



Impact of sex on 30-day complications and long-term functional outcomes following ileal pouch-anal anastomosis for chronic ulcerative colitis

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Abstract

Purpose To determine the impact of patient sex on operative characteristics, short-term complications, and long-term functional outcomes following ileal pouch-anal anastomosis (IPAA) for chronic ulcerative colitis (CUC).

Methods A retrospective review was performed on all patients undergoing two- or three-stage IPAA for CUC at our institution between January 2002 and August 2013. Patient demographics, operative characteristics, 30-day postoperative complications, and long-term functional outcomes from annual survey data were analyzed comparing men and women patients.

Results During the study period, 911 IPAAAs (542 men, 369 women) were performed. Men were older and were more often obese (both $p < 0.01$). Use of a three-stage approach and laparoscopic approach were similar between men and women, but operation length, intraoperative blood loss, and hospital length of stay were all higher in men (all $p < 0.05$). At 30 days, women had increased rates of superficial surgical site infections and urinary tract infections (both $p < 0.05$), while men had increased rates of urinary retention ($p = 0.03$). Five hundred forty-six patients (60%; 307 men, 239 women) responded to the annual post IPAA survey with a median follow-up of 5.1 and 5.0 years in men and women, respectively. Women reported increased frequency of daytime stools in the early follow-up period, but this difference resolved with time. Other functional outcomes were similar.

Conclusion Patient sex impacts intraoperative complexity, postoperative length of stay, 30-day postoperative outcomes, and initial long-term function. These findings underscore the need to adjust preoperative counseling regarding IPAA outcomes based on sex.

Keywords IPAA · CUC · Outcomes · Sex

Introduction

Restorative proctocolectomy with ileal pouch anal anastomosis (IPAA) was first described for chronic ulcerative colitis (CUC) in 1978 by Parks and Nicholls [1] and has become

the procedure of choice for CUC due to low postoperative morbidity, improved quality of life [2], and good long-term function [3]. While there has been extensive literature on pouch outcomes with relation to age [4–6], body mass index [7, 8], a diagnosis of Crohn's disease [9–11] or familial adenomatous polyposis [12–14], and pelvic sepsis [15, 16], there are limited reports on outcomes in relation to sex.

Previous studies have shown that sex affects the presentation of inflammatory bowel disease (IBD) and the disease course [17–19]. For example, women more often have extra-intestinal manifestations of IBD, undergo surgery for Crohn's disease, and have more relatives with IBD [18]. However, there is limited literature regarding the relationship of sex to pouch outcomes. To date, only one other large single center series has directly compared intraoperative variables, short-term outcomes, and long-term pouch outcomes with regard to sex. In this series, men had a diverting ileostomy at the time of IPAA more often, had a higher incidence of 30-day

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postoperative anastomotic separation [20], and an increased long-term risk of chronic antibiotic refractory pouchitis (CARP) and pouch sinus tracts [21]. Similarly, an additional report from the same center found that men had increased rates of pouchitis and sexual dysfunction, and importantly, difficulty with prostate cancer screening, biopsy, and treatment in the setting of a pouch [22]. However, when looking at long-term functional outcomes, women had an increased number of daytime bowel movements, daytime seepage, and 24-h pad usage at a median follow-up of 10 years [20].

The impact of patient sex on operative characteristics, short-term complications, and long-term functional outcomes following IPAA for CUC remains poorly defined. We used our single center pouch database of over 900 patients to determine the impact of sex on (1) intraoperative characteristics, (2) short-term 30-day postoperative complications, and (3) long-term pouch functional outcomes.

Methods

Following Institutional Review Board approval, all CUC patients who underwent either laparoscopic or open total proctocolectomy with IPAA (two-stage IPAA - CPT codes 44157, 44158, and 44211) or completion proctectomy with IPAA (three-stage IPAA - CPT code 45113) between January 2002 and August 2013 were identified using a prospectively maintained pouch database. Data collected included patient demographics (age, body mass index (BMI)), American Society of Anesthesiology (ASA) score, preoperative serum laboratory values, and preoperative immunosuppressive medications, operative characteristics (operative approach, operation length, estimated blood loss), and 30-day postoperative complications (surgical site infection, pelvic sepsis, urinary tract infection, partial small bowel obstruction/ileus, urinary retention, postoperative blood transfusion, dehydration, and venous thromboembolism). Pelvic sepsis was defined as a peripouch abscess or anastomotic leak. Partial small bowel obstruction/ileus were defined as the requirement for nasogastric tube decompression due to delayed return of intestinal function but not requiring return to the operating room. Dehydration was defined as readmission for the administration of intravenous fluids with or without elevation in creatinine.

Long-term functional data was gathered from annual survey data collected from a prospectively maintained pouch database as previously described [23]. Survey data collected included frequency of bowel movements, incontinence, need for stool bulking agents or pads, and various quality of life indicators. Pouch failure was defined as patients who underwent pouch excision or those who were diverted at time of last follow-up.

Operations and perioperative care

Throughout the manuscript, two-stage IPAA refers to the first step of a two-stage IPAA: total proctocolectomy with ileal pouch anal anastomosis. Three-stage IPAA refers to the second step of a three-stage IPAA: completion proctectomy with ileal pouch anal anastomosis. All patients underwent intestinal diversion at the time of pouch formation. The subtotal colectomy operation (step 1 of a three-stage IPAA approach) and loop ileostomy reversal were not studied. All operations were performed for a preoperative diagnosis of CUC. Menopause was defined using the average age of menopause in the USA of 51 years [24].

Perioperative care was the same for all patients, with the only change being the introduction of an enhanced recovery pathway (ERP) for all patients starting in 2011. In the pre-ERP era, patients were started on clear liquid diet the day of surgery, and currently patients are initiated on a regular diet immediately after surgery. Patients are discharged once pain is controlled on oral medications, oral intake is adequate, and ileostomy output is in an acceptable range (<1.5 L). Our perioperative care pathway in the enhanced recovery era has been previously described [25].

Statistics

Summary statistics were presented as mean and percentage for categorical variables and median and interquartile range for continuous variables. Univariate analysis was performed using Wilcoxon rank sum tests for continuous variables and Pearson's chi-squared tests for categorical variables.

To account for variable times between IPAA and survey response, the responses for daytime bowel movements were grouped based on time from IPAA. This created three groups (response within the first 18 months, response at 4 to 6 years, and response at 7 to 10 years). The groups were constructed in this way to maximize the number of patients included based on their response at various time points, with the recognition that this would result in some patient responses being censored. A similar methodology has been used previously by Delaney et al. [5]. Analysis in this manner allows the evaluation of temporal trends in bowel movements per day. Other indicators of pouch function, including pad usage and incontinence, are reported at 4 to 6 years after surgery. Pouch survival analysis was conducted using the Kaplan-Meier method.

Significance was set at $p \leq 0.05$. Data management and analyses were performed using JMP®, Version 10.0.0. SAS Institute Inc., Cary, NC, 1989–2007.

Results

Patient demographics

A total of 911 IPAA (542 men, 369 women) were performed between January 2002 and August 2013. Men were older ($p = 0.02$), had higher ASA scores ($p < 0.01$), and had higher preoperative hemoglobin ($p < 0.01$) (Table 1). A total of 310 women (84%) were less than 51 years old and presumed premenopausal.

Operative characteristics

The use of a three-stage approach was similar between men and women. However, a laparoscopic approach was more common in women than men for patients undergoing a two-stage procedure. Operation length for two-stage procedures ($p < 0.01$), estimated blood loss for two-stage ($p < 0.01$) and three-stage ($p = 0.01$) procedures, and length of stay for two- and three-stage procedures (both $p = 0.02$) were all greater in men (Table 2).

30-day postoperative complications

At 30 days postoperatively, women suffered from increased rates of superficial surgical site infection (sSSI) ($p = 0.03$), dehydration ($p = 0.02$), and urinary tract infections (UTI) ($p < 0.01$), while men suffered from increased rates of urinary retention ($p = 0.03$). The most striking difference in complications between men and women was the almost two times occurrence of ileus/partial small bowel obstruction in men compared to women ($p < 0.01$) (Table 3).

Long-term functional outcomes

Sixty percent of patients (307 men, 239 women) responded to the annual post IPAA survey at least once with a median follow-up of 5.1 and 5.0 years in men and women, respectively (Tables 4 and 5). At up to 1.5 years after IPAA, women reported an increased median number of daytime bowel movements compared to men (median [IQR]—men, 6 [5–8]; women, 7 [6–9], $p = 0.02$). This difference persisted at follow-up 4–6 years after IPAA (median [IQR]—men, 6 [5–8]; women, 7 [5–8], $p = 0.02$) but disappeared at follow-up at 7–10 years after IPAA (median [IQR]—men, 6 [5–8]; women, 6 [5–8], $p = 0.22$).

For patients replying 4 to 6 years after IPAA ($N = 311$; 181 men, 130 women), women reported an increased percentage of daytime pad usage, but other functional outcomes were similar (Table 6). With respect to quality of life at 4–6 years after surgery, men reported increased social life restrictions, but otherwise men and women had similar rates of restrictions across eight domains including work, travel, and sexual life (Table 7). Pouch failure was similar in men and women at both 5 years (10.6% men, 9.8% women) and at 9 years (13.8% men, 11.7% women).

Discussion

While outcomes following IPAA have been well studied with regard to age [4–6, 26] and diagnosis [9–14], there remains a paucity of literature regarding pouch outcomes in relation to sex. Using our single institution pouch database of more than 900 patients, we found male patients underwent more open

Table 1 Demographics and preoperative variables

	Men (n = 542)	Women (n = 369)	P value
Patients, n (%)	542 (59.5)	369 (40.5)	–
Age at surgery, median (IQR)	38 (27–46)	35 (27–48)	0.02
BMI ≥ 30 , n (%)	89 (16.5)	64 (17.4)	0.72
ASA, n (%)			< 0.01
I	27 (5)	27 (7)	
II	434 (80)	311 (84)	
III	81 (15)	31 (9)	
Hemoglobin, median (IQR)	13.7 (12.0–14.7)	12.1 (10.8–13.4)	< 0.01
White blood cells, median (IQR)	7.7 (5.8–10.3)	7.4 (5.8–9.5)	0.28
Albumin, median (IQR)	4.1 (3.7–4.5)	4.1 (3.7–4.4)	0.57
Steroids [‡] , n (%)	194 (55.0)	128 (58.7)	0.38
Immunomodulators [‡] , n (%)	117 (33.1)	64 (29.4)	0.35
Biologics [‡] , n (%)	71 (20.2)	48 (22.1)	0.58

IQR interquartile range

[‡] Only includes 569 patients undergoing two-stage IPAA

Table 2 Operative characteristics

	Men (n = 542)	Women (n = 369)	P value
Three-stage operation, n (%)	190 (35.1)	152 (41.2)	0.06
Urgent surgery [‡] , n (%)	44 (12.5)	25 (11.5)	0.72
Stapled, n (%)	514 (94.8)	360 (97.6)	0.04
Laparoscopic, n (%)			
Two-stage	232 (65.9)	161 (74.2)	0.04
Three-stage	44 (23.5)	48 (31.8)	0.09
Operation length (minutes), median (IQR)			
Two-stage	268 (229–333)	254 (202–310)	< 0.01
Three-stage	195 (161–248)	200 (155–238)	0.69
Estimated blood loss (mL), median (IQR)			
Two-stage	200 (100–300)	150 (100–200)	< 0.01
Three-stage	200 (100–300)	100 (100–200)	< 0.01
Length of stay (days), median (IQR)			
Two-stage	7 (5–9)	6 (5–8)	0.02
Three-stage	5 (4–7)	5 (4–6)	0.02

Urgent surgery defined as an operation during same hospitalization as admission for medically refractory disease
IQR interquartile range

[‡] Only includes 569 patients undergoing two-stage IPAA

total proctocolectomies with IPAA, with increased operative times, blood loss, and postoperative hospital lengths of stay. However, women had higher rates of surgical site infections and urinary tract infections, as well as episodes of dehydration in the first 30-days postoperatively. Women also experience an increased frequency of daytime bowel movements in the first two follow-up periods, but this difference resolved by the latest follow-up period. Other functional outcomes and quality of life were largely similar between men and women patients at 4 to 6 years of follow-up. Thus, despite the seemingly increased intraoperative difficulty in the male patient, our findings suggest women and men have similar long-term outcomes.

When looking at intraoperative variables, previous reports from Cleveland Clinic have found male patients were more often diverted, but a similar proportion of men and women underwent laparoscopic surgery [20]. In contrast, we found a

decreased use of laparoscopy for total proctocolectomy with IPAA, longer operative times, and increased estimated blood loss in men. This suggests a more difficult operation in male patients as has been previously reported [27]. This is likely secondary to a number of factors including the increased BMI among male patients in our series and known narrower confines of the male pelvis. Previous investigation has shown obesity is associated with increased intraoperative abandonment of IPAA due to increased technical difficulty [7, 8] and that obesity contributes to increased operative times and estimate blood loss in IPAA [28, 29]. Further, a narrow pelvis limits the use of laparoscopy, which leads to an increased length of stay [30], as we saw in the male cohort in our series.

Reflecting this increased complexity in the male patients was the higher rate of postoperative ileus/partial small bowel obstruction. Several factors likely contributed to this including the higher proportion of open cases in men and the longer

Table 3 30-day complications

Complication	Men (n = 542)	Women (n = 369)	P value
Pelvic sepsis, n (%)	43 (7.9)	31 (8.4)	0.80
Superficial surgical site infection, n (%)	50 (9.2)	51 (13.8)	0.03
Partial small bowel obstruction/Ileus, n (%)	102 (18.8)	41 (11.1)	< 0.01
Urinary retention, n (%)	51 (9.4)	20 (5.4)	0.03
Blood transfusion, n (%)	41 (7.6)	41 (11.1)	0.07
Dehydration, n (%)	20 (3.7)	26 (7.1)	0.02
Urinary tract infection, n (%)	12 (2.2)	48 (13.0)	< 0.01
Venous thromboembolism, n (%)	34 (6.3)	22 (6.0)	0.84
ICU admission, n (%)	13 (2.4)	7 (1.9)	0.61

Table 4 IPAA survey results

	Men	Women	<i>P</i> value
Total patients (%)	542 (59.5)	369 (40.5)	–
Number responded (%)	307 (57.8)	239 (66.0)	0.01
Median follow-up, years (IQR)	5.1 (3.3–5.3)	5.0 (3.3–5.4)	0.82
Minimum follow-up, years	0.62	0.58	–
Maximum follow-up, years	11.2	10.8	–

operative duration suggesting increased manipulation of the bowel. Male sex, open surgery, and increased operative duration are well-established risk factors for postoperative ileus [31, 32]. Interestingly, while the intraoperative characteristics and the increased incidence of ileus indicate increased operative complexity in the male patient, we did not find a difference in the occurrence of pelvic sepsis between men and women at up to 30 days postoperatively.

Several other postoperative complications were higher in women than men however. An increased percentage of women received a blood transfusion postoperatively, consistent with previous reports [20]. This is likely secondary to the transfusion threshold of 7 g/dL in patients without a cardiac history regardless of sex [33], despite women having a lower normal hemoglobin range [34]. The preoperative lab values reflect this difference with the median hemoglobin level being almost 2 g/dL lower in the women patients. Superficial surgical site infection and urinary tract infection also occurred more frequently in women. It is well established that women are more prone to urinary tract infections due to anatomic differences including a shorter urethra [35]. Previous literature has shown an association between men sex and infectious complications in patients undergoing abdominal surgery [36]. In our study, women were more often on corticosteroids or biologic medications preoperatively which both have a known association with wound infection and could account for the slight difference we see in superficial surgical site infection rate [37, 38]. Women also underwent blood transfusion at a higher rate than men. Blood transfusion has a known immunomodulatory effect and has been shown to increase surgical site infections in patients undergoing IPAA [39].

With respect to long-term function, we found evidence of decreased function measured by number of daytime bowel movements in women initially. This is concordant with prior reports that women have an increased number of daytime bowel movements [20]. This difference in function resolved

Table 5 IPAA survey response rate by follow-up period

Time frame	Men	Women
0.5 to 1.5 years, <i>n</i> (%)	120 (22)	97 (26)
4 to 6 years, <i>n</i> (%)	181 (33)	130 (35)
7 to 10 years, <i>n</i> (%)	51 (9)	41 (11)

with time with men and women having an equivalent number of daytime bowel movements at 7–10 years of follow-up, which suggests accommodation with time. This theory has been previously proposed by Michelassi et al., and our findings add credence to this [40].

At 4 to 6 years of follow-up, women reported increased pad usage compared to men, but did not report differences across other functional domains including daytime and nighttime incontinence. Similarly, previous literature from Cleveland found women had an increased frequency of daytime pad usage. However, they also found increased daytime stools, daytime seepage, and pad usage during the day and night at a median of 10 years for women, but they did not account for time to follow-up, so it is unclear if these results would persist if stratified by time. Lastly, quality of life was largely similar between men and women across several functional domains. Men did report increased social life restrictions. The mechanism behind this is unclear, but it could be related to male patients being more reluctant to use a pad, thus resulting in more social life restrictions. Importantly, no difference was seen in travel or sexual restrictions between sexes.

Our series is limited by it being a retrospective study from a single institution. While there is some bias due to our center being an IBD referral center, our series includes over 900 patients, representing a large patient experience thereby minimizing any bias in our findings. In addition, our long-term functional results are limited by overall survey response rates of 66 and 58% in women and men, respectively. It is possible that due to incomplete reporting, our findings are not a true representation of overall function. Lastly, we do not have information on how child birth affects pouch function within

Table 6 Long-term functional at 4–6 years in men versus women

	Men	Women	<i>P</i> value
Daytime incontinence*, <i>n</i> (%)	44 (25.4)	36 (30.0)	0.39
Daytime pad use ^Ω , <i>n</i> (%)	10 (5.8)	24 (19.5)	<0.01
Nighttime incontinence*, <i>n</i> (%)	94 (54.3)	65 (52.9)	0.80
Nighttime pad use ^Ω , <i>n</i> (%)	42 (24.3)	32 (26.0)	0.73
Stool thickening medication, <i>n</i> (%)	95 (53.7)	71 (55.5)	0.76
Pouchitis, <i>n</i> (%)	85 (49.1)	65 (52.4)	0.58

*Includes occasional and frequent incontinence

^ΩIncludes sometimes and frequently wearing a pad

Table 7 Quality of life at 4–6 years after IPAA

Domain	Men	Women	<i>p</i> value
Social life restriction, n (%)	82 (47.4)	45 (36.0)	0.0496
Sports restrictions, n (%)	66 (42.6)	41 (38.3)	0.49
Housework restrictions, n (%)	32 (18.5)	18 (14.5)	0.37
Recreation restrictions, n (%)	75 (44.1)	47 (37.9)	0.29
Family restrictions, n (%)	28 (16.4)	19 (15.7)	0.88
Travel restrictions, n (%)	89 (51.2)	53 (42.7)	0.15
Work restrictions, n (%)	38 (23.0)	23 (20.2)	0.57
Sexual restrictions, n (%)	50 (31.1)	46 (42.6)	0.05

Data presented as percent of patients reporting restrictions in the various domains

this study. However, we have previously shown that it does that child birth does not adversely affect pouch function [4].

Conclusion

Patient sex has an impact on both intraoperative complexity and frequency of postoperative complications including urinary tract infection and ileus. However, long-term function is largely similar over time. Thus, men and women can anticipate equivalent long-term functional outcomes.

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