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Observations and Research

Dietary Patterns Are Not Associated With Disease Activity Among Patients With Inflammatory Conditions of the Pouch in a Prospective Cohort

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Background: Evidence-based recommendations regarding the influence of diet on inflammatory conditions of the pouch after restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) are limited.

Methods: We analyzed dietary patterns at enrollment in a prospective registry of patients with 1 of 4 inflammatory conditions of the pouch (acute pouchitis, chronic antibiotic-dependent pouchitis, chronic antibiotic refractory pouchitis, and Crohn's disease of the pouch). We analyzed dietary intake by disease activity at enrollment and then compared dietary patterns among patients who remained in remission throughout the 12-month follow-up to those patients who experienced a disease relapse. We also compared dietary patterns among patients with inflammatory conditions of the pouch to the United States Department of Agriculture (USDA) recommended daily goals.

Results: Among 308 patients, there were no differences in dietary patterns among patients with 1 of the 4 disease states at enrollment. Additionally, among the 102 patients in remission at baseline, there were no significant differences noted among patients who went on to experience a disease flare in the 12 months after enrollment compared to those patients who remained in remission. However, patients with inflammatory conditions of the pouch demonstrated decreased intake of several food groups and macronutrients including dairy, fruits, vegetables, whole grains, and fiber when compared to USDA recommendations.

Conclusions: In a prospective cohort, we demonstrated no impact of dietary patterns on disease activity. The relative deficiencies in several food groups and macronutrients among patients after IPAA indicate the potential role of targeted nutritional counseling in this population.

Lay Summary

In a prospective patient cohort with inflammatory conditions after restorative proctocolectomy with ileal pouch–anal anastomosis, dietary factors were not associated with disease activity. However, patients with inflammatory conditions of the pouch consumed lower United States Department of Agriculture levels of multiple macronutrients and food groups.

Key Words: Pouchitis, diet, nutrition, Crohn's-like disease of the pouch, PROP-RD

Introduction

Given that the inflammation seen in pouchitis and other inflammatory conditions of the pouch is assumed to be driven by dysbiosis and a dysregulated immune response, there has been continued interest in the influence of diet on these inflammatory states after restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) for ulcerative colitis (UC). Environmental factors such as diet play a key role in shaping the gut microbiota, thus the role of diet as a potential risk factor for pouchitis as well as a therapy for inflammatory conditions of the pouch has been explored in recent years.[1–3]

Despite the suspected influence of diet on outcomes after IPAA and inflammatory conditions of the pouch, there is a lack of consensus regarding the effects of diet on the clinical course of pouchitis and other pouch-related disorders.[3,4]

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Additionally, patients' dietary perceptions can significantly impact nutritional status,[5] and self-imposed dietary restrictions can be associated with both macronutrient and micronutrient deficiencies. Although prior comparisons to recommendations from United States Department of Agriculture (USDA) have been proposed by the Crohn's & Colitis Foundation and other organizations,[5] the comparison of food intake among patients with inflammatory conditions of the pouch to USDA recommendations has not been well explored.

Given that the influence of diet on the disease course after IPAA is not well understood, we integrated a validated dietary questionnaire[6] into the enrollment assessment for patients in A Prospective Registry for the Study of Outcomes and Predictors or Pouchitis and Pouch-Related Disorders (the PROP-RD Study).[7] Specifically, we aimed to evaluate the impact of dietary patterns on disease activity at the time of enrollment and risk for disease relapse/increased disease activity after enrollment among patients in remission at enrollment. Additionally, we sought to compare dietary patterns among patients with the 4 inflammatory conditions of the pouch assessed in PROP-RD (acute pouchitis, chronic antibiotic refractory pouchitis [CARP], chronic antibiotic-dependent pouchitis [CADP], and Crohn's disease [CD] of the pouch) and in comparison to established dietary guidelines.[8]

Methods

Study Population

The design of the PROP-RD study has been described in detail previously.[7] Briefly, patients were enrolled after a confirmed diagnosis of acute pouchitis, CADP, CARP, or CD of the pouch from 1 of 8 participating medical centers. Enrollment was not restricted by a predefined disease activity score, as patients could have active disease or be in clinical remission at the time of enrollment. Similarly, enrollment was not restricted by baseline therapy for inflammatory conditions of the pouch, as patients could be treated with any available antibiotic, probiotic, biologic, and/or small molecule therapy per the discretion of the treating physician. After enrollment, patients completed electronic follow-up via a secure portal at 3, 6, and 12 months after baseline, including questions related to medication use patterns as well as clinical outcome assessments (detailed below).

Dietary Assessment

To assess the impact of dietary patterns on the disease course among patients with inflammatory conditions of the pouch, all patients completed the Dietary Screener Questionnaire (DSQ) at the time of enrollment.[6] Each of the items included in the DSQ was initially selected due to an existing relationship with 1 or more dietary factors of interest in dietary guidance and the scoring algorithms for the DSQ underwent subsequent evaluation and validation after their initial development.[9] Additionally, the DSQ has previously been used in studies of diet modification among patients with inflammatory bowel disease.[10] For comparison to the USDA daily goals,[8] a median of recommendations for females and males age 19 and older or a median of all recommendations for specific daily intake of calories were used.

Outcomes

The primary outcome of the study was a comparison of dietary patterns and disease activity. Clinical remission was defined using the clinical portion of the modified Pouchitis Disease Activity Index (mPDAI),[11] based on a clinical mPDAI score of ≤2 with both the bowel frequency and urgency subscores ≤1. The comparison among dietary factors and disease activity was performed at baseline among all enrolled patients, and in several stratified analyses, including by inflammatory condition of the pouch. In prespecified analyses, we also compared dietary patterns among all patients in remission at enrollment, comparing diet responses among patients who remained in remission throughout the 12-month follow-up to those patients who experienced disease relapse.

Statistical Analysis

Continuous variables are described using medians and interquartile range (IQR). In comparisons across the 4 categories of inflammatory conditions of the pouch, Kruskal–Wallis testing was utilized. In all other comparisons, Wilcoxon rank-sum testing was utilized. A decision to employ adjustments for multiple testing only if significant findings were demonstrated was made *a priori*. For all analyses, 2-sided *P*-values of .05 or less were considered statistically significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC).

Results

Between June 5, 2019, and August 3, 2020, we enrolled 308 patients with inflammatory conditions of the pouch who also completed dietary questionnaires. Specifically, 32 (10%) had acute pouchitis, 85 (28%) had CADP, 35 (11%) had CARP, and 156 (51%) had CD of the pouch. When examining baseline dietary intake patterns, there were no significant differences noted by disease state (Table 1).

In comparisons of specific food groups and macronutrients, patients with CD of the pouch had the lowest fiber intake (median 0.59 g day^{-1}, $P = .656$) and vegetable intake (1.43 cup equivalents per day, $P = .714$). The median body mass index (BMI) of the cohort was 25.9 kg m^{-2} (IQR 22.8–29.5), with no differences in BMI when comparing the 4 inflammatory conditions of the pouch ($P = .468$).

When examining dietary patterns at the time of enrollment among patients in each disease state, stratified by active disease or remission, there were also no significant differences noted (Table 2). However, when comparing these dietary patterns to USDA daily recommendations, patients with inflammatory conditions of the pouch demonstrated decreased intake of several food groups and macronutrients including dairy, fruits, vegetables, whole grains, and fiber (all groups less than the median of recommendations for females and males age 19 + or median of all calorie levels [range 1000–3200 calories per day], as presented in Table 1).

When examining the 102 patients in remission at baseline, there were no significant differences noted among patients who went on to experience a disease flare in the 12 months after enrollment compared to those patients who remained in remission (Table 3). Although nonsignificant, in the stratified analysis, 26 patients with CADP who experienced a disease flare demonstrated numerically decreased median fruit intake compared to 9 patients who remained in remission throughout

Table 1. Dietary patterns at time of enrollment, assessed by inflammatory condition of the pouch and compared to United States Department of Agriculture daily nutritional goals.

		Acute pouchitis		Chronic antibiotic-dependent pouchitis		Chronic antibiotic refractory pouchitis		Crohn's disease of the pouch		*P*-value[a]	USDA Daily Nutritional Goals[b]
		n = 32		*n* = 85		*n* = 35		*n* = 156			
		Median	IQR	Median	IQR	Median	IQR	Median	IQR		median
	Body mass index (kg m^{-2})	24.67	22.8–27.4	25.53	22.3–29.2	26.3	22.1–29.8	26.8	22.8–29.8	.468	–
Fiber	Fiber (g day^{-1})	17.09	14.42–19.79	16.19	13.96–18.64	16.97	13.63–19.79	15.61	13.90–19.11	.770	28
	Whole grains (ounce equivalents per day)	0.65	0.44–0.85	0.63	0.46–1.07	0.75	0.49–1.22	0.59	0.40–0.86	.227	3.75
Calcium	Calcium (mg per day)	1036.28	825.11–1131.57	989.14	874.64–1193.52	952.68	851.33–1242.63	1016.47	877.65–1187.06	.972	1000
	Dairy (cup equivalents per day)	1.51	1.36–1.89	1.65	1.22–1.94	1.63	1.27–2.02	1.68	1.32–2.10	.631	3
Fruits and vegetables	Fruits (cup equivalents per day)	0.84	0.64–1.22	0.77	0.60–1.06	0.83	0.53–0.99	0.86	0.59–1.18	.654	2
	Vegetables, including legumes (cup equivalents per day)	1.32	1.10–1.58	1.37	1.17–1.62	1.34	1.19–1.65	1.43	1.26–1.70	1.32	2.75
Sugars	Total added sugars (tsp equivalents per day)	15.79	12.85–20.71	16.13	13.03–22.38	16.54	13.73–21.58	16.74	13.86–21.78	.841	<10% kcal
	Added sugars from sugar-sweetened beverages (tsp equivalents per day)	6.11	4.44–8.96	6.01	4.58–9.42	6.93	4.73-8.43	5.87	4.58–9.12	.891	-

Abbreviations: IQR, interquartile range; USDA, United States Department of Agriculture.
[a]*P*-value from Kruskal–Wallis test.
[b]USDA Daily Nutritional Goals presented as median of recommendations for females and males age 19+ or median of all calorie levels (range 1000–3200 calories per day).

Table 2. Dietary patterns at time of enrollment, assessed by remission or active disease in patients with inflammatory conditions of the pouch.

	Acute pouchitis, in remission		Acute pouchitis, active disease		*P*-value	Chronic antibiotic-dependent pouchitis, in remission		Chronic antibiotic-dependent pouchitis, active disease		*P*-value
	n = 12		*n* = 19			*n* = 36		*n* = 49		
	Median	IQR	Median	IQR		Median	IQR	Median	IQR	
Calcium (mg day^{-1})	1077.50	955.44-1132.31	935.01	800.96–1228.33	.454	993.13	926.31–1169.05	986.33	830.28–1213.16	.486
Dairy (cup equivalents per day)	1.72	1.45–2.12	1.42	1.26–1.76	.110	1.71	1.20–1.94	1.61	1.25–1.94	.880
Fiber (g day^{-1})	16.85	14.19–22.53	16.28	14.71–18.93	.598	16.48	15.07–19.03	15.25	13.60–18.47	.117
Fruits (cup equivalents per day)	0.92	0.63–1.53	0.85	0.64–0.98	.674	0.79	0.65–1.10	0.77	0.58–1.02	.588
Vegetables, including legumes (cup equivalents per day)	1.41	1.23-1.69	1.51	1.20–1.65	.875	1.60	1.46–1.95	1.39	1.21–1.68	.024
Whole grains (ounce equivalents per day)	0.61	0.46–0.94	0.72	0.44–0.85	.822	0.68	0.51–1.19	0.59	0.41–0.89	.187
Total added sugars (tsp equivalents per day)	16.19	12.71–21.02	15.59	13.55–20.71	.774	16.13	12.59–20.84	17.53	13.03–23.28	.371
Added sugars from sugar-sweetened beverages (tsp equivalents per day)	6.06	4.59–10.24	5.87	4.44–9.42	.700	6.14	4.77–7.89	5.90	3.96–10.14	.674
	Chronic antibiotic refractory pouchitis, in remission		Chronic antibiotic refractory pouchitis, active disease		*P*-value	Crohn's disease of the pouch, in remission		Crohn's disease of the pouch, active disease		*P*-value
	n = 9		*n* = 26			*n* = 63		*n* = 92		
	Median	IQR	Median	IQR		Median	IQR	Median	IQR	
Calcium (mg day^{-1})	961.17	879.17–1167.45	983.45	848.47–1256.74	.702	1044.56	941.11–1182.73	997.27	837.31–1187.24	.141
Dairy (cup equivalents per day)	1.73	1.58–1.87	1.50	1.19–2.15	.372	1.71	1.41–2.03	1.68	1.23–2.18	.468
Fiber (g day^{-1})	18.89	16.97–19.79	16.51	13.56–20.58	.346	15.66	14.36–19.22	15.60	13.56–18.79	.330
Fruits cup equivalents per day)	0.96	0.83–1.02	0.67	0.53–0.98	.073	0.82	0.62–1.43	0.89	0.59–1.18	.821
Vegetables, including legumes (cup equivalents per day)	1.40	1.24–1.58	1.46	1.29–1.62	.969	1.43	1.30–1.71	1.41	1.21–1.68	.354
Whole grains (ounce equivalents per day)	0.64	0.49–1.26	0.76	0.49–1.21	.845	0.58	0.46–0.95	0.59	0.40–0.81	.369
Total added sugars (tsp equivalents per day)	15.93	13.96–26.85	16.60	13.63–20.86	.587	16.13	13.56–20.76	17.63	14.27–23.34	.059
Added sugars from sugar-sweetened beverages (tsp equivalents per day)	6.98	4.74–8.43	6.8	4.61–8.09	.678	5.72	4.58–8.87	6.04	4.58–9.21	.353

Abbreviation: IQR, interquartile range.
P-values obtained via Wilcoxon rank-sum test.

Table 3. Dietary patterns among those in remission at enrollment, according to whether they remained in remission throughout the 12-month study period or experienced a disease flare at any follow-up (all 4 inflammatory conditions of the pouch combined).

	Overall, remain in remission		Overall, disease flare		*P*-value[a]
	n = 46		*n* = 56		
	Median	IQR	Median	IQR	
Fiber (g day^{-1})	16.34	15.17–19.86	16.91	14.64–19.57	.731
Whole grains (ounce equivalents per day)	0.61	0.44–0.95	0.62	0.51–1.02	.377
Calcium (mg day^{-1})	1070.15	967.03–1208.85	991.64	912.03–1158.22	.333
Dairy (cup equivalents per day)	1.76	1.41–2.00	1.67	1.37–1.95	.847
Fruits (cup equivalents per day)	0.84	0.64–1.22	0.79	0.65–1.26	.960
Vegetables, including legumes (cup equivalents per day)	1.35	1.23–1.59	1.40	1.17–1.63	.847
Total added sugars (tsp equivalents per day)	16.20	14.60–21.11	16.13	12.60–19.26	.272
Added sugars from sugar-sweetened beverages (tsp equivalents per day)	6.41	4.75–9.28	5.35	4.58–7.88	.163

Abbreviation: IQR, interquartile range.
[a]*P*-value from Wilcoxon rank-sum test.

the 12-month period (0.67 cup equivalents per day vs 0.96 cup equivalents per day, $P = .073$). Among patients with CD of the pouch, the 92 patients who experienced a disease flare in the 12 months following enrollment demonstrated numerically higher median total added sugars compared to 63 patients who remained in remission (17.63 tsp equivalents per day vs 16.13 tsp equivalents per day, $P = .059$).

Discussion

In this prospective cohort of 308 patients with inflammatory conditions of the pouch, we demonstrated no impact of dietary patterns on disease activity. Despite these findings, the influence of diet on inflammatory conditions of the pouch and the potential for dietary modifications to affect disease activity remains a significant area of interest given our limited knowledge of risk factors for inflammatory conditions of the pouch and a relative therapeutic plateau among existing therapies. Additionally, the relative deficiencies in several food groups and macronutrients in comparison to USDA recommendations are striking.

There has been significant emphasis placed on the impact of diet and the microbiome on the pathogenesis and disease course of patients with IBD.[5,12] The impact of dietary patterns on symptom activity among patients with CD and UC has been well recognized, with evaluations of specific dietary clusters yielding potential lower odds of active symptoms.[13] However, in the most recent recommendations from the International Organization for the Study of Inflammatory Bowel Diseases, no comments specifically dedicated to patients with pouchitis or other inflammatory conditions of the pouch were outlined.[12] Similarly, reviews assessing the nutritional adequacy of diets for patients with IBD have revealed limited evidence among patients after IPAA.[5] Given the lack of evidence-based dietary regimens for patients with pouchitis and other inflammatory conditions of the pouch, many recent authors have sought investigational approaches to dietary therapy for the treatment of pouch-related disorders[3,14,15] and examined associations between dietary factors and inflammatory conditions of the pouch.[1,2,16,17]

In comparison to USDA guidelines,[8] patients with inflammatory conditions of the pouch consumed a median fiber intake that was approximately 60% of daily recommended nutritional goals. Additionally, patients with inflammatory conditions of the pouch appeared to be consuming lower than recommended portions of vegetables, fruits, and whole grains when compared to the 2020–2025 USDA dietary goals. These findings suggest that patients with inflammatory conditions of the pouch may have significantly altered their diets with the goal of maximizing pouch function. In the current analyses, this hypothesis could not be tested given that all patients enrolled in PROP-RD had 1 of 4 inflammatory conditions of the pouch, without a control population for comparison. In particular, without a control population it is unknown whether patients without inflammatory conditions of the pouch would pursue similar changes in dietary intake. Although we did not demonstrate any significant differences among patients with active disease compared to those in remission, in an analysis of a prospective internet-based cohort, Cohen et al. found that patients with an IPAA for UC and active disease reported less consumption of fruit and red meat compared to patients without active disease.[18]

When taken together, each of these findings suggest that patients may benefit from specialized nutritional counseling with guidance on methods of achieving a balanced diet and symptom control, which may also provide an opportunity to combat misinformation that may exist with regard to nutritional needs after IPAA.

The decreased fruit consumption demonstrated by patients in PROP-RD in comparison with USDA guidelines is also interesting given prior findings by Godny and colleagues demonstrating that patients in the lowest tertile of fruit consumption were at increased risk for pouchitis in a prospective evaluation from a comprehensive pouch clinic.[1] In the analysis by Godny et al., fruit consumption correlated with increased microbial diversity while a decrease in fruit consumption over time was associated with recurrence of pouchitis and a reduction in microbial diversity. One pilot study indicated that a low in fermentable oligo-, di-, and mono-saccharides and polyols (FODMAPs) was associated with decreased stool frequency; however, these effects were not as dramatic in patients with pouchitis.[14] Additionally, the relative decreased fiber consumption demonstrated

by patients in PROP-RD is potentially problematic, especially given prior studies demonstrating a potential beneficial effect of fiber supplementation after IPAA, including a reduction in inflammation of the pouch.[19] Given the recent suggestion that adherence to a Mediterranean diet is associated with a decrease in calprotectin among patients with an IPAA,[2] future work evaluating the role of fiber and the impact on the microbiome may demonstrate important relationships between dietary intake and pouch health/function.

Our study has several strengths including the rigorous and standardized diagnostic criteria used at enrollment as well as the validated dietary questionnaires utilized. However, studying the impacts of diet on disease activity in an observational cohort has several limitations, including determining whether dietary patterns are a cause of or reaction to inflammatory conditions of the pouch. Given that we only assessed dietary patterns at enrollment, we were unable to capture dietary changes that individual patients may have pursued during the 12-month follow-up period and it is unknown if an initial assessment of diet at enrollment predicts dietary patterns for the subsequent 12 months. Despite the prospective nature of this study, this was not an inception cohort, and all patients enrolled had a prior diagnosis of an inflammatory condition of the pouch. Additionally, the DSQ was chosen for the ease of administration, and thus more granular dietary assessments may be necessary to improve our understanding of the link between dietary factors (eg, emulsifiers, artificial sweeteners) and pouch-related inflammation. However, there is currently no validated instrument specifically created to evaluate the nutritional status of patients after IPAA. Similarly, paired microbial analyses and dietary assessments may be most useful in evaluating the correlation between diet and inflammatory conditions of the pouch. Additionally, while we were able to assess symptoms attributed to inflammatory conditions of the pouch, endoscopic confirmation of disease activity was not required in this study, and thus dietary changes may have been pursued in an attempt to manage symptoms that were not related to inflammation (irritable pouch syndrome) or other inflammatory conditions of the pouch (such as cuffitis).

In conclusion, among 308 patients with inflammatory conditions of the pouch, we demonstrated no significant differences in diet when stratifying patients by disease state or disease activity. However, patients with inflammatory conditions of the pouch consumed less than recommended daily allowances of multiple food groups or macronutrients. These data may be helpful to counsel patients with inflammatory conditions of the pouch and to inform multidisciplinary practices regarding the need for routine nutritional assessments after IPAA.

Author Contributions

E.L.B.: Study design, study oversight and management, data collection, statistical analysis, writing of original draft of manuscript, revision of manuscript. P.B.-P., P.D., L.R., M.K., M.D., S.C., P.D.R.H., J.I.B., R.K.C., M.D.L., and H.H.H.: Study oversight and management, data collection, revision of manuscript. C.A.: Study oversight and management, statistical analysis, revision of manuscript.

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Conflicts of Interest

E.L.B. has served as a consultant for AbbVie, Bristol-Meyers Squibb, Eli Lilly, and Target RWE. P.D. has served as a consultant or on an advisory board for Janssen, Pfizer, Prometheus Biosciences, Boehringer Ingelheim, AbbVie, Arena Pharmaceuticals, Takeda Pharmaceuticals LLC, Roche Genentech, Bristol Myers Squibb and Scipher Medicine Corporation. He has also received funding under a sponsored research agreement unrelated to the data in the paper from Takeda Pharmaceutical, Arena Pharmaceuticals, Bristol Myers Squibb-Celgene, Janssen, Landos Pharma, Teva Pharma, Iterative scopes, CorEvitas and Boehringer Ingelheim. P.D. holds the position of Associate Editor for *Crohn's & Colitis 360* and has been recused from reviewing or making decisions for the manuscript. P.B.-P. has received honorarium from the Takeda speaker's bureau. L.R. has served on an advisory board for Janssen. LR holds the position of Associate Editor for *Crohn's & Colitis 360* and has been recused from reviewing or making decisions for the manuscript. M.D. has served as a consultant or has received advisory board fees from Abbvie, Arena, BMS, Eli Lilly, Gilead, Janssen, Pfizer, Prometheus Labs, Takeda. She has received grant support from Janssen, Abbvie. She also has the following relationships: Licenser of software: Takeda; Co-Founder, Equity ownership and board of director for Trellus Health

Shannon Chang has served as a consultant for AbbVie, BMS, and Pfizer. R.K.C. has participated in advisory boards for AbbVie, Bristol Myers Squibb, Fresenius Kabi, and has served as a consultant for Fzata, Magellan Health, Pfizer, and Samsung Bioepis. He is on the Data Safety Monitoring Board for Adiso, is a member of the Executive Committee for the IBD Education Group and is Co-Director of the CorEvitas Registry. M.D.L. has served as a consultant for AbbVie, UCB, Takeda, Janssen, Pfizer, Salix, Valeant, Target Pharmasolutions and has received research support from Pfizer and Takeda. H.H.H. has served as a consultant for Alivio, AMAG, BMS, ExeGI Finch, Gilead, Janssen, Lycera, Merck, Otsuka, Pfizer, PureTech, Seres and has received research support from Pfizer and Artizan Biosciences. M.K., P.D.R.H., J.B., and C.A. have no relevant disclosures.

Data Availability

Data not publically available. However, requests for raw copies of the data can be submitted to the corresponding author.

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