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ORIGINAL ARTICLE

Factors Associated with Long-Term Quality of Life After Restorative Proctocolectomy with Ileal Pouch Anal Anastomosis

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Abstract

The aim The aim of this study was to analyze factors associated with quality of life (QoL) after ileal pouch anal anastomosis (IPAA).

Methods Patients who underwent IPAA (1983–2015) and replied to QoL questionnaire were identified from an IRB-approved prospectively maintained IPAA-database. QoL was assessed using Cleveland Global Quality of Life (CGQL) questionnaire at 1, 3, 5, and 10 years postoperatively. Patient cohort was divided in two groups: overall QoL score ≤ 0.7 (low) and > 0.7 (high). Demographics, perioperative morbidity, and functional results were analyzed.

Results A total of 4059 patients replied to the questionnaire at the most recent follow-up and were included. A total of 2889 (71%) had overall QoL > 0.7 (group 1) and 1170 (29%) patients had overall QoL ≤ 0.7 (group 2). Patients in group 1 had lower rates of early (44.6 vs. 50.4%, $p = 0.003$) and late (55.7 vs. 64.5%, $p < 0.003$) postoperative complications. Kaplan-Meier survival analysis demonstrated significantly higher rates of pouch failure among patients with lower QoL. Pouchitis, obstruction, fistulas, higher number of stools, and IPAA performed during the most recent decade (2005–2015) were significantly associated with lower QoL (≤ 0.7), while S-pouch configuration was associated with higher QoL (> 0.7).

Conclusion Patient's characteristics and minimal perioperative complications impact patient's QoL following IPAA not only in the short term, but also in the long term.

Keywords Ileal pouch anal anastomosis · Quality of life · Inflammatory bowel disease

Introduction

The opportunity to maintain transanal defecation and avoid a permanent ileostomy is the major benefit of ileal pouch anal-anastomosis (IPAA) surgery.[1,2] For those who have an existing ileostomy, restoration of GI continuity is a revolutionary life event that leads to disease-specific adjustment, change in body image, and psychosocial life. Over the last decades, the surgical technique of IPAA has evolved, as well as anesthesia, perioperative care, and patients' postoperative expectations. A generally accepted quality of life (QoL) definition is a gap between patient's expectations and outcomes. Patients undergoing IPAA are generally young with long life expectancy.

It has previously been reported that long-term QoL after IPAA is either good or excellent, and most patients are highly satisfied with the results of RP. Importantly, most patients would be willing to recommend RP to others or undergo the procedure themselves again, if necessary.[1,3–5] Conversely, IPAA procedure is technically demanding and can be associated with serious postoperative complications (i.e., anastomotic leak, pelvic sepsis, strictures), which could compromise long-term ileal pouch function. Although QoL has been reported to be good or excellent in the majority of patients after IPAA, approximately 20% of patients would rate their QoL as low or poor after IPAA.[1,2,6,7] The relationship between the functional outcomes and QoL in the short term after IPAA has been previously reported.[8–12] Yet, less is known whether pre- and perioperative factors, including postoperative

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complications in the immediate and late postoperative periods, impact QoL after IPAA in the long term.[13]

We hypothesized that patients' baseline demographic characteristics and perioperative complications have an impact not only on short-term outcomes, but also on long-term QoL after IPAA. We aimed to determine the evolution of QoL over several decades and determine the factors associated with long-term QoL after IPAA.

Methods

After institutional review board approval, a prospectively maintained ileal pouch database was queried for all patients who underwent index IPAA surgery and answered a quality of life questionnaire at the Department of Colorectal Surgery, Cleveland Clinic from 1983 to 2015. Individuals who underwent trans-abdominal salvage redo/revision of their IPAA were excluded.

Assessment of Quality of Life

Cleveland Clinic Global Quality of Life (CGQL) Pelvic Pouch Questionnaire, a validated and reliable self-administered questionnaire, was used to assess QoL[1] at the most recent follow-up to include 1, 3, 5, and 10 years (± 6 months) after IPAA. This questionnaire consists of three parameters: current QoL, current quality of health, and current energy level. Each parameter was assessed on a scale of 0 to 10 (0 = worst; 10 = best). The overall CGQL score was obtained by adding the three parameters and dividing by 30 (range 0–1; 0 being worst, 1 best).[1]

Functional outcome was determined by questionnaire as well. Patients were asked about bowel frequency (number of bowel movements per 24 h, day time and nocturnal), stool seepage (soiling during the day or night), use of pads. Dietary, social, work, and sexual restrictions at the most recent follow-up were also studied. Long-term QoL data was obtained during either annual clinic visits or by mailed questionnaire. Patients that replied to QoL questionnaires and were followed for at least 12 months after surgery were included.

The mean overall QoL score among all patient cohort was 0.7 ± 0.1. The entire cohort was divided in two groups: overall QoL score > 0.7 (high QoL, group 1) vs. ≤ 0.7 (low QoL, group 2).

Parameters of Interest and Definitions

Demographic characteristics included the patient's age at time of surgery, gender, American Society of Anesthesiologist (ASA) score, body mass index (BMI), diagnosis [ulcerative colitis (UC), indeterminate colitis (IC), familial adenomatous polyposis (FAP), Crohn's disease (CD)], date of diagnosis, and medical therapy (steroids, antitumor necrosis factor (TNF) inhibitor use). The time of surgery was classified on decade basis: decade 1 = 1983–1993, decade 2 = 1994–2004, and decade 3 = 2005–2015 and was considered as a separate parameter. The diagnosis was established based on permanent pathological examination of the resected specimen. At the latest follow-up, the clinical diagnosis was re-evaluated aiming to reveal subtle conversions to CD. Patients with J- and S-pouch configuration were included in the study, as well as stapled and hand-sewn anastomosis technique. Single-stage IPAA combines total proctocolectomy with an ileal pouch anal anastomosis but without a loop ileostomy. Two-staged IPAA is defined by an initial total proctocolectomy and IPAA with a loop ileostomy, followed by ileostomy closure. Three-staged IPAA is a sequence of subtotal colectomy/end ileostomy, followed by completion proctectomy with IPAA and loop ileostomy, and finally closure of ileostomy.

Postoperative complications were classified as early (within 90 days of IPAA or diverting loop ileostomy closure) and late (post 90 days or after loop ileostomy closure). Postoperative complications included anastomotic leak, pelvic sepsis, fistula, strictures, pouchitis, small bowel obstruction (SBO), wound infection, and pouch failure. Pouch failure was defined as either excision of ileal anal pouch with permanent end ileostomy or indefinite diverting loop ileostomy while leaving the constructed dysfunctional ileal pouch in situ.

Statistical Analysis

Analyses were performed using R version 2.15.1 (www.r-project.org). Categorical variables were compared using the Fisher's exact (when any group contains < 10 data points) or χ^2 test, while quantitative and ordinal variables were compared using the Wilcoxon rank-sum test. P values < 0.05 were considered statistically significant. Associations between QoL and baseline characteristics were assessed using univariable Cox regression models, which yielded log-rank test p values for categorical variables and Wald p values for quantitative variables. In the case of univariate multiple comparisons, Bonferroni's correction was applied as noted. Stepwise multivariate (MV) regression models were developed based on univariate regression analysis. The models were based on time at the most recent follow-up and at 1, 3, 5, or 10 years postoperatively. In addition, they were analyzed based on diagnosis including UC, IC, CD, and FAP. Hazard ratios, likelihood ratios, and 95% confidence intervals (CI) were also produced using the Cox models. For each model, the final variables were selected among candidates using a stepwise process, with Akaike's information criterion (AIC) used to select the most influential variables for the model. Candidate variables were removed from the model, if it did not add predictive ability to the model with the variables already present.

A Kaplan-Meier pouch survival analysis was performed to estimate pouch longevity across the follow-up period.

Results

Out of 4502 patients who underwent IPAA between 1983 and 2016, a total of 4059 patients responded to the CGQL questionnaire and met inclusion criteria. The overall integrative quality of life score at the latest follow-up for all patients was 0.7 ± 0.1. Of the 4059 patients, 2889 (71%) patients had overall QoL > 0.7 (group 1) and 1170 (29%) patients had overall QoL ≤ 0.7 (group 2). CGQL scores were stable with minor fluctuations over 10 years (Table 1). The median follow-up was significantly longer in the group 1, 8.7 (3.3–15.7) years vs. 8.1 (2.7–15.1) years in group 2 ($p < 0.001$); however, this difference is negligible from clinical standpoint. At the most recent follow-up after surgery, a total of 1394 (34%) patients had dietary restrictions, 767 (19%) social, 845 (21%) working, 807 (20%) sexual. Table 1 represents postoperative trend of QoL restrictions. Almost all patients (2375, 97.5%) in group 1 would recommend IPAA surgery to others vs. 764 (88%) patients in group 2 ($p < 0.001$); 2319 (95%) patients in group 1 would undergo IPAA surgery again if needed, compared to 735 (85%) patients in group 2 ($p < 0.001$).

Regardless of diagnoses, CGQL scores and dietary restrictions were consistent over years in long term after IPAA (Table 2).

Patients' characteristics at the time of surgery stratified by groups are shown in Table 3. Overall, men rated postoperative QoL higher than women at the time of most recent follow-up (73.2% males in group 1 and 26.8% in group 2, $p < 0.002$, vs. 68.7% of females in group 1, and 33.1% in group 2). Patients with better QoL were significantly younger, with a lower BMI and lower ASA scores, and more frequently underwent a two-stage IPAA. There was no difference in diagnosis distribution (UC the most common), steroids, or biologic use between the groups. J-pouch and stapled IPAA were the most common pouch configuration and type of anastomosis in both groups, but patients in group 1 had a higher rate of S-pouch construction (10 vs. 6.3%, $p < 0.001$). Of note, the majority of S-pouches (92.2%) were constructed prior to the year 2000.

Perioperative Morbidity and Quality of Life

Patients with better QoL scores had lower rates of early (44.6 vs. 50.4%, in group 1 vs. 2, $p = 0.003$) and late (55.7 vs. 64.5%, in group 1 vs. 2, $p < 0.003$) postoperative complications (Table 4). The rates of early anastomotic separation, pelvic sepsis, and wound infection were all significantly higher in patients with lower QoL. Late postoperative complications including fistula, obstruction, pelvic sepsis, and pouchitis were also significantly more frequent among those with lower QoL (group 2). Despite almost one third of patients (1281, 31.5%) developing pouchitis at the most recent follow-up, pouch loss due to pouchitis occurred only in 26 patients.

Kaplan-Meier survival analysis demonstrated significantly higher rates of pouch failure among patients with a lower QoL (Fig. 1, Table 5). Pouch dysfunction was the most frequent reason to lose a pouch among those with low QoL, while fistula was the most prevalent cause among those with good QoL. There was no significant association between other reasons of pouch failure and QoL.

Factors Associated with Quality of Life

Cox regression model identified pouchitis, obstruction, fistulas, stool frequency, and IPAA performed during the most recent decade (2005–2015), as significant factors associated with lower QoL score (≤ 0.7) (Table 6). Diagnosis was not a significant factor associated with QoL outcome. Further subanalysis estimated factors associated with worse QoL in each particular diagnosis (Table 7). Anastomotic separation and stool frequency were associated with worse QoL regardless of diagnosis, including UC, IC, CD, and FAP. Stool frequency

Table 1 Changes in quality of life and restrictions at 1, 3, 5 and 10 years after ileal pouch anal anastomosis

Variable/year after surgery	1 year, $n = 2133$	3 years, $n = 2305$	5 years, $n = 2533$	10 years, $n = 2013$
CGQL score	0.8 ± 0.1	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1
Quality of life	8.1 ± 1.7	8.4 ± 1.6	8.1 ± 1.7	8.0 ± 1.8
Quality of health	8.2 ± 1.7	8.2 ± 1.6	8.3 ± 1.6	8.2 ± 1.7
Energy level	7.5 ± 1.9	7.6 ± 1.9	7.4 ± 2.0	7.3 ± 2.0
Dietary restrictions	866 (37.4)	784 (32.6)	787 (30.4)	566 (28.2)
Social restrictions	343 (16)	338 (15)	372 (15)	294 (15)
Working restrictions	366 (17)	325 (14.1)	390 (15.4)	291 (15)
Sexual restrictions	322 (14.5)	367 (15.6)	379 (15)	322 (16.2)

CGQL Clevealnd Global Quality of Life

All data represented as *n*, %; mean ± standard deviation

Table 2 Changes in quality of life and restrictions on diagnosis basis at 1, 3, 5, and 10 years after ileal pouch anal anastomosis

Diagnosis/year after surgery	UC $n = 2812$	IC $n = 851$	CD $n = 161$	FAP $n = 235$	p value
CGQL score					
1 year	0.7 ± 0.1	0.8 ± 0.	0.8 ± 0.1	0.8 ± +0.1	0.62
3 years	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.89
5 years	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.86
10 years	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.2	0.92
Dietary restrictions	962 (34.2)	264 (31)	52 (32.5)	78 (33.3)	0.66
Social restrictions	529 (18.6)	166 (19.5)	28 (17.2)	42 (18)	0.29
Working restrictions	570 (20.3)	165 (19.4)	32 (20)	54 (23.1)	0.19
Sexual restrictions	529 (18.8)	187 (22.0)	31 (19.5)	43 (18.2)	0.73

CGQL Clevealnd Global Quality of Life, *UC* ulcerative colitis, *IC* indeterminate colitis, *CD* Crohn's disease, *FAP* familial adenomatous polyposis

All data represented as *n*, %; mean ± standard deviation

and anastomotic separations leading to pelvic sepsis were significant factors associated with QoL among patients with FAP. Pouchitis, obstruction, and higher number of stools were associated with worse QoL among patients with UC and IC diagnosis.

Multivariate logistic regression analysis at 1, 3, 5, and 10 years (Table 8) showed that some factors had persistent impact on QoL, while others would change and play a role in QoL only temporarily at separate time points. Stool frequency and pouchitis impact QoL at any time point after

Table 3 Demographics and intraoperative details stratified by quality of life score > 0.7 and < 0.7 after restorative proctocolectomy with ileal pouch anal anastomosis

Variable	Group 1 (QoL > 0.7) $n = 2889$ (71.2%)	Group 2 (QoL < 0.7) $n = 1170$ (28.8%)	p value
Age at surgery, years	38.2 ± 13.3	39.2 ± 13.4	*0.04*
Body mass index, kg/m^2	25.7 ± 5.6	26.1 ± 5.3	*0.03*
Gender			*0.002*
Male	1675 (58)	610 (52)	
Female	1214 (42)	560 (48)	
ASA score			*< 0.001*
1.2	2224 (77)	784 (67)	
3.4	665 (23)	386 (33)	
Diagnosis			0.21
UC	1993 (69)	819 (70)	
IC	606 (21)	245 (21)	
CD	115 (4)	46 (4)	
FAP	173 (6)	60 (5)	
Duration of disease, years	6.2 (2.4–12)	6.0 (2.42–13.2)	0.89
Pre-operative albumin, g/dL	4.3 (4.1–4.5)	4.3 (4–4.5)	0.29
Pre-operative hemoglobin, g/dL	12.7 (11.2–14.1)	12.4 (10.6–13.7)	*0.005*
Biologics usage	751 (26)	327 (28)	0.38
Steroids usage	1155 (40)	690 (39)	0.79
Procedure			*0.02*
2-staged IPAA	1588 (55)	585 (50)	
3-staged IPAA	1300 (45)	585 (50)	
Pouch configuration			*< 0.001*
J	2600 (90)	1663 (94)	
S	289 (10)	107 (6)	
Anastomosis fashion			0.11
Stapled	2542 (88)	1593 (90)	
Handsewn	347 (12)	177 (10)	
Duration of operation, hours,	3.2 ± 1.1	3.3 ± 1.1	*0.03*
Length of hospital stay, days	7.4 ± 4.0	7.9 ± 4.6	*0.004*
Intraoperative blood loss, mls	276.8 ± 276.5	273.5 ± 265.9	0.62

ASA American Society of Anesthesiology, *QoL* quality of life, *UC* ulcerative colitis, *IC* indeterminate colitis, *CD* Crohn's disease, *FAP* familial adenomatous polyposis, *IPAA* ileal pouch anal anastomosis

All data represented as *n*, %; mean ± standard deviation. Significant *p* values are in italics

Table 4 Comparison of postoperative complications in early and late postoperative periods after restorative proctocolectomy with ileal pouch anal anastomosis based on quality of life scores

Variable	Group 1 (QoL > 0.7) $n = 2889$ (71.2%)	Group 2 (QoL < 0.7) $n = 1170$ (28.8%)	p value
Anastomotic separation*	144 (5)	141 (8)	*0.01***
Anastomotic separation within 90 days	115 (4)	106 (6)	*0.03***
Anastomotic separation post 90 days	57 (2)	35 (2)	0.21**
Anastomotic stricture*	404 (14)	247 (14)	0.95
Anastomotic stricture within 90 days	173 (6)	85 (5)	0.28
Anastomotic stricture post 90 days	260 (9)	177 (10)	0.33
Fistula*	231 (8)	177 (10)	*0.02***
Fistula within 90 days	57 (2)	35 (2)	0.20
Fistula post 90 days	173 (6)	141 (8)	*0.06***
Small bowel obstruction*	577 (20)	424 (24)	*0.03***
Obstruction within 90 days	288 (10)	177 (10)	0.45
Obstruction post 90 days	318 (11)	283 (16)	*< 0.003***
Pelvic sepsis*	202 (7)	212 (12)	*< 0.003***
Pelvic sepsis within 90 days	144 (5)	82 (7)	*0.003***
Pelvic sepsis post 90 days	57 (2)	88 (5)	*0.003***
Pouchitis*	895 (31)	432 (37)	*< 0.003***
Pouchitis within 90 days	57 (2)	12 (1)	0.48
Pouchitis post 90 days	866 (30)	421 (36)	*< 0.003***
Wound infection*	231 (8)	194 (11)	*0.01***
Wound infection within 90 days	172 (6)	885 (9)	*0.02***
Any of the complications within 90 days	1300 (45)	579 (50)	*0.003***
Any of the complications post 90 days	1617 (56)	1150 (65)	*< 0.003***
Pouch failure *	101 (3)	79 (7)	*< 0.001*
Follow-up	8.7 (3.3–15.7)	8.1 (2.7–15.1)	*< 0.001*

All data represented as n, %; median and range. Significant p values are in italics

*At most recent follow-up. *QoL* quality of life, *IPAA* ileal pouch anal anastomosis

**Corrected for multiple comparisons

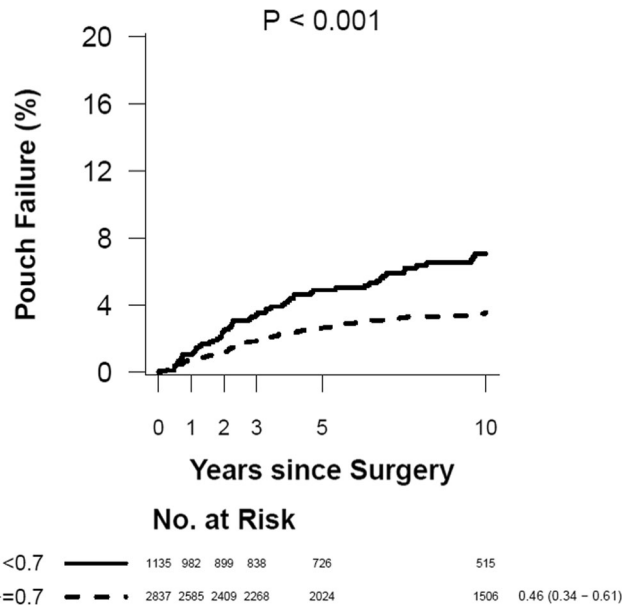

Fig. 1 Pouch Failure Based on Quality of Life Scores at 1, 3, 5, and 10 years after restorative proctocolectomy with ileal pouch anal anastomosis

IPAA. Patient's age and BMI significantly influenced QoL only at 1 and 3 years postoperatively. Technical details were noted to appear in models starting from 3 years after surgery up to 10 years. In particular, a handsewn anastomotic technique was associated with worse QoL. Finally, pelvic sepsis was noted to have significant impact on QoL at 1 and 10 years postoperatively, while anastomotic separation was incorporated into models at 3 years.

Table 5 Kaplan-Meier pouch survival analysis between groups

Year	Group 1 (QoL > 0.7)	Group 2 (QoL < 0.7)	p value
1	99% (98–99%)	99% (98–99%)	*0.001*
2	98% (98–99%)	97% (96–98%)	
3	98% (97–98%)	97% (95–97%)	
5	97% (96–98%)	95% (93–96%)	
10	96% (95–97%)	93% (91–95%)	

Data represented as 95% confidence intervals of pouch survival over years between groups

Table 6 Stepwise multivariate logistic regression model for overall quality of life after IPAA based on dichotomous outcome < 0.7 vs. 0.7 at the most recent follow-up between groups

Variable	Likelihood ratio *p* value	Parameter estimate (SE)	Odds ratio (95% CI)	Wald *p* value
Pouchitis	< 0.001	− 0.5973 (0.0987)	0.550 (0.454–0.668)	*< 0.001*
Obstruction	0.004	− 0.2977 (0.1024)	0.743 (0.608–0.908)	*0.004*
Fistula	0.023	− 0.3337 (0.1446)	0.716 (0.540–0.951)	*0.021*
Time of the operation	0.048			
1983–1993		0		
1994–2004		− 0.2183 (0.1227)	0.804 (0.632–1.022)	0.08
2005–2015		− 0.3618 (0.1490)	0.696 (0.520–0.933)	*0.015*
Stool frequency	< 0.001	− 0.0465 (0.0093)	0.955 (0.937–0.972)	*< 0.001*

Significant *p* values are in italics

Discussion

Quality of life is usually maintained after RP on the long-term with minimal restrictions; however, a certain number of patients will have sub-optimal outcomes. We sought to evaluate perioperative factors that may affect QoL after IPAA. Overall, we found that both early and late complications, such as pouchitis, anastomotic separation, pelvic sepsis, and recurrent obstructions, are associated with decreased QoL. We also found that although pouchitis is common, pouch loss due to pouchitis is rare, even if QoL is low in this cohort. Stool frequency and pouchitis appear to be major factors influencing QoL among patients with colitis, and their influence persists as time goes on following IPAA. Occurrence of anastomotic separation, either within early or late postoperative period, also had a detrimental effect on QoL. Finally, we found that

Table 7 Stepwise multivariate logistic regression model for overall quality of life after IPAA at the most recent follow-up on the diagnosis basis

Variable	Likelihood ratio *p* value	Parameter estimate (SE)	Odds ratio (95% CI)	Wald *p* value
Patients with ulcerative colitis				
Pouchitis	< 0.001	− 0.7321 (0.1304)	0.481 (0.372–0.621)	*< 0.001*
Obstruction	0.008	− 0.3475 (0.1302)	0.706 (0.547–0.912)	*0.008*
Pelvic sepsis	0.09	− 0.3353 (0.1947)	0.715 (0.488–1.047)	0.09
Stool frequency	< 0.001	− 0.0436 (0.0122)	0.957 (0.935–0.980)	*< 0.001*
Age (per 5-year increase)	0.007	− 0.0596 (0.0220)	0.942 (0.902–0.984)	*0.007*
Decade of surgery	0.11			
1983–1993				
1994–2004		− 0.0178 (0.1510)	0.982 (0.731–1.321)	0.91
2005–2015		− 0.3173 (0.1791)	0.728 (0.513–1.034)	0.08
Patients with indeterminate colitis				
Pouchitis	0.003	− 0.5658 (0.1876)	0.568 (0.393–0.820)	*0.003*
Anastomotic separation	0.051	− 0.6634 (0.3336)	0.515 (0.268–0.990)	*0.047*
Steroid use	0.06	− 0.3591 (0.1896)	0.698 (0.482–1.013)	0.06
Obstruction	0.11	− 0.3511 (0.2166)	0.704 (0.460–1.076)	0.10
Stool frequency	0.05	− 0.0270 (0.0139)	0.973 (0.947–1.000)	0.051
Patients with Crohn's colitis				
Anastomotic separation	0.038	1.4256 (0.7458)	4.160 (0.965–17.945)	0.06
Pelvic sepsis	0.1	− 0.7759 (0.4700)	0.460 (0.183–1.156)	0.10
Stool frequency	0.002	− 0.1238 (0.0416)	0.884 (0.814–0.959)	*0.003*
Patients with FAP				
Anastomotic separation	0.043	− 1.5642 (0.7872)	0.209 (0.045–0.979)	*0.045*
Stool frequency	0.036	− 0.1179 (0.0568)	0.889 (0.795–0.993)	*0.038*

IPAA ileal pouch anal anastomosis, *CI* confidence interval, *QoL* quality of life, *FAP* familial adenomatous polyposis. Significant *p* values are italicized

Table 8 Factors associated with overall quality of life scores after IPAA at 1, 3, 5, and 10 years of follow-up

Variable	Likelihood ratio *p* value	Parameter estimate (SE)	Odds ratio (95% CI)	Wald *p* value
Factors at 1 year				
Stool frequency	< 0.001	− 0.1340 (0.0224)	0.875 (0.837–0.914)	*< 0.001*
Pouchitis	< 0.001	− 1.0332 (0.2035)	0.356 (0.239–0.530)	*< 0.001*
Age (per 5-year increase)	0.003	− 0.0833 (0.0278)	0.920 (0.871–0.972)	*0.003*
Pelvic sepsis	0.07	− 0.4615 (0.257)	0.630 (0.385–1.032)	0.07
Time of surgery	0.052			
1983–1993				
1994–2004		− 0.0694 (0.3438)	0.933 (0.476–1.830)	0.84
2005–2015		− 0.4435 (0.3542)	0.642 (0.321–1.285)	0.21
Factors at 3 years				
Handsewn (vs. stapled) anastomosis	0.15	− 0.405 (0.2763)	0.669 (0.389–1.149)	0.15
Stool frequency	< 0.001	− 0.1753 (0.0234)	0.839 (0.802–0.879)	*< 0.001*
Disease duration (per 5 years increase)	0.004	− 0.1094 (0.0377)	0.896 (0.833–0.965)	*0.004*
Pouchitis	0.001	− 0.629 (0.1901)	0.533 (0.367–0.774)	*0.001*
Anastomotic separation	0.06	− 0.5415 (0.2763)	0.582 (0.339–1.000)	0.05
BMI (per 5 units increase)	0.019	− 0.1641 (0.680)	0.849 (0.743–0.970)	*0.016*
Fistula	0.049	− 0.6087 (0.2995)	0.544 (0.302–0.979)	*0.042*
Time of surgery				
1983–1993				
1994–2004	< 0.001	− 0.4286 (0.4207)	0.651 (0.286–1.486)	0.31
2005–2015		− 1.2345 (0.4317)	0.291 (0.125–0.678)	*0.004*
Factors at 5 years				
Time of surgery	0.003			
1983–1993				
1994–2004		− 0.2201 (0.650)	0.802 (0.581–1.109)	0.18
2005–2015		− 0.6590 (0.1982)	0.517 (0.351–0.763)	*0.001*
Handsewn (vs. stapled) anastomosis	0.041	− 0.4263 (0.2028)	0.653 (0.439–0.972)	*0.036*
Stool frequency	< 0.001	− 0.1792 (0.0190)	0.836 (0.805–0.868)	*< 0.001*
Wound infection	0.011	− 0.4949 (0.1887)	0.610 (0.421–0.882)	*0.009*
Pouchitis	< 0.001	− 0.4957 (0.1412)	0.609 (0.462–0.803)	*< 0.001*
Factors at 10 years				
Time of surgery				
1983–1993	0.017			
1994–2004		− 0.4216 (0.1505)	0.656 (0.488–0.881)	*0.005*
2005–2015		− 0.1664 (0.2921)	0.847 (0.478–1.501)	0.57
Stool frequency	< 0.001	− 0.2291 (0.0219)	0.795 (0.762–0.830)	*< 0.001*
Obstruction	0.006	− 0.4353 (0.1549)	0.647 (0.478–0.877)	*0.005*
Sepsis	0.018	− 0.5748 (0.2363)	0.563 (0.354–0.894)	*0.015*
Pouchitis	0.049	− 0.2723 (0.1380)	0.762 (0.581–0.998)	*0.04*

IPAA ileal pouch anal anastomosis, *BMI* body mass index. Significant *p* values are in italics

other factors associated with QoL vary significantly over time, some of which play a role persistently over time, and some that fade away as time goes by after surgery. Patient's demographics such as age, BMI, and ASA score were significant factors only at separate time points after surgery on multivariate analysis. Perhaps, this more aptly reflects difficulties in adapting to new life limitations after acquiring an ileal pouch compared among patients who differ demographically.

It is important to emphasize that better QoL scores from patients that underwent a two-stage IPAA can potentially be related to better preoperative health and nutrition status, which are usually compromised among those who undergo three-

stage IPAA. The former were medically treated for a longer time, had more severe disease preoperatively, and presented to surgery later in their course. Seirfath et al. also described worse QoL among patients after three-stage IPAA.[14]

Perioperative complications, either early or late after surgery, are detrimental for QoL in the long term.[15–17] Anastomotic separation was a significant predictors of QoL regardless of diagnosis, including UC, IC, as well as FAP and Crohn's colitis. Pouchitis was also a factor among colitis individuals, as it is rarely seen among patient with FAP after IPAA. Pouchitis is one of the most common complications after IPAA, occurring in the majority of patients and was associated with significant decline in QoL.[18] Of note, it was not the most common reason for loss of ileal pouch in the long term, and patients were willing to undergo additional treatments to retain the functioning pouch for as long as possible. This also highlights an important message about how a patient's motivation plays a key role in the success of IPAA surgery. Recurrent small bowel obstructions are another long-standing challenge on the long-term QoL for patients with IPAA. Previously, Erkek et al. reported SBO to be associated with increased frequency of stools after IPAA in long term, without impact on QoL. In our series, recurrent SBO was a factor diminishing postoperative QoL.[19]

Ileal pouch function and stool frequency in particular appear to be the most crucial factors in association with patients QoL after IPAA. This study showed strong relationship between higher stool frequency and lower QoL over a decade of observation. This also supports multiple previous reports about correlation of pouch function and QoL.[20–22]

The patient's preoperative and postoperative expectations also play a tremendous role in determining ultimate QoL. IPAA procedure is now considered a standard procedure for restoration of gastrointestinal continuity after removal of colorectum. Moreover, this procedure is now available broadly over the world; however, during 1980s, when IPAA was offered only in several centers, it was the only unique opportunity to avoid permanent ostomy for very motivated selected patients. Our analysis showed that IPAA performed during the most recent decade was associated with worse QoL. We believe that this is related to changes of patients' expectations over decades, as previously we reported decreased postoperative complication rate during recent decade after IPAA.[23] Certainly, these expectations are age- and sex-dependent and tend to change over time. Previously, Raviram et al. reported that the underlying indications for an IPAA itself plays important role for QoL, as those with severe UC and higher stool frequency report improved QoL almost immediately after surgery, while those who developed dysplasia from long-standing mild UC and required colorectal resection had a longer and more difficult adjustment to life after IPAA—likely due to increased stool frequency, similar to findings seen after IPAA for FAP.[5]

We acknowledge certain limitations to the present analysis. Many treatment strategies have occurred over the long-time period of the study—more than three decades. Not only have surgical techniques changed, but also patients, dietary habits, expectations, medications, as well as staff turnover, the introduction of laparoscopy, and implementation of enhanced recovery protocols. It is almost impossible to study the change of patients' expectations over decades. Collectively, these changes make it very hard to single out factors associated with QoL. We also were unable to address the preoperative QoL and see how that changed from pre- to postoperatively, as well as over time. Despite these limitations, to our knowledge, this study represents the largest study with longest follow-up reporting of QoL after IPAA published to date and adds incrementally to the available literature on the topic.

Conclusions

Overall, QoL after IPAA is excellent with minimal fluctuations and gives motivated patients an opportunity to avoid permanent ostomy in the long term. Both early and late complications are strongly associated with long-term QoL after IPAA. Predictors of QoL after IPAA tend to vary over time as the patient, and the pouch, age. Finally, pouchitis, although common, rarely results in pouch loss. This study has demonstrated that "high-quality operation" with minimal intraoperative complications and subsequent avoidance of perioperative complications can improve QoL following IPAA not only in short term, but also in the long term.

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Compliance with Ethical Standards

Disclosure None.

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