Pouch-Related Symptoms and Quality of Life in Patients with Ileal Pouch–Anal Anastomosis

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Background: Restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) has become the standard surgical treatment for the majority of patients with inflammatory bowel disease (IBD) who require colectomy. We evaluated the prevalence of pouch-related symptoms among the Crohn's and Colitis Foundation of America Partners cohort and the effect of pouch-related symptoms on Patient-Reported Outcome Measurement Information System measures.

Methods: We performed analyses nested in the Crohn's and Colitis Foundation of America Partners cohort. We used bivariate analyses to compare demographics and medication use among patients with ulcerative colitis or indeterminate colitis and pouch-related symptoms and those with IPAA without symptoms. We also compared Patient-Reported Outcome Measurement Information System domains (measured in T-scores) and short IBD questionnaire quality of life scales between symptomatic pouch patients (over the past 6 mo) and those without symptoms.

Results: Among 243 patients reporting a history of IPAA, 199 (82%) reported a history of pouch symptoms. Patients with recent pouch symptoms demonstrated higher mean T-scores in pain interference (53.0 versus 45.3; $P < 0.001$), depression (51.0 versus 46.4; $P = 0.002$), and fatigue (56.3 versus 47.0; $P < 0.001$). Symptomatic pouch patients reported lower mean scores in social role satisfaction (47.4 versus 54.6) and short IBD questionnaire (4.8 versus 5.8) (both $P < 0.001$). These differences were all clinically meaningful.

Conclusions: In a large sample of patients with IBD, nearly all patients with IPAA reported a history of pouch symptoms. Patients experiencing symptoms within the 6 months before the survey assessment demonstrated clinically meaningful decrements in patient-reported outcomes in multiple domains of physical and psychosocial functioning.

(Inflamm Bowel Dis 2017;23:1218–1224)

Key Words: pouch-related symptoms, pouchitis, PROMIS measures, quality of life

Approximately 20% to 35% of patients with ulcerative colitis (UC) eventually will require colectomy due to refractory disease or histologically proven dysplasia.[1–3] Given the ability to accomplish the major goals of eliminating the diseased segment of intestine while maintaining fecal continence, restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) has become the standard surgical treatment for the majority of patients who require colectomy. Additionally, the pouch procedure has been shown to significantly improve the health-related quality of life (QOL) of patients while reducing the risk for colitis-associated neoplasia.[4]

There are known complications that can occur after IPAA surgery. Among the potential complications, pouchitis is the most common long-term complication after IPAA, affecting 50% to 79% of patients after IPAA for UC.[1,5–13] Several risk factors for pouchitis have been suggested in previous studies, including extensive UC,[14,15] a concurrent diagnosis of primary sclerosing cholangitis,[16–18] backwash ileitis,[18,19] nonsmoking status,[14,15] the regular use of nonsteroidal anti-inflammatory drugs,[14,17] and ischemia.[20]

The majority of the studies that have evaluated pouchitis and pouch-related impact thus far have been performed in single-center cohorts. However, as clinical outcomes may vary depending on the center where pouch procedures are performed,[2] a broader understanding of pouchitis and the effect of pouch-related symptoms on related clinical outcomes is needed. The primary objective of our study was to use the Crohn's and Colitis Foundation of America (CCFA) Partners infrastructure to evaluate

Received for publication February 2, 2017; Accepted March 8, 2017.

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Supported by a grant from The Broad Medical Research Program at the Crohn's and Colitis Foundation of America and by the National Institutes of Health [5U01DK092239, P30DK034987]. This work is also supported by Patient Centered Outcomes Research Institute and the Crohn's and Colitis Foundation of America (M.D.K., R.S.S.).

Millie D. Long, MD, MPH, is a consultant for Abbvie, Takeda, Pfizer, and Theravance. The other authors report no disclosures or conflicts of interest relevant to this study.

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the prevalence of pouch-related symptoms and the impact of pouch-related symptoms on patient-reported outcomes (PROs) in participants with a history of IPAA. We used the Patient-Reported Outcomes Measurement Information System (PROMIS) measures including anxiety, depression, sleep disturbances, fatigue, pain interference, and social satisfaction to compare symptomatic pouch patients with those without pouch-related symptoms.

METHODS

Study Population

We identified patients with a history of IPAA within CCFA Partners, an Internet-based cohort of patients with inflammatory bowel disease (IBD). The study cohort has been described in detail previously.[21] Briefly, patients were recruited to enroll in this online cohort registry through a variety of means, including invitations by means of e-mail, social media, and recruitment at CCFA educational events. More than 15,000 patients with self-reported IBD have enrolled in the cohort since its initiation in 2011, and cohort members are followed up at 6-month intervals. Baseline and follow-up surveys include a core survey with information on disease phenotype, activity, medication use, and PROs. Optional "modules" can also be completed alongside the core survey at 6-month intervals to assess specific areas of interest among patients with IBD, including pouch-related complications and QOL.

For inclusion in this study, patients needed to be older than 18 years, diagnosed with UC or indeterminate colitis (IC), and with a history of colectomy with IPAA. Patients with a diagnosis of Crohn's disease were excluded from this study. There were no other exclusion criteria.

Study Variables

All patients completed questionnaires regarding demographic and clinical information, in addition to validated scales including the short IBD questionnaire (SIBDQ),[22] and the PROMIS measures for pain interference, anxiety, depression, satisfaction with social role, sleep disturbance, and fatigue.[23,24] The SIBDQ has not specifically been validated in pouch populations; however, the instrument includes domains with clinical relevance to this IBD subpopulation, including bowel symptoms, systemic symptoms, emotional function, and social function and has been used in the evaluation of patients with Crohn's disease phenotypes of the pouch.[25]

In addition to the survey measures described above, patients were questioned regarding any history of symptoms of pouchitis, including abdominal pain, cramping, and urgent or frequent bowel movements and then separately regarding a history of pouch-related symptoms within the preceding 6 months. If a patient completed multiple surveys within the study period, all survey responses were analyzed for a positive history of pouch-related symptoms at any point. If a patient answered positively to the question regarding pouch-related symptoms in the preceding 6 months on multiple surveys, then the first survey where pouch-related symptoms were reported was analyzed for the evaluation of PROMIS measures. If a patient completed multiple surveys and never experienced pouch-related symptoms, then the last survey completed was analyzed for the evaluation of PROMIS measures. This method was chosen to allow for more complete capture of patients without pouch-related symptoms because the question regarding pouch-related symptoms in the preceding 6 months may not have been available in the baseline survey depending on how long an individual had participated in CCFA Partners.

The PROMIS measures have previously been assessed within the CCFA Partners cohort[24] and have been validated in other general and chronically ill populations for the self-reporting of outcomes.[26,27] PROMIS measures are calibrated using T-score metrics to provide mean values for each domain, with higher scores indicating higher levels of each domain being measured. Among generally healthy populations, the mean T-score for pain interference, depression, anxiety, satisfaction with one's social role, fatigue, and sleep disturbance is 50 with a standard deviation of 10. Based on previous studies evaluating the PROMIS measures in patients with IBD and other chronic conditions such as rheumatoid arthritis,[24,28–31] a minimally important difference of 2 was assigned when analyzing PROMIS measures.

Statistical Analysis

Baseline demographics and clinical characteristics were compared using proportions and 95% confidence intervals (CI), means with standard deviation, and medians with interquartile ranges as appropriate. Bivariate statistics using Pearson's chi-square test statistic, Fisher's exact, Wilcoxon's rank sum, and Student's *t* test as appropriate were used to compare symptomatic pouch patients with those with no reported history of symptoms. Logistic regression modeling was used to compare the effect of pouch-related symptoms within the prior 6 months on individual PROs as assessed by the PROMIS measures, after controlling for covariates. When using logistic regression, the minimally important difference of 2 in each PRO scale was used as the threshold for assessment. Categorical variables for each PROMIS domain were created using a threshold of >52 for pain interference, depression, anxiety, fatigue, and sleep disturbance and a threshold of <48 for satisfaction with social role. In multivariable analyses, an a priori decision was made to include age and sex in all models, given the potential for confounding. All statistical analyses were performed using SAS statistical software (version 9.4; SAS Institute, Cary, NC). The Institutional Review Board at the University of North Carolina at Chapel Hill approved the study protocol.

RESULTS

A total of 243 participants in CCFA Partners reported a history of colectomy with IPAA. Of these, 199 (82%) reported a history of pouch-related symptoms on at least 1 survey at any

time in the interval following their initial IPAA surgery. There were no significant differences in age, sex, or race when comparing symptomatic pouch patients with those without a history of pouch-related symptoms (Table 1). Significant differences were noted when analyzing the number of years since the diagnosis of IBD ($P = 0.034$), with 89% of patients with colitis for more than 11 years reporting at least 1 episode of pouch-related symptoms (Table 1). At each time point analyzed, a greater percentage of patients reported at least 1 episode of pouch-related symptoms when compared with those with a pouch who had not experienced symptoms (Fig. 1).

TABLE 1. Comparison of Demographics and Clinical Characteristics Among Patients from CCFA Partners with No History of Pouch-Related Symptoms and Symptomatic Pouch Patients

	Patients Without Pouch-Related Symptoms (n = 44)	Symptomatic Pouch Patients (n = 199)
Age, yr		
18–39	21 (48%)	109 (55%)
40–59	19 (43%)	74 (37%)
>60	4 (9%)	16 (8%)
Female	27 (61%)	141 (71%)
Race		
White	38 (86%)	182 (91%)
Black	0	3 (2%)
Other/not reported	6 (13%)	14 (8%)
Current smoker	0	5 (3%)
Time since IBD diagnosis, yr		
<1	3 (7%)	9 (5%)
1–5	17 (39%)	39 (20%)
6–10	11 (25%)	46 (23%)
11–15	4 (9%)	43 (22%)
>15	9 (20%)	62 (31%)
Current therapy		
Antibiotics	0	60 (30%)
Probiotics	10 (23%)	72 (36%)
Oral steroids	1 (2%)	14 (7%)
Aminosalicylates	0	20 (10%)
Biologic therapy	0	11 (6%)
Immunosuppressive therapy	0	7 (4%)
Narcotic pain medications	5 (11%)	29 (15%)
Current gastroenterology provider setting	n = 30	n = 162
University hospital	9 (30%)	46 (28%)
Community practice	15 (50%)	100 (62%)
Other/don't know setting	6 (20%)	16 (10%)
Number of times a gastroenterologist has been seen in the past year	n = 30	n = 162
None	7 (23%)	24 (15%)
1 or 2 times	15 (50%)	82 (51%)
3 or 4 times	4 (13%)	24 (15%)
5 or more times	4 (13%)	32 (20%)

Symptomatic pouch patients were more likely to report the use of antibiotics (30% versus 0; $P < 0.001$) and aminosalicylates (10% versus 0; $P = 0.030$) when compared with asymptomatic patients. No significant differences were noted in the use of probiotics, narcotic pain medications, oral steroids, biologic agents, or immunosuppressive therapies (Table 1). There was no significant difference in practice setting when comparing symptomatic pouch patients with those without symptoms; however, a minority of patients in both the groups reported being treated at a university hospital (Table 1).

When examining PROMIS measures, a total of 222 patients (91%) completed questionnaires regarding PROMIS and QOL measures. Of these, 187 (84%) reported pouch-related symptoms in the preceding 6 months. Symptomatic pouch patients demonstrated greater pain interference, depression, fatigue, and less satisfaction with their social role (Table 2). All of these differences were both statistically significant and clinically meaningful, as defined by the prespecified minimally important difference. Additionally, patients with symptoms in the preceding 6 months reported decreased QOL as defined by the SIBDQ when compared with those without pouch-related symptoms (mean SIBDQ, 4.8 versus 5.8; $P < 0.001$).

Using multivariable logistic regression to evaluate the independent association between pouch-related symptoms within the preceding 6 months on PROs, several significant associations were demonstrated. In both unadjusted analysis and adjusted analyses, symptomatic pouch patients demonstrated worse outcomes on several PROs as defined by PROMIS measures (Table 3). After adjusting for age and sex, symptomatic pouch patients in the preceding 6 months demonstrated greater pain interference (adjusted odds ratio, 3.99; 95% confidence interval, 1.53–10.41) and fatigue (adjusted odds ratio, 4.52; 95% confidence interval, 2.88–10.90). Patients with pouch-related symptoms in the preceding 6 months also reported decreased satisfaction with their social role (adjusted odds ratio, 0.24; 95% confidence interval, 0.09–0.63).

DISCUSSION

In an analysis of a large, geographically diverse cohort of patients with UC or IC reporting a history of proctocolectomy with IPAA for IBD, we evaluated the prevalence of patient-reported pouchitis symptoms, which is the most common long-term complication associated with IPAA. Our population was treated in multiple practice settings, with a majority of symptomatic pouch patients being treated in a community-based practice. We demonstrated that pouch-related symptoms occur frequently in patients who undergo restorative proctocolectomy with IPAA for IBD-related reasons and that antibiotics and probiotics seem to be the most frequently used therapy. Symptomatic pouch patients

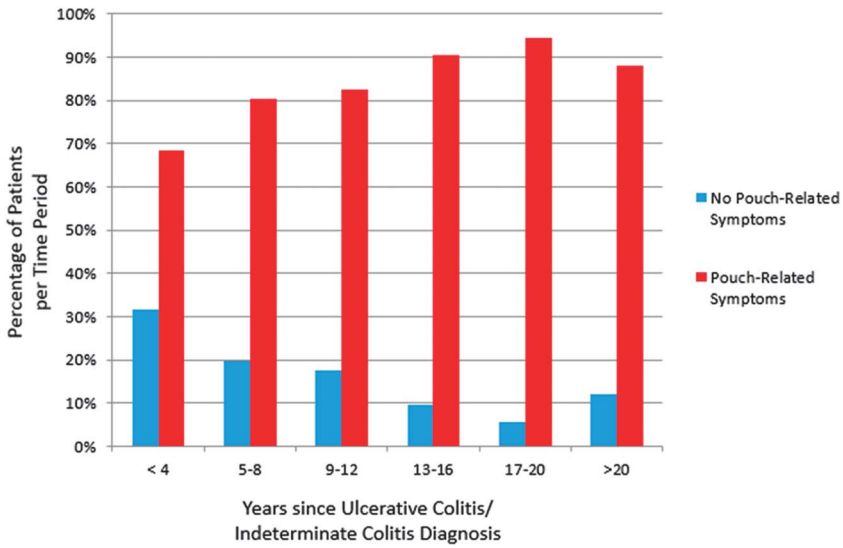

FIGURE 1. The percentage of patients with and without pouch-related symptoms compared with the number of years since diagnosis of UC/IC.

with symptoms in the previous 6 months demonstrated worse PROs as defined by PROMIS measures, including increased pain interference, depression, and fatigue, as well as decreased satisfaction with the social role and decreased QOL as defined by the SIBDQ.

The frequency of reported pouch-related symptoms after colectomy of 82% in our cohort study is higher than previously assessed in most of the single-center studies.[1,5–8] The higher incidence of pouch-related symptoms could be due to the variable window of assessment of pouchitis symptoms used in our surveys compared with other studies. Another potential explanation is that patients are also treated for pouch-related symptoms by their primary care providers and thus do not always report their symptoms to the center that performed the colectomy with IPAA. Additionally, we were unable to verify a diagnosis of self-reported pouchitis symptoms by means of endoscopy or review of the medical record.

TABLE 2. Comparison of PROMIS and QOL Measures Among Patients from CCFA Partners with a History of Pouch-Related Symptoms Within 6 Months of Survey and Patients with No History of Pouch-Related Symptoms

	Patients Without Pouch-Related Symptoms (n = 35)	Patients with Pouch-Related Symptoms in the Preceding 6 months (n = 187)	*P*
Pain interference	45.3 (6.4)	53.0 (10.9)	<0.001
Depression	46.4 (7.1)	51.0 (9.5)	0.002
Anxiety	48.8 (7.4)	51.9 (9.7)	0.075
Satisfaction with social role	54.6 (7.6)	47.4 (9.8)	<0.001
Fatigue	47.0 (8.2)	56.3 (10.5)	<0.001
Sleep disturbance	51.9 (3.6)	51.8 (3.8)	0.854
SIBDQ	5.8 (0.9)	4.8 (1.2)	<0.001

Scores reported as mean (standard deviation).

Gut microbiota may be involved in the pathogenesis of pouchitis through multiple mechanisms, including an alteration in commensal bacteria.[32–35] This focus on the microbiota was reflected in medication use patterns of the patients in our study because a significantly greater number of symptomatic pouch patients reported current use of antibiotics as compared with those with no history of pouch-related symptoms. A greater number of patients with pouch-related symptoms also reported the use of probiotics, although this result was not statistically significant. Although antibiotics such as ciprofloxacin or metronidazole are viewed as the first-line therapy for acute pouchitis,[4,36–38] our findings confirm that among a diverse survey of patients with IPAA, antibiotics and probiotics are being used more widely among symptomatic pouch patients than anti-inflammatory medications such as steroids, biologic therapy, or other immunosuppressive agents. Interestingly, 11% of patients were also treated with aminosalicylate for pouch-related symptoms, which has only proven to be effective for the local treatment of cuffitis but not pouchitis.[39,40]

Classically, the majority of pouch surgeries have been performed in young patients with long life expectancies following colectomy with IPAA. As patients age, the risk of developing pouchitis increases,[41] a finding that was suggested in our study. Our survey did not specifically ask the date of colectomy or ileostomy, and thus we were unable to analyze the time since the last surgery related to the IPAA. In prior longitudinal

TABLE 3. Odds of Experiencing Worse Outcomes as Defined by PROMIS Measures Among Patients from CCFA Partners with a History of Pouch-Related Symptoms Within 6 Months of Survey Compared with Those with No History of Pouch-Related Symptoms[a]

	Unadjusted Odds Ratio (95% Confidence Interval)	Adjusted Odds Ratio (95% Confidence Interval)[b]
Pain interference	4.15 (1.61–10.72)	3.99 (0.153–10.41)
Depression	2.27 (0.92–5.60)	2.07 (0.83–5.16)
Anxiety	2.19 (0.95–5.08)	2.09 (0.90–4.90)
Satisfaction with social role	0.24 (0.09–0.62)	0.24 (0.09–0.63)
Fatigue	4.79 (2.00–11.45)	4.52 (2.88–10.90)
Sleep disturbance	0.82 (0.36–1.83)	0.82 (0.36–1.87)

[a]For categorical analysis, PROMIS measures were divided at the point of clinically meaningful difference (>52 for pain interference, depression, anxiety, and fatigue; <48 for satisfaction with social role).
[b]Multivariable analysis adjusted for age and sex.

evaluations where cohorts were followed for up to 15 years after IPAA, up to 47% of patients had experienced at least 1 episode of pouchitis.[3,41,42] Although we were unable to evaluate time since IPAA, in our population, 33% of symptomatic pouch patients had been diagnosed with UC/IC more than 15 years ago. Additionally, the majority of patients who had undergone IPAA and had been diagnosed with IBD more than 11 years before completing the survey reported at least 1 episode of pouch-related symptoms. When evaluating time since diagnosis in this population of patients with IPAA, a greater proportion of patients had experienced pouch-related symptoms at every time point analyzed as compared with those without symptoms.

Early studies indicated that long-term QOL after ileal pouch surgery was excellent,[43] with similar cohorts demonstrating good QOL compared with the general population[44–47] despite the initial surgery-specific complications in some cases.[48] Improvements in QOL have been noted as early as 1 month after ileostomy.[49] However, other studies have demonstrated decreased QOL and functional outcomes among patients undergoing IPAA when compared with the general population,[50] whereas another study noted no major improvement in QOL after IPAA.[51] When QOL has been examined more specifically among patients with a history of pouchitis, the effects on QOL seem more significant. A history of pouchitis has been associated with negative effects on multiple QOL scales,[52] and patients experiencing chronic pouchitis have demonstrated decreased QOL and satisfaction with surgery.[53]

Although the PROMIS measures have been validated among patients with IBD, another key advantage of evaluating QOL with the PROMIS measures is the ability to compare with the general population. We found that patients with a pouch who were symptomatic within the preceding 6 months demonstrated clinically meaningful worsened outcomes in several areas assessed by PROMIS measures, including pain interference, depression, satisfaction with social role, and fatigue when compared with those without pouch-related symptoms. However, even symptomatic pouch patients demonstrated PROMIS T-scores within 1 standard deviation of 50, indicating that although pouch-related symptoms were associated with worse outcomes in several domains of QOL, these may not be as significant as in other chronic diseases.[54,55] These findings may be particularly helpful when discussing potential outcomes in the preoperative period while patients are considering colectomy. Additionally, those patients without pouch-related symptoms demonstrated PROMIS T-scores that were better than the mean scores of the general population in multiple domains.

Our study is the first to use the PROMIS measures to evaluate PROs among patients with IBD who have undergone proctocolectomy with IPAA. The PROMIS initiative of the National Institutes of Health was developed to advance the application of PROs in research and clinical practice.[23] Although other studies have evaluated QOL among patients with a history of IPAA, we believe that the use of the PROMIS measures in a geographically diverse sample is a strength of this study.

The majority of the prior studies that have evaluated pouchitis have largely been limited to single-center reports. Although these studies have significantly increased our understanding of the risk factors associated with the development of pouchitis among patients undergoing IPAA and the epidemiology of pouchitis among patients with IBD undergoing restorative proctocolectomy with IPAA, the fact that these cohorts arise from single centers of excellence may indicate that these studies are less representative of the experiences of patients undergoing IPAA in the general population. Our study evaluated the experiences of patients with IPAA across practice settings, including both university hospitals and community practices. Although there was no significant difference when evaluating a history of pouch-related symptoms among patients seen in differing practice settings, we view the ability to evaluate patients across a more broad geographic area and multiple practice settings as a strength.

Our study has limitations as well. Although a subset of the CCFA Partners cohort has been validated for factors such as disease diagnosis,[56] the history of pouchitis symptoms and IPAA surgery for this study are self-reported. The inability to validate patient-reported pouchitis may have led to a report of pouchitis when symptoms could have been due to other conditions such as irritable pouch syndrome or Crohn's disease of the pouch. Given our inability to validate the diagnosis of pouchitis, we have used a more appropriate diagnosis of pouch-related symptoms in our analyses. As noted previously, the inability to evaluate the relationship between time since IPAA surgery and the risk of development of pouch-related symptoms is a significant limitation.

Although we demonstrated a trend in overall time since IBD diagnosis, the more clinically meaningful relationship between time since surgery and symptoms could not be assessed. Despite nesting this study in a cohort of more than 15,000 participants, the population reporting a history of restorative proctocolectomy with IPAA was relatively small. The population of patients without pouch-related symptoms was even smaller, limiting the number of variables that we could include in our final multivariable analyses.

In conclusion, in an analysis of patients with UC or IC who underwent restorative proctocolectomy with IPAA, those patients with pouch-related symptoms within the past 6 months demonstrated significantly worse PROs including pain interference, depression, satisfaction with social role, and fatigue. Given that symptomatic pouch patients demonstrated worse PROs, increased awareness by providers of the impact of pouchitis symptoms on the QOL of an individual patient appears warranted. In addition to the standard treatment for pouchitis including antibiotics, symptomatic pouch patients may require alternative treatments targeting PROs, such as depression, pain, and social satisfaction.

REFERENCES

1. Hahnloser D, Pemberton JH, Wolff BG, et al. Results at up to 20 years after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Br J Surg.* 2007;94:333–340.
2. Parc Y, Reboul-marty ÃJ, Lefevre JH, et al. Restorative proctocolectomy and ileal pouch-anal anastomosis. *Ann Surg.* 2015;262:849–854.
3. Shannon A, Eng K, Kay M, et al. Long-term follow up of ileal pouch anal anastomosis in a large cohort of pediatric and young adult patients with ulcerative colitis. *J Pediatr Surg.* 2016;51:1181–1186.
4. Shen B. Pouchitis: what every gastroenterologist needs to know. *Clin Gastroenterol Hepatol.* 2013;11:1538–1549.
5. Sandborn WJ, Tremaine WJ, Batts KP, et al. Pouchitis after ileal pouch-anal anastomosis: a pouchitis disease activity index. *Mayo Clin Proc.* 1994;69:409–415.
6. Penna C, Dozois R, Tremaine W, et al. Pouchitis after ileal pouch-anal anastomosis for ulcerative colitis occurs with increased frequency in patients with associated primary sclerosing cholangitis. *Gut*. 1996;38: 234–239.
7. Romanos J, Samarasekera DN, Stebbing JF, et al. Outcome of 200 restorative proctocolectomy operations: the John Radcliffe hospital experience. *Br J Surg.* 1997;84:814–818.
8. Svaninger G, Nordgren S, Oresland T, et al. Incidence and characteristics of pouchitis in the Kock continent ileostomy and the pelvic pouch. *Scand J Gastroenterol.* 1993;28:695–700.
9. Nagar H, Rabau MDM, Tulchinsky MDH. Long-term functional and quality-of-life outcomes after IPAA in children. *Dis Colon Rectum.* 2013;56:198–204.
10. Patton D, Gupta N, Wojcicki JM, et al. Postoperative outcome of colectomy for pediatric patients with ulcerative colitis. *J Pediatr Gastroenterol Nutr.* 2010;51:151–154.
11. Farouk R, Glasg F, Pemberton JH, et al. Functional outcomes after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Ann Surg.* 2000; 231:919–926.
12. Simchuk EJ, Thirlby RC. Risk factors and true incidence of pouchitis in patients after ileal pouch-anal anastomoses. *World J Surg.* 2000;24: 851–856.
13. Peyrin-Biroulet L, Germain A, Patel AS, et al. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. *Aliment Pharmacol Ther.* 2016;44:807–816.
14. Achkar JP, Haddad MAL, Lashner B, et al. Differentiating risk factors for acute and chronic pouchitis. *Clin Gastroenterol Hepatol.* 2005;3565: 60–66.
15. Shen BO, Fazio VW, Remzi FH, et al. Risk factors for diseases of ileal pouch–anal anastomosis after restorative proctocolectomy for ulcerative colitis. *Clin Gastroenterol Hepatol.* 2006;3565:81–89.
16. Hata K, Watanabe T, Shinozaki M, et al. Patients with extraintestinal manifestations have a higher risk of developing pouchitis in ulcerative colitis: multivariate analysis. *Scand J Gastroenterol*. 2003;38: 1055–1058.
17. Lepistö A, Kärkkäinen P, Järvinen HJ. Prevalence of primary sclerosing cholangitis in ulcerative colitis patients undergoing proctocolectomy and ileal pouch-anal anastomosis. *Inflamm Bowel Dis.* 2008;14: 775–779.
18. White E, Melmed GY, Vasiliauskas EA, et al. A prospective analysis of clinical variables, serologic factors, and outcome of ileal pouch-anal anastomosis in patients with backwash ileitis. *Dis Colon Rectum.* 2010;53: 987–994.
19. Schmidt CM, Lazenby AJ, Hendrickson RJ, et al. Preoperative terminal ileal and colonic resection histopathology predicts risk of pouchitis in patients after ileoanal pull-through procedure. *Ann Surg.* 1998;227: 654–662; discussion 663–665.
20. Shen B, Plesec TP, Remer E, et al. Asymmetric endoscopic inflammation of the ileal pouch: a sign of ischemic pouchitis? *Inflamm Bowel Dis.* 2010; 16:836–846.
21. Long MD, Kappelman MD, Martin CF, et al. Development of an internet-based cohort of patients with inflammatory bowel diseases (CCFA Partners): methodology and initial results. *Inflamm Bowel Dis.* 2012;18:2099–2106.
22. Irvine EJ, Zhou Q, Thompson AK. The short inflammatory bowel disease questionnaire: a quality of life instrument for community physicians managing inflammatory bowel disease. CCRPT Investigators. Canadian Crohn's relapse prevention trial. *Am J Gastroenterol.* 1996; 91:1571–1578.
23. Ader DN. Developing the patient-reported outcomes measurement information System (PROMIS). *Med Care.* 2007;45(5 suppl 1): S1–S2.
24. Kappelman MD, Long MD, Martin C, et al. Evaluation of the patient-reported outcomes measurement information system in a large cohort of patients with inflammatory bowel diseases. *Clin Gastroenterol Hepatol.* 2014;12:1315–1323.e2.
25. Shen B, Fazio VW, Remzi FH, et al. Clinical features and quality of life in patients with different phenotypes of Crohn's disease of the ileal pouch. *Dis Colon Rectum.* 2007;50:1450–1459.
26. Cella D, Yount S, Rothrock N, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH roadmap cooperative group during its first two years. *Med Care.* 2007;45(5 suppl 1):S3–S11.
27. Rothrock NE, Hays RD, Spritzer K, et al. Relative to the general US population, chronic diseases are associated with poorer health-related quality of life as measured by the Patient-Reported Outcomes Measurement Information System (PROMIS). *J Clin Epidemiol.* 2010;63: 1195–1204.
28. Abdalla M, Sandler R, Kappelman M, et al. The impact of ostomy on quality of life and functional status of Crohn's disease patients. *Inflamm Bowel Dis.* 2016;22:2658–2664.
29. Thissen D, Liu Y, Magnus B, et al. Estimating minimally important difference (MID) in PROMIS pediatric measures using the scale-judgment method. *Qual Life Res.* 2016;25:13–23.
30. Kroenke K, Zu Y, Wu J, et al. Operating characteristics of PROMIS four-item depression and anxiety scales in primary care patients with chronic pain. *Pain Med.* 2014;15:1892–1901.
31. Hays RD, Spritzer KL, Fries JF, et al. Responsiveness and minimally important difference for the Patient-Reported Outcomes Measurement Information System (PROMIS) 20-item physical functioning short form in a prospective observational study of rheumatoid arthritis. *Ann Rheum Dis.* 2015;74:104–107.
32. Nasmyth DG, Godwin PG, Dixon MF, et al. Ileal ecology after pouch-anal anastomosis or ileostomy. A study of mucosal morphology, fecal bacteriology, fecal volatile fatty acids, and their interrelationship. *Gastroenterology.* 1989;96:817–824.
33. Duffy M, O'Mahony L, Coffey JC, et al. Sulfate-reducing bacteria colonize pouches formed for ulcerative colitis but not for familial adenomatous polyposis. *Dis Colon Rectum.* 2002;45:384–388.

34. Komanduri S, Gillevet PM, Sikaroodi M, et al. Dysbiosis in pouchitis: evidence of unique microfloral patterns in pouch inflammation. *Clin Gastroenterol Hepatol.* 2007;5:352–360.
35. Sokol H, Lay C, Seksik P, et al. Analysis of bacterial bowel communities of IBD patients: what has it revealed? *Inflamm Bowel Dis.* 2008;14:858–867.
36. Madden MV, McIntyre AS, Nicholls RJ. Double-blind crossover trial of metronidazole versus placebo in chronic unremitting pouchitis. *Dig Dis Sci.* 1994;39:1193–1196.
37. Shen B, Achkar JP, Lashner BA, et al. A randomized clinical trial of ciprofloxacin and metronidazole to treat acute pouchitis. *Inflamm Bowel Dis.* 2001;7:301–305.
38. Singh S, Stroud A, Holubar S, et al. Treatment and prevention of pouchitis after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Cochrane Database Syst Rev.* 2015;11:CD001176.
39. Holubar SD, Cima RR, Sandborn WJ, et al. Treatment and prevention of pouchitis after ileal pouch-anal anastomosis for chronic ulcerative colitis. *Cochrane Database Syst Rev.* 2010;CD001176.
40. Wu B, Lian L, Li Y, et al. Clinical course of cuffitis in ulcerative colitis patients with restorative proctocolectomy and ileal pouch–anal anastomoses. *Inflamm Bowel Dis.* 2013;19:404–410.
41. Hahnloser D, Pemberton JH, Wolff BG, et al. The effect of ageing on function and quality of life in ileal pouch patients: a single cohort experience of 409 patients with chronic ulcerative colitis. *Ann Surg.* 2004;240: 615–621; discussion 621–623.
42. Suzuki H, Ogawa H, Shibata C, et al. The long-term clinical course of pouchitis after total proctocolectomy and IPAA for ulcerative colitis. *Dis Colon Rectum.* 2012;55:330–336.
43. Fazio VW, O'Riordain MG, Lavery IC, et al. Long-term functional outcome and quality of life after stapled restorative proctocolectomy. *Ann Surg.* 1999;230:575–584; discussion 584–586.
44. Robb B, Pritts T, Gang G, et al. Quality of life in patients undergoing ileal pouch-anal anastomosis at the University of Cincinnati. *Am J Surg.* 2002; 183:353–360.
45. Thirlby RC, Sobrino MA, Randall JB. The long-term benefit of surgery on health-related quality of life in patients with inflammatory bowel disease. *Arch Surg.* 2001;136:521–527.
46. Camilleri-Brennan J, Steele RJ. Objective assessment of quality of life following panproctocolectomy and ileostomy for ulcerative colitis. *Ann R Coll Surg Engl.* 2001;83:321–324.
47. Carmon E, Keidar A, Ravid A, et al. The correlation between quality of life and functional outcome in ulcerative colitis patients after proctocolectomy ileal pouch anal anastomosis. *Colorectal Dis.* 2003;5: 228–232.
48. Fazio VW, Kiran RP, Remzi FH, et al. Ileal pouch anal anastomosis: analysis of outcome and quality of life in 3707 patients. *Ann Surg.* 2013;257:679–685.
49. Muir AJ, Edwards LJ, Sanders LL, et al. A prospective evaluation of health-related quality of life after ileal pouch anal anastomosis for ulcerative colitis. *Am J Gastroenterol.* 2001;96:1480–1485.
50. Andersson T, Lunde OC, Johnson E, et al. Long-term functional outcome and quality of life after restorative proctocolectomy with ileo-anal anastomosis for colitis. *Colorectal Dis.* 2011;13:431–437.
51. Berndtsson I, Oresland T. Quality of life before and after proctocolectomy and IPAA in patients with ulcerative proctocolitis–a prospective study. *Colorectal Dis.* 2003;5:173–179.
52. Koerdt S, Jehle EC, Kreis ME, et al. Quality of life after proctocolectomy and ileal pouch-anal anastomosis in patients with ulcerative colitis. *Int J Colorectal Dis.* 2014;29:545–554.
53. Turina M, Pennington CJ, Kimberling J, et al. Chronic pouchitis after ileal pouch-anal anastomosis for ulcerative colitis: effect on quality of life. *J Gastrointest Surg.* 2006;10:600–606.
54. Lai JS, Beaumont JL, Jensen SE, et al. An evaluation of health-related quality of life in patients with systemic lupus erythematosus using PROMIS and Neuro-QoL. *Clin Rheumatol.* 2017;36:555–562.
55. Hahn EA, Beaumont JL, Pilkonis PA, et al. The PROMIS satisfaction with social participation measures demonstrated responsiveness in diverse clinical populations. *J Clin Epidemiol.* 2016;73:135–141.
56. Randell RL, Long MD, Cook SF, et al. Validation of an internet-based cohort of inflammatory bowel disease (CCFA partners). *Inflamm Bowel Dis.* 2014;20:541–544.