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Efficacy of Mediterranean Diet vs. Low-FODMAP Diet in Patients With Nonconstipated Irritable Bowel Syndrome: A Pilot Randomized Controlled Trial

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ABSTRACT

Introduction: Mediterranean diet (MD) has been proposed as a dietary therapy for irritable bowel syndrome (IBS) but its efficacy remains unclear. We compared the efficacy of MD to a diet low in fermentable oligo-, di-, monosaccharides, and polyols (LFD).

Methods: In this pilot-feasibility, randomized controlled trial (RCT), adult patients with diarrhea-predominant IBS (IBS-D) or mixed bowel pattern (IBS-M) were randomized to MD versus LFD for 4 weeks. Meals were provided for both groups (ModifyHealth, GA). Daily variables included abdominal pain intensity (API) and bloating, while IBS symptom severity score (IBS-SSS) and IBS adequate relief (IBS-AR) were scored weekly. The primary endpoint was the proportion of patients with ≥ 30% decrease in API for ≥ 2/4 weeks.

Results: Of 26 randomized patients, 20 finished the study (10 per group). Seventy-three percent of the MD group met the primary endpoint compared to 81.8% of the LFD group ($p = 1.0$). Although not statistically significant, a numerically higher proportion of the LFD group reported adequate relief and met the responder endpoint for IBS-SSS (50-point reduction) compared to the MD group (54.6% vs. 27.3% for IBS-AR and 81.8% vs. 45.5% for IBS-SSS, $p = 0.39$ and 0.18, respectively). The LFD group also had a significantly greater reduction in IBS-SSS score over the 4-week treatment period compared to the MD group (−105.5 vs. −60, $p = 0.02$).

Conclusion: MD provides symptom relief in IBS-D and IBS-M; however, the magnitude of relief was higher with the LFD. Larger diet comparison studies in real-world settings are needed before MD can be routinely recommended to IBS patients.

Trial Registration: Clinicaltrials.gov: NCT05807919.

1 | Introduction

Irritable bowel syndrome (IBS) is a disorder of gut-brain interaction, characterized by abdominal pain associated with altered bowel habits, and is estimated to affect 4%–11% of people globally [1, 2]. A majority of patients perceive their symptoms to be food-related; therefore, it is not surprising that many patients with IBS prefer dietary therapies over other forms of therapy such as pharmacotherapy [3]. A diet low in fermentable oligo-, di-, monosaccharides and polyols (low-FODMAP diet, or LFD) improves symptoms in about 50%–60% of patients with IBS, and a recent network meta-analysis found it superior to other

Summary

- A Mediterranean diet (MD) improves abdominal symptoms in the majority of patients with nonconstipated IBS.
- The magnitude of improvement in IBS symptoms was greater with the low-FODMAP diet compared to the MD.
- Larger, real-world studies are needed before the MD can be recommended to patients with IBS.

dietary interventions in improving global IBS symptoms [4, 5]. However, many patients find it difficult to implement given its complex and restrictive nature. Moreover, there are concerns about diet-induced changes in the gut microbiota as well as the potential for nutrient deficiencies [6]. Furthermore, there are concerns about recommending a restrictive diet like the LFD to patients with disordered eating or an eating disorder [7]. Thus, there remains a need for alternative dietary strategies for managing the symptoms of IBS.

The Mediterranean diet (MD) is a time-honored diet rich in plant-based foods including fruits, vegetables, legumes, whole grains, nuts, and olive oil while being low in saturated fats and red meat. MD has been shown to be beneficial for a variety of health conditions including cardiovascular and metabolic diseases as well as cognitive disorders and overall mortality [8]. It is hypothesized that a MD could be beneficial in reducing bowel symptoms as well, due to beneficial effects on the gut microbiota, gut mucosal inflammation, gut barrier function, and activation of the gastrocolic reflex [9–11]. Observational studies have yielded conflicting results, with some suggesting a higher likelihood of IBS symptoms in those with lower adherence to a MD while others have reported the opposite (i.e., more severe gastrointestinal symptoms with MD adherence or specific MD foods) [12–14]. These studies are challenging to interpret given their potential for unrecognized confounding. A nonrandomized cross-over trial found improvement in IBS symptoms with a MD; however, the study had several methodological limitations including a small sample size, high likelihood of carry-over effects as well as lack of randomization, blinding, or assessment of adherence to the diet interventions [15]. More recently, a pilot, feasibility, randomized controlled trial (RCT) found the MD superior to a habitual diet in patients with IBS [16]. To date, no RCT has compared the efficacy of a MD with the LFD, the most evidence-based dietary therapy for patients with IBS.

In this pilot feasibility study, our objective was to compare the clinical efficacy of a MD with the LFD in patients with IBS in a single-center, parallel group, RCT. We hypothesized that both a MD and LFD would achieve similar improvements in abdominal pain, bloating, and overall improvement in IBS symptom severity.

2 | Materials and Methods

The study was approved by the Institutional Review Board at the University of Michigan, Ann Arbor (HUM00227491). The study was registered at Clinicaltrials.gov (NCT05807919). All subjects provided written informed consent for the study.

2.1 | Patient Population

Subjects aged 18–70 who met Rome IV criteria for irritable bowel syndrome with diarrhea (IBS-D) or irritable bowel syndrome with mixed bowel habits (IBS-M) were recruited from gastroenterology and primary care clinics at the University of Michigan and via online advertising. Subjects were required to have an average worst daily abdominal pain intensity (API) score of ≥ 3.0 on a 10-point visual analog scale (VAS) during the 7-day baseline period. Subjects with alarm features (rectal bleeding, weight loss, nocturnal diarrhea) or relevant comorbid conditions (personal history of celiac disease, microscopic colitis, inflammatory bowel disease, poorly controlled diabetes, eating disorder, prior small bowel or colonic surgery, known food allergies to eggs, peanuts, tree nuts, milk or seafood) were excluded. Subjects who received antibiotics in the 3 months prior to enrollment were excluded. Pregnant and lactating subjects were also excluded. At least 80% compliance in daily questionnaire entries was required during a 7-day screening period. Subjects who had adhered to any dietary IBS treatment (low-fat, LFD, MD, gluten-free) in the previous 6 months were excluded. Subjects were allowed to remain on their current IBS medications, provided the dose was stable over the past 30 days. Subjects agreed to not change their lifestyle or exercise routines significantly during the study period.

2.2 | Study Protocol

Eligible subjects were asked to participate in a study that would test the efficacy of two diets thought to be beneficial for IBS symptoms. Potential subjects underwent a 7-day screening period during which they were asked to fill out a daily symptom questionnaire. Those eligible for randomization (average daily API score ≥ 3.0, 80% adherence with symptom surveys) were randomized via computer generation in a 1:1 ratio to MD or LFD for a 4-week period. Study visits occurred at the screening visit, at the beginning of the dietary intervention (day 0), and at the end of the dietary intervention (day 28).

Three meals a day and additional snacks were provided to all participants for the entire study period by a company that provides medically tailored meals including MD and LFD (ModifyHealth, Atlanta, Georgia). In addition, additional recipes for snacks and meals in accordance with their randomization were provided to each subject. Subjects were instructed not to eat food outside of what was provided. Meals for both groups were packaged identically and were not labeled as MD or LFD. The MD cohort received foods consistent with a MD (plant-based foods, olive oil, legumes, nuts, vegetables and fruits, whole grains, fish and poultry as meat, etc.). The LFD meals were Monash certified for the restriction phase of the LFD and mean (±SD) total FODMAP content per serving was 0.36 g (±0.13 g). The mean total FODMAP content per serving for the MD group was significantly higher than the LFD group at 1.51 g (±1.04 g) ($p < 0.001$). Individual FODMAP group content for both meal plans is listed in Table 1. As expected, the

TABLE 1 | Total and individual FODMAP content per serving in meals provided in both groups.

	MD	LFD	*p*
Total FODMAP content	1.51 (1.03)	0.36 (0.12)	< 0.0001
Excess fructose	0.17 (0.11)	0.15 (0.12)	0.36
Fructans	0.92 (0.65)	0.14 (0.08)	< 0.0001
Galacto-oligosaccharides	0.35 (0.47)	0.03 (0.03)	< 0.0001
Lactose*	0.00	0.00	NA
Polyols	0.07 (0.12)	0.04 (0.07)	0.70

*No lactose present in either meal plan.

MD group had significantly higher levels of fructan, galacto-oligosaccharides, and polyols compared to the LFD group ($p < 0.05$ for each, Table 1). Additional details about the meal plans are provided in Supporting Information.

2.3 | Measures

Subjects completed daily, weekly, and pre/post-study symptom surveys. Subjects rated API, abdominal discomfort, and bloating in a daily log on an 11-point Likert scale (0–10). Stool consistency was measured using the Bristol stool form scale (BSFS) and recorded daily for each bowel movement. Subjects completed the Irritable Bowel Syndrome Symptoms Severity Scale (IBS-SSS) weekly. IBS-SSS measures five items: severity of abdominal pain, number of days with abdominal pain, severity of abdominal distension, dissatisfaction with bowel habits, and interference with quality of life, each on a 0–100 scale. IBS-SSS scores can range from 0 to 500, with higher scores indicating greater symptom frequency and/or severity [17]. A 50-point reduction in IBS-SSS is considered the minimal clinically important difference and was used as a cut-off to define the IBS-SSS responder [17]. To evaluate for adequate relief of IBS (IBS-AR), subjects were asked to provide a binary (yes/no) response about the adequacy of relief of their IBS symptoms. Subjects filled out IBS-SSS and IBS-AR at the beginning of the diet phase and then weekly thereafter. Irritable Bowel Syndrome Quality of Life (IBS-QoL) is a 34-item questionnaire assessing quality of life along eight domains [18]. All of the final IBS-QoL scores were transformed into a 0–100 score, with quality of life improving as the score increases. The Generalized Anxiety Disorder Screener (GAD7) is a seven-question anxiety questionnaire that has been validated in the general population [19]. Subjects filled out IBS-QoL and GAD7 at the beginning and end of the diet phase.

2.4 | Outcomes

The primary outcome was the proportion of subjects meeting the Food and Drug Administration (FDA) weekly responder definition for API for at least 2 of 4 weeks. A weekly responder was defined as a 30% decrease in the weekly average for API compared to the baseline period.

Secondary endpoints included responders for bloating and discomfort (calculated similarly to API responder definition above), 50% or greater reduction in the number of days per week with at least one abnormal stool (defined as BSFS 1 or 2, or 6 or 7), the proportion of subjects who had adequate relief of symptoms in at least 2 of 4 weeks of the treatment period, the proportion of subjects who were IBS-SSS responders for at least 2 of 4 weeks (50-point reduction in IBS-SSS compared to baseline) and mean IBS-SSS change between the start and end of the diet phase.

Exploratory endpoints were mean changes in abdominal symptoms, IBS-QOL, and GAD-7 scores.

2.5 | Diet Adherence

After proper instruction, study participants filled out a 3-day food diary at the beginning and end of the study (week 4). A three-day food record has been shown to be more accurate than 24-h or 5-day diet recall [20]. The week 4 three-day food diaries were reviewed by an expert GI dietitian (CLK) and each recorded meal was designated as "compliant" or "not compliant" with the allocated randomization. The percentage of "compliant" and "noncompliant" meals was calculated for every subject and the percentage of compliance for the group was calculated by averaging the compliance percentages for subjects in that group. Standardized questionnaires such as MD screener adherence was not used to measure compliance as participants were not aware of how the meals were prepared (to maintain blinding) and therefore would not have been able to answer questions which composed these questionnaires such as what oil was used for preparation, how much olive oil, or ingredients of sauce (when sofrito based sauce was used in meals). Instead, we felt review of food diaries by an expert GI dietitian was a better way to assess compliance in a feeding intervention such as ours.

2.6 | Statistical Analysis

As this was a pilot study, we aimed to enroll approximately 30 subjects to achieve the goal of 20 subjects finishing the study (10 in each arm). Analysis was done using modified intention to treat (mITT) as well as per-protocol. All subjects who finished the study and those who dropped out due to adverse events were included in mITT analysis, while only those who finished the study were included in per-protocol analysis. For mITT analysis, the nonresponder imputation approach was used for imputing missing data for binary variables that assumes non-response for all missing data (given the 2 dropouts were due to side effects). All continuous variables were tested for normality using the Shapiro–Wilk test. For a continuous variable, the Student t-test and Mann Whitney test were performed as appropriate. The chi-square test and Fisher exact tests were used as appropriate. p-Value < 0.05 was considered significant.

3 | Results

Twenty-six subjects with IBS-D/M were enrolled: 15 were randomized to MD and 11 to LFD. One subject received antibiotics

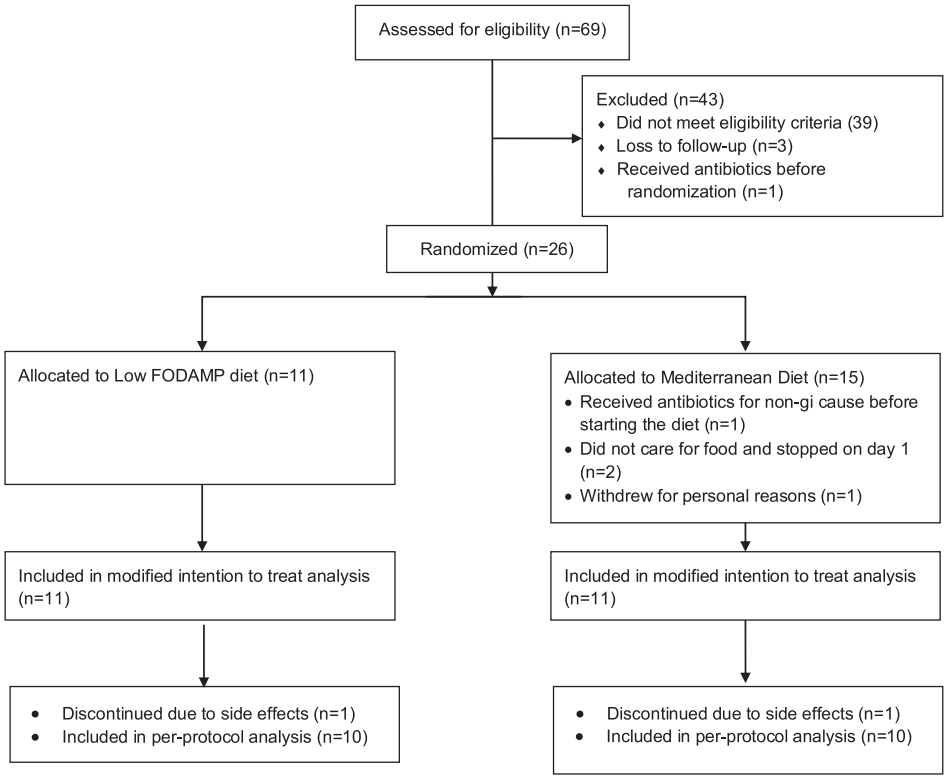


FIGURE 1 | Consort flow diagram.

TABLE 2 | Baseline characteristics of the two groups.

Baseline characteristic	MD ($n=15$)	LFD ($n=11$)	p
Age, mean (SD)	38.13 (11.3)	45.09 (19.5)	0.26
Female	93.3% (14)	81.8% (9)	0.36
IBS subtype			
IBS-D	53.3% (8/15)	54.5% (6/11)	1.0
IBS-M	46.7% (7/15)	45.5% (5/11)	
API[a]	5.4 (4.3, 6.4)	5.1 (4.1, 5.8)	0.5
Bloating[a]	5.1 (4.5, 6.1)	5.7 (4.6, 7.2)	0.3
Discomfort[a]	5.7 (5.3, 7.0)	6.1 (4.7, 6.5)	0.7
IBS-SSS[a]	338.9 (82.5)	346.2 (54.4)	0.80

Abbreviations: API, abdominal pain intensity; IBS, irritable bowel syndrome; IBS-D, diarrhea-predominant IBS; IBS-M, IBS with mixed bowel pattern; IBS-SSS, IBS symptom severity scale (0–500).
[a]Average daily score assessed during 7-day baseline period. Bloating, Discomfort, and API were measured on a 0–10 scale. Results presented as mean (95% CI) or mean (SD).

for a nongastrointestinal issue after randomization and therefore did not start the diet phase. Of 25 subjects who started the diet, three withdrew consent (two who did not care for the meals they were receiving and withdrew consent on day 1 of the diet and one for personal reasons not related to the study). The remaining 22 subjects were included in the mITT analysis. Finally, two subjects withdrew from the study due to side effects (one in each group). Therefore, 20 subjects finished the study and were included in the per protocol analysis (10 in each group) (Figure 1). Baseline characteristics were similar between the two groups (Table 2).

3.1 | Primary Efficacy Endpoint

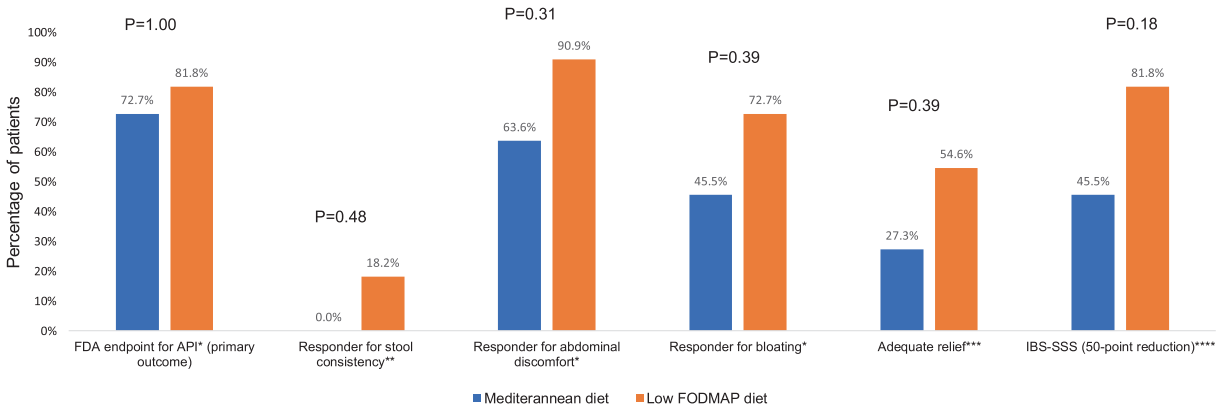
In mITT analysis, 72.7% (8/11) of the subjects in the MD group met the FDA responder definition for API (i.e., $\geq$30% reduction in worst abdominal pain score for at least 2 of the 4-week treatment period) compared to 81.8% (9/11) in the LFD group ($p=1.00$) (Figure 2).

3.2 | Secondary Efficacy Endpoints

Although not statistically significant, all secondary outcomes including the proportion of subjects meeting the responder definition for abdominal discomfort, bloating, stool consistency, IBS-SSS (using 50-point cutoff), and adequate relief were numerically higher in the LFD group (Figure 2).

3.3 | Per-Protocol Analysis

In per-protocol analysis, 80% (8/10) of the subjects in the MD group met the primary endpoint of the FDA responder definition for API compared to 90% (9/10) in the LFD group ($p=1.00$). There were no significant differences between the two groups with respect to any of the secondary outcomes described above and continued to favor the LFD group (Table 3). Finally, when the absolute decrease in the mean IBS-SSS scores between the beginning and end of the treatment period was compared



*≥30% reduction in weekly average of daily symptom severity for at least 2/4 weeks
**≥50% reduction in the number of days with Bristol stool form scale 6-7 or 1-2 stool for at least 2/4 weeks
*** Those reporting adequate relief for at least 2/4 weeks
****≥50-point and 100-point reduction in IBS-SSS for at least 2/4 weeks
mITT= modified intention to treat, FDA=Food and Drug Administration, API= abdominal pain intensity, IBS-SSS= Irritable bowel symptom severity score

FIGURE 2 | Comparison of primary and secondary outcomes between the two groups per modified intention-to-treat analysis.

TABLE 3 | Per protocol analysis for clinical outcomes between the two groups.

	MD ($n=10$)	LFD ($n=10$)	p
Primary outcome			
FDA endpoint for API* (primary outcome)	80% (8)	90% (9)	1.00
Secondary outcomes			
Responder for stool consistency**	0% (0)	20% (2)	1.00
Responder for abdominal discomfort*	70% (7)	100% (10)	0.21
Responder for bloating*	50% (5)	80% (8)	0.35
Adequate relief***	30% (3)	60% (6)	0.37
IBS-SSS responder****	50% (5)	90% (9)	0.14
Mean change in IBS-SSS mean (95% CI)	-60 (57, −227)	−105.5 (−66, −260)	**0.02**
Exploratory outcomes			
Mean percent change in abdominal pain	46.7%	63.2%	0.26
Mean percent change in abdominal discomfort	42.4%	62.4%	0.08
Mean percent change in bloating	37.2%	58.9%	0.17
Mean change in IBS-QoL (SD)	−9.4 (17.3)	26.2 (20.6)	0.09
Mean change in GAD-7 (SD)	−0.1 (3.0)	−4.1 (6.4)	0.056

Abbreviations: API, abdominal pain intensity; FDA, food and drug administration; GAD-7, generalized anxiety and disorder-7; IBS-SSS, irritabl1e bowel symptom severity score, IBS-QoL, quality of life.
*≥ 30% reduction in weekly average of daily symptom severity for at least 2/4 weeks.
**≥ 50% reduction in the number of days with BSFS 6–7 or 1–2 stool for at least 2/4 weeks.
***Those reporting adequate relief for at least 2/4 weeks.
****≥ 50-point reduction in IBS-SSS for at least 2/4 weeks.

between the two groups, subjects in the LFD group had a significantly higher decrease in IBS-SSS compared to the MD group (105.5 vs. 60, $p=0.02$).

3.4 | Exploratory Endpoints

Subjects in the LFD group had a numerically greater mean percent change in API, abdominal discomfort, and bloating from baseline to week 4 compared to the MD group, but these differences did not reach statistical significance (Table 3).

While the MD group did not report a significant change in the mean GAD7 scores, GAD7 scores decreased in the LFD group between week 4 and baseline (−0.1 vs. −4.1, $p=0.056$). Similarly, the mean disease-specific quality of life scores between week 4 and baseline did not improve in the MD group, while they increased in the LFD group (−9.4 vs. 26.2, $p=0.09$, Table 3).

3.5 | Safety Endpoints

Two of the 26 randomized patients dropped out of the study due to side effects: one due to worsening constipation (LFD group) and another due to worsening abdominal pain (MD group).

3.6 | Compliance

Compliance was calculated as described above. In the MD arm, the average compliance to the principles of MD was 93.8% (range 78%–100% for 10 patients) i.e., subjects in the MD group were compliant with the MD for 93.8% of meals recorded in the 3-day food diary at the end of the treatment period, which were consistent with the principles of MD, and for the rest 6.2%, subjects were not compliant. Similarly, in the LFD arm, the average compliance to the elimination phase of LFD was 94% (range 75%–100% for 10 patients), and for the rest of the meals, subjects were not compliant.

4 | Discussion

In this feeding trial, we compared the efficacy of MD with the LFD in patients with IBS. We found that both interventions were comparable in meeting the primary endpoint of 30% or more improvement in API scores for at least 2 of 4 intervention weeks. However, the LFD group had a significantly greater decrease in the IBS-SSS score compared to the MD group. Furthermore, though not statistically significant, there was a statistical trend toward greater benefit with the LFD over the MD for improvements in GAD-7 and IBS-QoL scores. Similarly, at the end of the study, the LFD group had a numerically (but not statistically) higher percent decrease in the weekly average scores for abdominal pain, bloating, and discomfort compared to the MD group.

In our study, the majority of patients in the MD group had improvement in symptoms of abdominal discomfort, pain, and bloating. Indeed, 80% of the patients in the MD group met the FDA responder definition for abdominal pain. The MD group had ~40% decrease in the mean weekly scores of abdominal pain, discomfort, and bloating. This is consistent with a recent RCT as well as a nonrandomized clinical trial, both of which reported a positive impact of MD on abdominal symptoms in patients with IBS [15, 16]. We found that none of the patients in the MD group met our endpoint of ≥ 50% increase in the number of days/week with only normal bowel movements (BSFS 3–5). This is also consistent with the abovementioned RCT, which did not find a significant impact of MD on bowel symptoms [16]. It is important to note that while all patients in our study fulfilled criteria for IBS-D and IBS-M, IBS-C was the largest IBS subgroup in the previous RCT [16]. Taken together, this suggests that irrespective of the IBS subtype, a MD appears to improve abdominal symptoms, but based upon the currently available evidence, does not impact bowel symptoms in patients with IBS.

Although our data and previously published literature suggest that a MD might be beneficial in improving abdominal symptoms in a subset of patients with IBS, it is unclear how it compares to other dietary interventions with known efficacy for IBS symptoms such as the LFD. Although our study was not powered to compare the efficacy of the two dietary interventions, multiple endpoints suggested that the LFD may provide a greater magnitude of improvement in abdominal pain and bloating compared to MD. The MD group had a numerically lower mean decrease in abdominal pain and bloating scores, a lower decrease in mean IBS-SSS score, and a lower proportion of patients meeting the responder definition for adequate relief and IBS-SSS (using a 50-point cutoff) compared to the LFD group. Larger comparative effectiveness studies are needed to confirm or refute the suggestions raised by our study. We only studied the restriction phase of LFD because it is the most scientifically validated and standardized phase of LFD. However, unlike MD, the restriction phase of LFD is not meant to be a long-term dietary modification and should only be used for 4–8 weeks [21]. Future trials should consider comparing the long-term effectiveness of the two diets by comparing the personalized phase of LFD with MD.

Ours is the first RCT comparing MD with an active comparison arm in IBS as the previous RCT compared the MD with a habitual diet, where patients were instructed to continue their usual diet. Another study that compared MD with LFD and gluten-free diet was not a randomized trial and had various other methodological limitations including high likelihood of carryover effects, and lack of blinding, or assessment of adherence to the dietary interventions [15]. This raises several important questions. Firstly, it is unclear how a MD compares to other dietary interventions such as LFD or NICE diet in patients with IBS. Secondly, the term "MD" has been applied to a wide range of dietary interventions. For example, while the principles of MD in our study and Staudacher et al. were fairly similar, a "balanced" MD used by Paduano et al. focused on increasing fiber intake and avoiding meal-skipping while allowing foods containing FODMAPs and gluten [15, 16]. However, they did not provide any details about other integral parts of their MD such as the consumption of olive oil, vegetables, fruits, whole grains, or legumes in the diet [15]. This should be explored in future studies evaluating a MD in patients with IBS. Finally, the LFD and a MD are conceptually very different diets, and even if they both are effective in managing IBS symptoms, it is unlikely they work through the same mechanism. For example, the LFD has been shown to decrease the abundance of saccharolytic bacteria while a MD has been shown to increase their abundance [22, 23]. While both the LFD and a MD have been shown to improve intestinal barrier function, the LFD has been shown to positively impact barrier function via targeting LPS-mediated mast cell activation and a MD via increasing SCFA production [24–26]. Therefore, it is possible, perhaps even likely, that the patients with IBS who benefit from the LFD and a MD may be different. It is also possible the biomarker discovery and validation strategies for these two diets will also differ but nonetheless, hold the promise of improving clinical response rates.

Our study has several strengths. We provided all the meals and most of the snacks for the duration of the study, thereby improving compliance, ensuring that the interventions were true to the LFD or a MD, and reducing the variation in nutritional contents during the intervention phase. This allowed us to compare the effects of both dietary interventions in a very controlled manner. Second, patients did not know which diets were being compared

in the study, allowing us to maximize blinding. Third, we collected very detailed clinical outcomes, including daily diaries on abdominal and bowel symptoms.

Our study has several important limitations. First, this was intended to be an exploratory, pilot study. As such, the study was not powered to achieve significant results for the primary or secondary endpoints assessed. For this reason, the results of this study should be viewed as hypothesis-generating rather than definitive. This study provides important preliminary data to power a future, methodologically rigorous, randomized, controlled trial. Second, six of the 26 patients who were randomized dropped out of the study, but it is important to note that only two of these dropouts were due to an adverse event (constipation and worsening abdominal pain in the LFD group) suggesting a MD is well tolerated in IBS patients. Finally, as this was a feeding study in which we provided all of the food during the intervention phase, it could be argued that our results may not be generalizable to the "real world." As this was a pilot study with a limited sample size, we felt that a feeding study was the best option to improve standardization of the diet interventions and compliance.

5 | Conclusion

In summary, in this pilot study, we have shown that a MD improves abdominal symptoms in the majority of patients with IBS-D and IBS-M. Larger, adequately powered, real-world studies comparing the efficacy of a MD with LFD and NICE diet are needed to validate these preliminary findings and to help patients and providers to know if a MD should be added to the list of effective, evidence-based diet interventions for patients with IBS.

Author Contributions

The authors confirm their contribution to the paper as follows: Study conception and design: Prashant Singh, Shanti Eswaran, William Chey. Data collection: Prashant Singh, Gregory Dean, Sofia Iram, Sam W. Chey. Analysis and interpretation of results: Samara Rifkin, Prashant Singh, Gregory Dean, Sam W. Chey, William Chey. Drafting of the manuscript: Prashant Singh and Gregory Dean wrote the initial draft of the manuscript. All authors critically reviewed the manuscript and revised it as necessary. All authors approved the final version of the manuscript.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Deidentified individual participant data that underlie the reported results may be made available 3 months after publication for 5 years after the publication date. Proposals for access should be sent to singhpr@med.umich.edu. The study protocol is included as a data supplement available with the online version of this article.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.