiority trial.

Statistical analyses

Categorical variables were described using frequencies and percentages were used. For quantitative variables, means (and standard deviations) or medians (and interquartile ranges) were used.

Intention to treat (ITT) analysis included all randomised cases (with the exception of those who did not attend the colonoscopy appointment and lack information regarding the main outcome). Per protocol (PP) analysis included only those patients in whom adherence to diet was complete, intake of bowel preparation solution was ≥ 75% and colonoscopy was complete. Patients in whom

colonoscopy was incomplete because of improper cleansing were also considered as not achieving the primary outcome in the ITT analysis. Comparisons between diet groups were assessed using Student's T-tests or the U-Mann Whitney for continuous variables. The chi-square test or the Fisher's exact test were used for categorical variables.

A non-inferiority analysis for the primary outcome "adequate preparation" was performed. It was a priori planned that, if non-inferiority was demonstrated, the primary and secondary outcomes (excellent preparation, tolerability, adenoma detection rate, polyp detection rate and colonoscopy exploration times) were assessed for superiority.

Univariate logistic regression models were used to estimate the effect of diet on the adequate bowel preparation and to identify other associated factors. Multivariate logistic regression models included the designated diet and covariates that were significant in the univariate models, providing the adjusted ORs. Statistical significance was considered as a p value less than 0.05. Statistical analysis was performed using the IBM Statistical Package for the Social Sciences (SPSS) program version 25.0 (SPSS, Inc. Chicago, IL) and R 3.1.0 (R Foundation for Statistical Computing, Vienna, Austria). Reporting of the study was performed according to the CONSORT statement recommendations [29].

RESULTS

Participants characteristics

A total of 1.697 consecutive subjects were assessed for eligibility, of whom 855 were randomised into the study (429 in 1-day group and 426 in the 3-day group). Causes of ineligibility for the study were unwillingness to participate (n=834) and inability to give informed consent (n=8) (Figure 1).

ITT population included 836 patients (420 in the 1-day group and 416 in the 3-day group), with a mean age of 54.91± 6.16 years and a mean BMI of 27.5 ± 4.4 kg/m^2 and including 56.9% of men. In both groups, 68.2% were overweighted or obese (BMI > 25). PP population included 826 patients (417 in the 1-day group and 409 in the 3-day group (see flow chart in Figure 1). Reasons of exclusion from the PP population included incomplete preparation intake, incomplete diet or incomplete colonoscopy due to reasons other than inadequate cleansing. Baseline and clinical characteristics were similar between groups (Table 1).

All participants assigned to the 1-day diet completed the regimen, 4 subjects (1%) failed to complete the 3-day LRD. Constipation needing additional bisacodyl rates were similar in both groups (15.2% vs 13.7%, p = 0.604). No differences were observed in the baseline characteristics (Table 1). There were no significant differences in the days lapsed from the study enrolment until the colonoscopy (36.6 days vs 38.5 days; p = 0.095) as well as in the time lapsed from the end of the preparation until the beginning of the colonoscopy (3 hours 20 minutes (56 minutes) vs. 3 hours 22 minutes (53 minutes), p=0.417).

Primary outcome

The percentages of patients with adequate preparation was similar between groups: in the ITT population, 97.9% of subjects in 1-day LRD and 96.9% in 3-

day LRD. In the PP population, adequate preparation rates were 98.0% and 97.7% respectively.

Non-inferiority ITT analysis show a difference of 0.98 (unilateral 95% CI -1.07, p <0.001) and in the case of PP analysis 0.53 (unilateral 95% CI -1.39, p <0.001) (Table 2). The study requirements for demonstrating non-inferiority of 1-day LRD are achieved (Figure 2).

Secondary outcomes

The proportion of patients achieving an excellent preparation

Adequacy of the cleansing per segment (BBPS score ≥ 2) in proximal, transverse and distal colon) was similar in both groups and all differences included in the non-inferiority margin. ITT data are shown in Table 3 and PP data in *Table S2*. Only the proportion of subjects with a BBPS score of 3 in the proximal colon was higher in the 1-day vs. the 3-day LRD arm (55% vs. 47.9%, respectively p=0.03).

Regarding the tolerability of each regimen, 1-day LRD was significantly better tolerated than the 3-day diet, with 47.7% vs 28.7% rating the diet as easy to follow and not interfering in normal activities (Likert 1 $p < 0.05$), and with 77.0% vs 60.9% having an aggregated Likert-scale scores of 1 and 2 ($p < 0.01$) (Table 4). Laxative preparation (PEG+Asc) tolerability was similar in both groups (67.8% vs. 63.6% of patients with Likert scale scores of 1 and 2 (p=0.209) and for each score (Table 4).

No differences were observed either in the ITT nor PP analyses in the cecal intubation and withdrawal time. Adenoma and polyp detection rate were similar in both arms (72.4% vs. 72.6% p=0.94 and 77.9% vs. 75.2% p=0.37 respectively). Incomplete colonoscopies were due to inadequate preparation in 6 cases. Five of them occurred in the 3-day LRD group (p=0.09). Additional incomplete explorations were due to stenosis (2), loop formation (1) and adherences (1).

The most frequent diagnosis during colonoscopy were polyps (73.4% in 1-day LRD group and 72.6% in 3-day LRD), followed by diverticula (7.7% vs 5.65) and hemorrhoids (5.0% vs 5.6%).

Risk factors and control of confounding variables

In order to control interobserver variability in the evaluation of the BBPS we adjusted for the individual endoscopist in a logistic regression model. Neither in the univariate analysis, nor in the logistic regression model any individual variable was associated with an adequate cleansing *(Table S3).*

On the other hand, regarding excellent bowel cleansing (BBPS ≥8) multivariate analysis disclosed older age, higher BMI, constipation and treatment with opioids as risk factors for not achieving it. After adjusting for other variables, 1-Day LRD was the only variable directly associated with BBPS ≥ 8 in the multivariate analysis and the binary logistic regression model (OR 1.5 95% CI 1.1 – 2.0 p<0.01) (Table 5)

DISCUSSION

In our study, designed for a non-inferiority testing, we have clearly demonstrated that the 1-day LRD is as effective as the 3-day diet to achieve an adequate colon

preparation in both the non-inferiority and superiority analyses. Furthermore, rates of excellent colon cleansing were superior in the 1-day LRD groups. Another related and important finding of the present study is that 1-day LRD was significantly better tolerated than 3-day diet, as expected due to the reduction by a third in diet duration.

To our knowledge, it is the first time that the 1-day diet has been demonstrated to be non-inferior to the 3-day diet. In this sense, two recent clinical trials, comparing 1-day versus 3-day LRD, did not find statistically significant differences in the cleansing quality and in the polyp/adenoma rates, but these studies where not designed to assess non-inferiority and included small samples of subjects [19,30] . Better tolerability of 1-day LRD when compared to longer diet durations has already been reported in previous trials. This fact is also in consonance with a higher probability to complete 1-day LRD and the observation that this regimen may provide a better preparation [19,30]. As it was observed in the univariate analysis 1-day LRD was associated with a higher probability of BBPS scores ≥ 8, which represents a high-quality preparation. Additionally, these results were further confirmed in the multivariate logistic regression analysis. One-Day LRD remained the only variable predictive of an excellent preparation after adjusting for confusing variables such as low tolerability to diet, treatment with bisacodyl and opioids and endoscopist.

The study has some limitations. First of all, the study was performed in a sample of low comorbidity asymptomatic subjects. Therefore, the results cannot be directly extrapolated to individuals with high risk of poor cleansing as, for

example, symptomatic, elderly patients or to the inpatient setting. Second, we did not use a validated tool for assessing diet and preparation tolerability, as there was no free access to scales or simple questionnaires validated in Spanish or Catalan. Finally, we were neither able to record colonoscopies nor to undergo a centralized single operator evaluation or a consensus assessment of the bowel cleansing. However, the relevance of these limitations was limited by the large sample size and the effect of the randomisation and blinding. Furthermore, we performed a multivariate and logistic regression model that revealed no effect on the results and that in real life BBPS can be biased.

Data of our study are robust enough to support the routine use of 1-day LRD diet, at least in the setting of routine preparation for CRC screening. This may help to reduce the burden of colonoscopy preparation for the patients. One-day LRD preparation has additional advantages: for example, reducing the number of days needed to perform LRD may help to manage waiting lists, as colonoscopies could be planned only one or two days in advance, thus allowing for example substitution of last-minute cancellations.

Furthermore, the right colon has the highest rate of missed adenomas and flat/serrated polyps as well as interval or missed colorectal cancer, which are the main concern for endoscopists due to the difficulty to detect them [11,31–36]. One reason for this fact, is the difficulty to obtain good colonic preparation in this particular segment [19,24,30,37,38]. In this sense, the analysis of bowel preparation per segments in the present study revealed a higher proportion of subjects with adequate preparation in the right or proximal segment in the 1-day LRD arm.

One-day preparation may, therefore, help to reduce the rate of missing lesions and interval cancer.

Finally, these results can lead to new insights in the management of colon preparation, in which diet could gain less importance than previously recognized. To date, however, these results have been obtained only in clinical trials and, therefore, in a selected population. Therefore, we consider that these results should also be confirmed in observational studies in routine clinical practice.

In conclusion, we have shown that 1-day LRD provides non-inferior results to 3-day LRD, in terms of bowel preparation, globally and per segments. It is better tolerated and achieves a higher adherence. Also, 1-day LRD is associated with increased probability of high-quality preparation. These results support a change in bowel preparation restricting diet to only the day before colonoscopy in average risk colorectal cancer screening.

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Figure legends

Figure 1. Study flow chart

Figure 2. Difference in the percentage (%) of patients that achieved adequate preparations between diets with 95% CI.

Supplementary table legends

Table S1 Diet and preparation tolerability 5 point Likert scale survey

Table S2 Per protocol segments cleansing and colonoscopy performance

Table S3 Factors related to an adequate cleansing. Results of univariate analysis.

TABLES

Table 1. Baseline and clinical characteristics

Variable	Category	1-Day LRD 420 (50.2%)	3-Day LRD 416 (49.8%)	*p-value*
Participants characteristics				
Age (years)		58.9 (5.4)	59.3 (5.5)	ns
BMI (kg/m2)		27.5 (4.3)	27.5 (4.5)	ns
BMI	≤ 25	31.8%	31.8%	ns
	> 25	68.2%	68.2%	
Sex	Male	55.7%	58.2%	ns
	Female	44.3%	41.8%	
Inadequate cleasing factors				
Hepatic Cirrhosis		1.2%	1.0%	ns
Constipation		15.2%	13.7%	ns
Reduced mobility		3.3%	2.9%	ns
Antidepressant treatment		11.0%	7.7%	ns
Opioid treatment		2.9%	2.9%	ns
Preparation and colonoscopy factors				
Preparation volume adherence	≥ 3/4	418 (96.2%)	416 (97.4%)	ns
	< 3/4	2 (0.5%)	0 (0%)	
Addition of bisacodyl		15.2%	13.7%	ns
Days until colonoscopy		36.6 (17.0)	38.5 (28.8)	ns

Table 2. Non-inferiority analysis (adequate colon preparation according to BBPS)

	1-Day LRD n/N (%)	3-Day LRD n/N (%)	*Difference (one-sided 95% CI)*	*p-value* (non-inferiority)
Intention to treat analysis				
Adequate preparation or segmental BBPS ≥2. n(%)				
Global BBPS	411/420 (97.9)	403/416 (96.9)	0.98 (-1.07.)	<0.001
Proximal BBPS	414/418 (99.0)	403/410 (98.3)	0.75 (-0.80.)	<0.001
Transverse BBPS	416/419 (99.3)	408/412 (99.0)	0.25 (-1.03.)	<0.001
Distal BBPS	414/420 (98.6)	405/416 (97.4)	1.21 (-0.63.)	<0.001
Per protocol analysis				
Adequate preparation or segmental BBPS ≥2. n(%)				
Global BBPS	409/417 (98.1)	399/409 (97.6)	0.53 (-1.39.)	<0.001
Proximal BBPS	412/416 (99.0)	400/407 (98.3)	0.76 (-0.80.)	<0.001
Transverse BBPS	414/417 (99.3)	404/407 (99.3)	0.02 (-0.97.)	<0.001
Distal BBPS	411/417 (98.6)	401/409 (98.0)	0.52 (-1.20.)	<0.001

Table 3. ITT segments cleansing and colonoscopy performance

Variable	1-Day LRD 420 (50.2%)	3-Day LRD 416 (49.8%)	*p-value*
Colonoscopy related times			
Cecal intubation time (m:s)	5:00 (4:00)	5:00 (3:00)	0.292
Time lapse between end preparation and colonoscopy (h:m)	3:20 (0:56)	3:22 (0:53)	0.417
Withdrawal time (m:s)	13:0 10:0)	14:00 (9:00)	0.867
Total colonoscopy time (m:s)	19:00 (12:00)	19:00 (11:00)	0.322
Cleansing			
Proximal BBPS			**0.029**
0-1	4 (1.0%)	7 (1.7%)	
2	185 (44.3%)	208 (50.7%)	
3	229 (54.8%)	195 (47.6%)	
Transverse BBPS			**0.047**
0-1	3 (0.7%)	4 (1.0%)	
2	130 (31.0%)	154 (37.4%)	
3	286 (68.3%)	254 (61.7%)	
Distal BBPS			0.566
0-1	6 (1.4%)	11 (2.6%)	
2	187 (44.5%)	184 (44.2%)	
3	227 (54.0%)	221 (53.1%)	
Global BBPS ≥ 8	254 (60.5%)	221 (53.1%)	**0.032**

Performance			
Adenoma detection	304 (72.4%)	302 (72.6%)	0.944
Polyp detection	327 (77.9%)	313 (75.2%)	0.372

Table 4. Tolerability and colonoscopy findings

Variable	**1-Day LRD 420 (50.2%)**	**3-Day LRD 416 (49.8%)**	***p-value***
Tolerability			
Agregate diet tolerability			<0.001
Likert 1-2	318 (77.0%)	248 (60.9%)	
Likert 3-5	95 (23.0%)	159 (39.1%)	
Agregate preparation tolerability			ns
Likert 1-2	280 (67.8%)	259 (63.6%)	
Likert 3-5	133 (32.2%)	148 (36.4%)	
Complete diet adherence	420 (100%)	412 (99%)	ns
Complete colonoscopy	418 (99.5%)	408 (98.1%)	ns
Cause of uncomplete colonoscopy			ns
Inadequate cleansing	1 (0.2%)	5 (1.2%)	
Estenosis	1 (0.2%)	1 (0.2%)	
Loop formation	0 (0%)	1 (0.2%)	
Adherences	0 (0%)	1 (0.2%)	

Colonoscopy diagnostics			ns
Normal	34 (8.2%)	41 (10.0%)	
Colorectal cancer	12 (2.9%)	18 (4.4%)	
Polyps	306 (73.4%)	299 (72.6%)	
Inflammatory colitis	3 (0.7%)	4 (1.0%)	
Angiodysplasia	8 (1.9%)	1 (0.2%)	
Other tumors	0 (0%)	1 (0.2%)	
Diverticulae	32 (7.7%)	23 (5.6%)	
Hemorroids	21 (5.0%)	23 (5.6%)	
Other	1 (0.2%)	2 (1.5%)	
Side effects			
Adverse events	1 (0.2%)	5 (1.2%)	ns

Table 5. Factors associated to an excellent colon preparation (BBPS ≥ 8). Results of a multivariate logistic regression analysi

Variable	*p-value, univariate analysis*	OR (95% CI)	*p-value, multivariate analysis*	OR (95% CI)
Age (years)	0.003*	0.96 (0.94-0.98)	0.049*	0.97 (0.94-0.99)
BMI (kg/m2)	0.026*	0.96 (0.93-1.0)	0.013*	0.96 (0.92-0.99)
Sex (Male)	0.140	0.81 (0.61-1.1)		
Reduced mobility	0.002	0.27 (0.11-0.65)		
Antidepressant	0.202	0.74 (0.46-1.2)		
Opioids	0.001*	0.24 (0.1-0.62)	0.018*	0.29 (0.11-0.81)
1-Day LRD	0.032*	1.3 (1.0-1.8)	0.008*	1.5 (1.1-2.0)
Diet compliance	0.034*	2.3 (2.1-2.5)		
Low diet tolerance	0.996	1.0 (0.7-1.4)		
Constipation	0.019*	0.63 (0.43-0.93)	0.021*	0.60 (0.39-0.93)
Low preparation tolerance	0.092	0.80 (0.58-1.0)		
Days until colonoscopy	0.236	0.99 (0.99-1.0)		

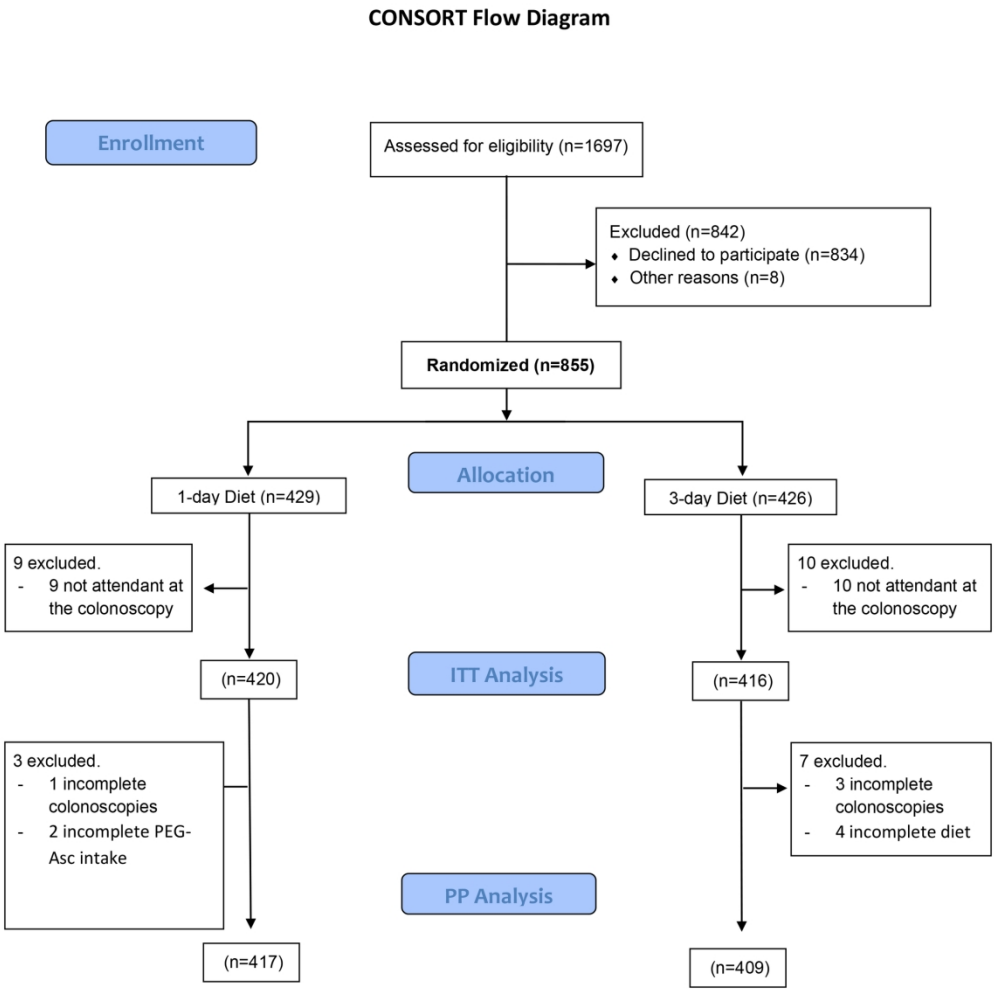

Figure 1 Study flow chart

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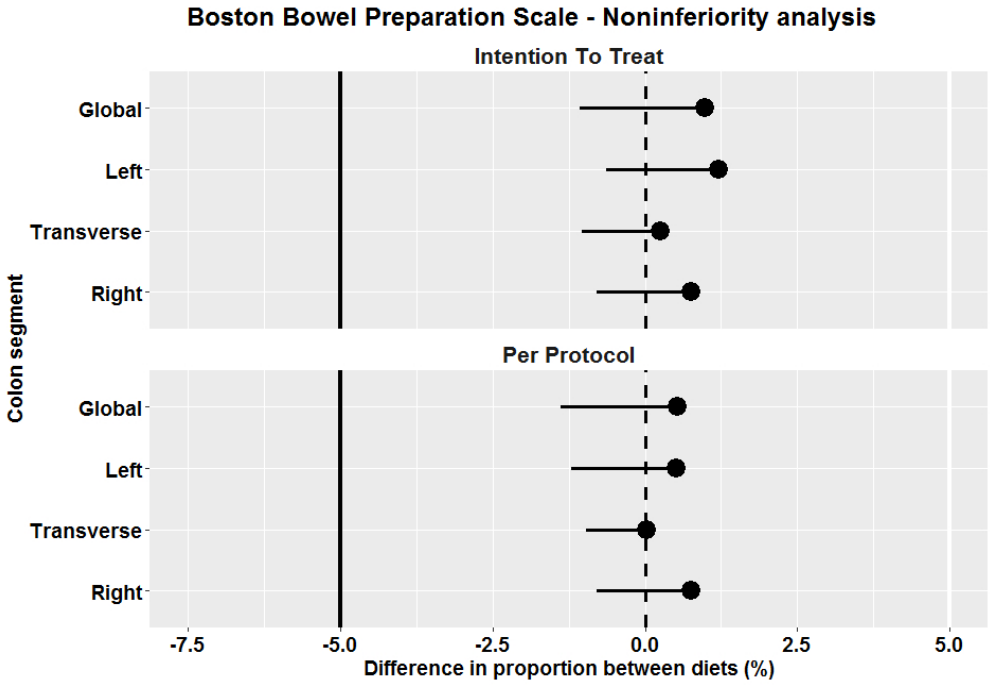

Figure 2 Difference in the percentage (%) of patients that achieved adequate preparations between diets with 95% CI.

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Supporting Information

Likert scores

Tolerance to the evacuating solution.

1 = Very tolerable preparation. I would have no problem repeating it again.

2 = Preparation quite tolerable. I have had some discomfort, but I would not mind repeating it again.

3 = Moderately tolerable preparation. I have had discomfort but if it is necessary, I would repeat it again.

4 = Very annoying preparation. I have had a lot of discomfort. I would only repeat it if it is strictly necessary.

5 = Intolerable preparation. I would never repeat it again.

Tolerance to the diet.

1 = Diet very easy to follow. It has not interfered with my normal life. I have had no discomfort.

2 = Diet easy to follow. I have had to change my habits a little, but I have continued to lead a normal life. I have not noticed any discomfort.

3 = Moderately easy diet to follow. I have had to change my habits. Restrictive amounts. I've been a little hungry. I have not noticed any other discomfort.

4 = Diet very difficult to follow. I have had to change my habits. Very restrictive amounts. I've been very hungry. I also felt very tired and have lost weight

5 = Diet almost impossible to follow. Very restrictive. I have been very hungry. I am very tired; I have insomnia and I have lost a lot of weight. I would never repeat it again.

Supporting Information

Additional table 2. **PP segments cleansing and colonoscopy performance**

Variable	Category	1-Day LRD	3-Day LRD	*p-value*
		417 (50.5%)	**409 (49.5%)**	
Colonoscopy related times				
Cecal intubation time (m:s)		5:00 (4:00)	5:00 (3:00)	ns
Time lapse between end preparation and colonoscopy (h:m)		3:20 (0:56)	3:22 (0:53)	ns
Withdrawal time (m:s)		13:00 (10:00)	14:00 (9:00)	ns
Total colonoscopy time (m:s)		19:00 (12:00)	19:00 (11:00)	ns
Cleansing				
Proximal BBPS	0-1	4 (1.0%)	7 (1.7%)	0.031*
	2	183 (44.0%)	205 (50.4%)	
	3	229 (55.0%)	195 (47.9%)	
Transverse BBPS	0-1	3 (0.7%)	3 (0.7%)	ns
	2	129 (30.9%)	152 (37.3%)	

	3	285 (68.3%)	252 (61.9%)	
Distal BBPS	0-1	6 (1.4%)	8 (2.0%)	ns
	2	185 (44.4%)	181 (44.3%)	
	3	226 (54.2%)	220 (53.8%)	
Global BBPS ≥ 8	Yes	254 (60.9%)	221 (54.0%)	0.046*
Performance				
Adenoma detection	Si	301 (72.2%)	299 (73.1%)	ns
Polyp detection	Si	325 (77.9%)	311 (76.0%)	ns

Supporting Information

Additional table 2. Factors associated to an adequate cleansing). Results of univariate analysis.

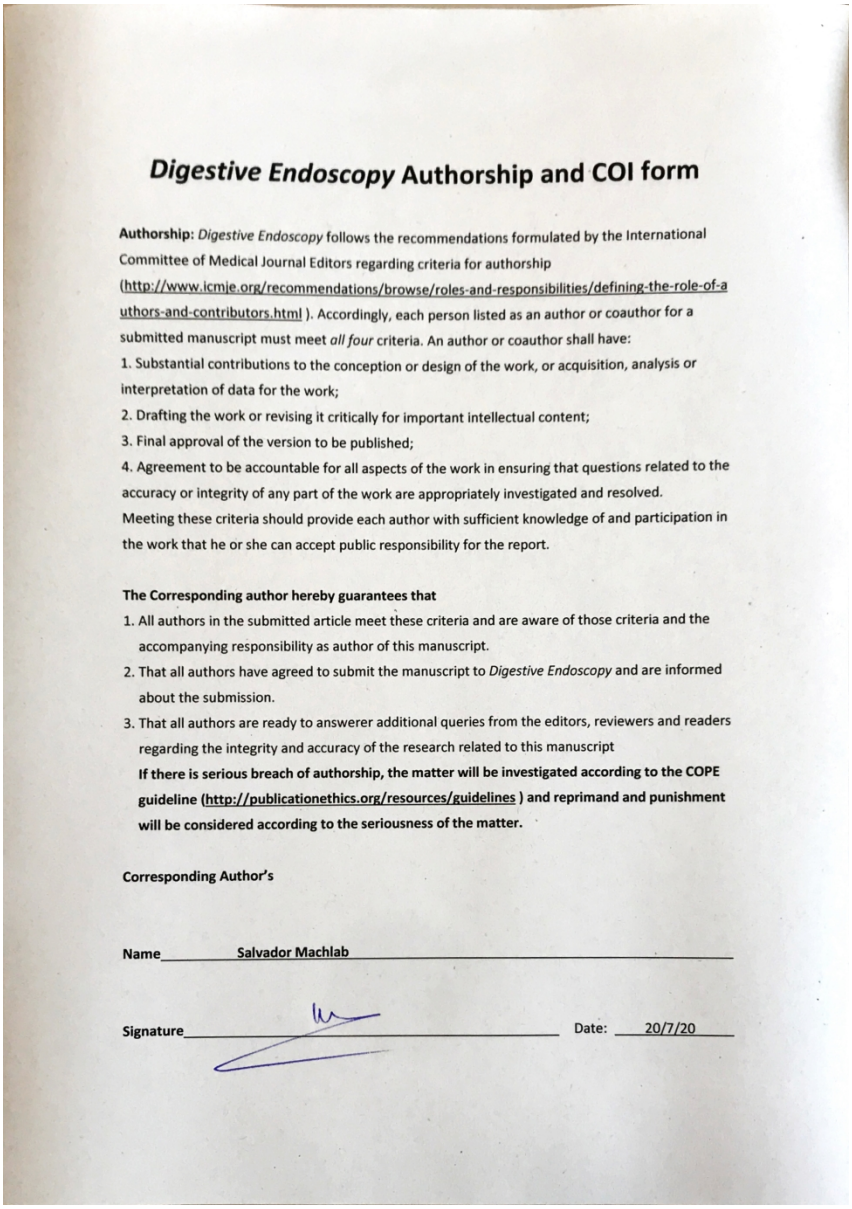
Variable	*p-value, univariate analysis*	OR (95% CI)
Age (years)	0.459	1.03 (0.95-1.1)
BMI (kg/m2)	0.582	0.97 (0.88-1.1)
Sex (Male)	0.818	1.10 (0.47-2.6)
Constipation	0.286	0.60 (0.23-1.55)
Antidepressant	0.148	0.45 (0.15-1.4)
1-Day LRD	0.502	1.47 (0.62-3.48)
Low diet tolerance	0.703	1.20 (0.46-3.1)
Low preparation tolerance	0.262	0.62 (0.26-1.45)
Days until colonoscopy	0.092	1.01 (0.99-1.02)

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4
	2b	Specific objectives or hypotheses	4, 5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons	
Sample size	7a	How sample size was determined	8
	7b	When applicable, explanation of any interim analyses and stopping guidelines	
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5,6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	6

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	9
	13b	For each group, losses and exclusions after randomisation, together with reasons	9
Recruitment	14a	Dates defining the periods of recruitment and follow-up	5
	14b	Why the trial ended or was stopped	5
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Done
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Done
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	9, 10
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Done
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	12
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	12
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	13
Other information			
Registration	23	Registration number and name of trial registry	5
Protocol	24	Where the full trial protocol can be accessed, if available	
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.



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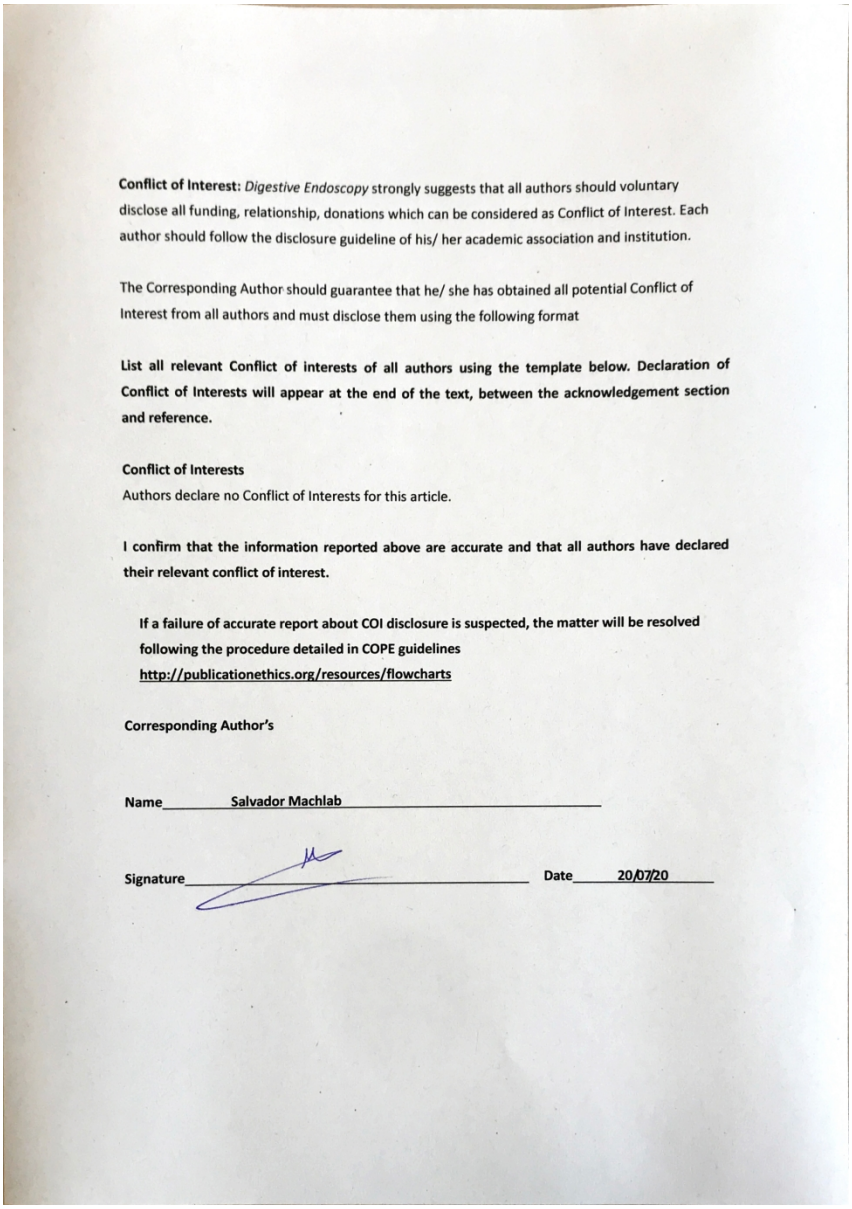

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