Original Article

Evaluation Of Pathophysiological Aspects And Surgery Outcomes Of Ulcerative Colitis: A Retrospective Study

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Abstract

Background: IPAA is one of the most preferred procedures for ulcerative colitis. However, it is associated with many complications that can be early or late complications. These early complications are comparable to those seen in abdominal surgeries and seen in 30-50% of cases. Late complications are seen after more than 90 days post-surgery of IPAA.
Aim: The present clinical study was conducted to evaluate the outcomes of IPPA and its designs on long-term functioning, neoplasia frequency in IPAA subjects, and IRA and IPAA outcomes in subjects having ulcerative colitis with concurrent PSC.
Methods: In 186 subjects, demographics, medical history, general physical examination, diagnosis, surgery performed, functional outcomes, histopathology, associated complications, and failure. Pouch Functional Score, Endoscopy, Pouchitis, and Proctitis was recorded. Complications following IRA or IPAA were also evaluated. The collected data were subjected to statistical evaluation and the results were formulated.
Results: With IPAA treatment, Bowel movement during daytime was scored as 0, 1, and 2 in 28.94% (n=11), 50% (n=19), and 15.78% (n=6) subjects respectively with UC and in 28.57% (n=2), 0, and 71.42% (n=5) subjects respectively with UC and PSC. Failure due to pouchitis was seen in 12.5% (n=2) of subjects having UC with PSC. More than 4 episodes of pouchitis were seen in 12.90% (n=4) subjects with UC alone and 62.5% (n=10) subjects having UC with PSC. Subjects having pouchitis were 32.25% (n=10) having UC alone and 81.25% (n=13) having UC with PSC. In IPAA, the subjects with UC with PSC and UC alone had 15% and 5% failure respectively which was statistically non-significant. However, in subjects treated with IRA, failure in subjects with UC alone and UC with PSC was 21% and 52% respectively.
Conclusion: The present study concludes that the best long-term functional outcomes were seen in K-pouch with stapled anastomosing in subjects with ulcerative colitis with a very low incidence of neoplasia following treatment. High failure rates and compromised functional outcomes are seen in subjects having UC and PSC treated with IRA. However, IPAA showed comparable outcomes in subjects having UC only or UC with PSC

Keywords: Complications, IPAA, IRA, neoplasia, Primary sclerosing cholangitis ulcerative colitis

INTRODUCTION

Ulcerative colitis is an inflammatory disease that affects the large intestine and is relapsing. Ulcerative colitis is mainly seen in young subjects. However, it can affect subjects of any age. Ulcerative colitis is caused by the interaction between various non-genetic and genetic factors. The pathophysiology of ulcerative colitis can be

attributed to the abnormal inflammatory response, in subjects that are genetically predisposed to bacteria present in the lumen of the intestine. Also, ulcerative colitis shares common genetic risks to Crohn's disease. However, non-genetic factors also play a role in the pathophysiology of ulcerative colitis.[1]

Mucosal cells in the intestine act as signaling agents as well as a barrier towards the microbial entry. The equilibrium between these two functions is disturbed in ulcerative colitis by disturbing the mucosal layer and junction between mucosal cells. This can lead to an inflammatory response by bacterial translocation which causes epithelial ulceration, erosions, and damage breaking local defense. Treatment of ulcerative colitis follows medical pharmacologic management as the first line of treatment utilizing 5-ASA, anti-TNF agents, immunomodulators, and corticosteroids.[2]

Pharmacologic treatment is effective in ulcerative colitis. However, nearly 30% of subjects with ulcerative colitis are either refractory or have colorectal neoplasia, and need surgical management. It is also needed in conditions risking life such as toxic megacolon, refractory bleeding, and/or perforation. Various aspects need to be considered including health-related quality of life, cost-related issues, pouchitis/proctitis risk, reproduction, failure rates, and postoperative complications. In surgical procedures, the first performed procedure is abdominal colectomy with/without ileostomy.[3] The aim of surgery is to restore bowel continuity and includes ileal pouch-anal anastomosis (IPAA), proctectomy, ileostomy, continent ileostomy (Kock pouch), or ileorectal anastomosis (IRA). Better functional outcomes are seen with Segmental colon resection. Anastomosis has to be made and could be made either with hand sewing or with the stapler.

IPAA is one of the most preferred procedures for ulcerative colitis. However, it is associated with many complications that can be early or late complications.[4] These early complications are comparable to those seen in abdominal surgeries and seen in 30-50% of cases. These include stenosis of the ileoanal anastomosis, intestinal obstruction, pelvic abscess, anastomosing leak, and/or bleeding. These can be managed, and if not repaired can lead to compromised long-term functions. Late complications are seen after more than 90 days post-surgery of IPAA. They include pouch failure, pouchitis, intestinal obstruction, pouch vaginal bleeding, stricture of the ileoanal anastomosis, pelvic fistulas, PSC (Primary sclerosing cholangitis), and/or pelvic sepsis (septic complications).[5] These late complications can also be surgically corrected with varied success rates. The present clinical study was conducted to evaluate the outcomes of IPPA and its designs on long-term functioning, neoplasia frequency in IPAA subjects, and IRA and IPAA outcomes in subjects having ulcerative colitis with concurrent PSC.

MATERIALS AND METHODS

The present clinical retrospective study was conducted to evaluate the outcomes of IPPA and its designs on long-term functioning, neoplasia frequency in IPAA subjects, and IRA and IPAA outcomes in subjects having ulcerative colitis with concurrent PSC. The present study was conducted at Department of General Surgery after obtaining clearance from the concerned Ethical committee. The study population was comprised of the records obtained from the Department of the surgery of the Institute of subjects managed by IPAA.

The inclusion criteria were complete records of the subjects managed by IPAA for ulcerative colitis or ulcerative colitis with concurrent Primary sclerosing cholangitis (PSC). The exclusion criteria were incomplete medical records of the IPAA subjects. The data extracted from the medical records were the subject's demographics, medical history, general physical examination, diagnosis, surgery performed, functional outcomes, histopathology, associated complications, and failure.

The study included a total of 186 subjects from both genders admitted to the department of Gastroenterology or surgery. For Pouch function assessment, a validated questionnaire was used along with VAS (Visual Analogue Scale) and HRQoL (Health-Related Quality of Life). Pouch Functional Score and rectal functions were assessed with Oresland score evaluating medication use, urgency, and incontinence grade. In addition, social restrictions, diet, perianal soreness, evacuation difficulties, antibiotic treatment, and stool consistency.

Endoscopy was done using gastroscopes and mucosal biopsies were done. The mucosa was assessed for ulcerations, lesions, polyps, edema, loss of vascularity, granularity, and friability by single examiner expertise in the field. The samples from anal transition zones were assessed for dysplasia and inflammation.

Pouchitis is the study subjects were assessed using PDAI (Pouchitis Disease Activity Index) evaluating histologic changes, endoscopic findings, and clinical symptoms on a scale of 0-6 for each criterion, whereas, Heidelberg

score evaluated inflammation and inflammatory changes. Proctitis was recorded at follow-up with the endoscope. Inflammation histopathologically was graded as absent, mild, moderate, or severe.
Complications following IRA or IPAA were considered when needed surgical or endoscopic management. The complications assessed in the present study were fistula, pelvic sepsis, small bowel obstruction, anastomotic stricture, anastomotic dehiscence, and bleeding. The complications were recorded using the Clavein-Dindo grading system dividing complications into anesthesia, failure, life-threatening complications, and death. IPAA failure was considered when pouch excision/diversion with proximal stroma for >1year, whereas, IRA failure was considered when diversion/proctectomy for >1year. The reason behind failure was also noted.

The collected data were subjected to the statistical evaluation using SPSS software version 21 (Chicago, IL, USA) and one-way ANOVA and t-test for results formulation. The data were expressed in percentage and number, and mean and standard deviation. The level of significance was kept at $p<0.05$.

RESULTS

The present clinical retrospective study was conducted to evaluate the outcomes of IPPA and its designs on long-term functioning, neoplasia frequency in IPAA subjects, and IRA and IPAA outcomes in subjects having ulcerative colitis with concurrent PSC. The study included a total of 186 subjects from both genders admitted to the department of Gastroenterology or surgery. The mean follow-up time for the study was 1.68±1.12 years. The study results showed that there was a statistically significant difference ($p<0.005$) between K-pouch and J-pouch with the design of the pouch and age of surgery being reliable predictors of the Oresland score. Functional scores were highest in cases with stapled J-pouch followed by handsewn J-pouch, handsewn K-pouch, and least with stapled K-pouch. Retarding drug use, protective pads use, and evacuation difficulties were higher in the J-pouch group.
In IPAA subjects for neoplasia, one subject showed low grade dysplasia in the pouch as seen by one pathologist among the two examiners. No high-grade dysplasia or carcinoma was seen in the study subjects. In acute inflammation, it was seen that Grade 2, 3, and 4 acute inflammation was seen in 20.96% (n=39) and 24.73% (n=46) subjects respectively by examiner 1 and 2, Grade 3 in 75.80% (n=141) and 51.07% (n=95) subjects respectively by examiner 1 and 2, and Grade 4 in 79.03% (n=147) and 59.13% (n=110) subjects respectively by examiner 1 and 2. For chronic inflammation, Grade 1, 2 and 3 was seen in 4.83% (n=9) subjects by examiner 2, 25.80% (n=48) and 23.11% (n=43), and 53.76% (n=100) and 73.11% (n=136) subjects respectively by examiner 1 and 2. Mucosal adaptation of Grade 1, 2, and 3 was seen in 25.80% (n=48), 5.91% (n=11), and 58.06% (n=108) subjects respectively by examiner 1. In ATZ area, Grade 1, 2, and 3 was seen in 3.76% (n=7), 18.81% (n=35), and 48.92% (n=91) subjects respectively (Table 1).
In subjects treated with IPAA, subjects with concurrent ulcerative colitis with Primary sclerosing cholangitis and with ulcerative colitis only, no difference was seen. However, the score of 8 or more was seen more in subjects with ulcerative colitis alone. In the IRA group, worse scores were seen in subjects with concurrent ulcerative colitis with Primary sclerosing cholangitis. Social handicap was seen in 5.26% (n=2) subjects with UC and 28.57% (n=2) having UC with PSC. Urgency was 2.63% (n=1) and 42.85% (n=3) subjects with UC and UC with PSC respectively. Bowel movement during night was 0, 1, and 2 in 50% (n=19), 31.57% (n=12), and 13.15% (n=5) subjects respectively in subjects with UC and in 0, 28.57% (n=2), and 57.14% (n=4) subjects having UC with PSC respectively. Bowel movement during daytime was scored as 0, 1, and 2 in 28.94% (n=11), 50% (n=19), and 15.78% (n=6) subjects respectively with UC and in 28.57% (n=2), 0, and 71.42% (n=5) subjects respectively with UC and PSC (Table 2).
Concerning pouchitis, it was seen that significantly more subjects with UC and PSC had pouchitis compared to subjects with UC only. Pouchitis was seen earlier in subjects having UC with PSC. Failure due to pouchitis was seen in 12.5% (n=2) of subjects having UC with PSC. More than 4 episodes of pouchitis were seen in 12.90% (n=4) subjects with UC alone and 62.5% (n=10) subjects having UC with PSC. Subjects having pouchitis were 32.25% (n=10) having UC alone and 81.25% (n=13) having UC with PSC. 1st pouchitis episode within 1 year of surgery was seen in 29.03% (n=9) subjects having ulcerative colitis only and in 62.5% (n=10) subjects having UC with concurrent PSC as shown in Table 3. Proctitis did not show any significance in subjects with UC alone or UC with PSC.
On assessing the surgical complications, it was seen that no significant difference was seen in subjects treated with IPAA or IRA in both having Ulcerative colitis only or subjects having ulcerative colitis with Primary

sclerosing cholangitis. Concerning failure, it was seen that the subjects treated with IPAA, the subjects with UC with PSC and UC alone had 15% and 5% failure respectively which was statistically non-significant. However, in subjects treated with IRA, failure in subjects with UC alone and UC with PSC was 21% and 52% respectively. This was statistically significant.

DISCUSSION

The present clinical retrospective study was conducted to evaluate the outcomes of IPPA and its designs on long-term functioning, neoplasia frequency in IPAA subjects, and IRA and IPAA outcomes in subjects having ulcerative colitis with concurrent PSC. The study results showed that there was no high-grade dysplasia or carcinoma was seen in the study subjects. In acute inflammation, it was seen that Grade 2, 3, and 4 acute inflammation was seen in 20.96% (n=39) and 24.73% (n=46) subjects respectively by examiner 1 and 2, Grade 3 in 75.80% (n=141) and 51.07% (n=95) subjects respectively by examiner 1 and 2, and Grade 4 in 79.03% (n=147) and 59.13% (n=110) subjects respectively by examiner 1 and 2. For chronic inflammation, Grade 1, 2 and 3 was seen in 4.83% (n=9) subjects by examiner 2, 25.80% (n=48) and 23.11% (n=43), and 53.76% (n=100) and 73.11% (n=136) subjects respectively by examiner 1 and 2. Mucosal adaptation of Grade 1, 2, and 3 was seen in 25.80% (n=48), 5.91% (n=11), and 58.06% (n=108) subjects respectively by examiner 1. In ATZ area, Grade 1, 2, and 3 was seen in 3.76% (n=7), 18.81% (n=35), and 48.92% (n=91) subjects respectively. These results were consistent with the findings of Anderson CA et al[6] in 2011 and Fazio VW et al[7] in 2013 where similar histopathologic characteristics of mucosa and inflammation were seen in subjects having UC or UC with PSC.

With IPAA treatment, subjects with concurrent ulcerative colitis with Primary sclerosing cholangitis and with ulcerative colitis only, no difference was seen. However, the score of 8 or more was seen more in subjects with ulcerative colitis alone. In the IRA group, worse scores were seen in subjects with concurrent ulcerative colitis with Primary sclerosing cholangitis. Social handicap was seen in 5.26% (n=2) subjects with UC and 28.57% (n=2) having UC with PSC. Urgency was 2.63% (n=1) and 42.85% (n=3) subjects with UC and UC with PSC respectively. Bowel movement during night was 0, 1, and 2 in 50% (n=19), 31.57% (n=12), and 13.15% (n=5) subjects respectively in subjects with UC and in 0, 28.57% (n=2), and 57.14% (n=4) subjects having UC with PSC respectively. Bowel movement during daytime was scored as 0, 1, and 2 in 28.94% (n=11), 50% (n=19), and 15.78% (n=6) subjects respectively with UC and in 28.57% (n=2), 0, and 71.42% (n=5) subjects respectively with UC and PSC. These results were in agreement with the findings of Mizoguchi A et al[8] in 2008 and Larsen S et al[9] in 2010 where similar functional outcomes were seen following treatment of ulcerative colitis in their respective studies.

Concerning complications and failures, pouchitis was seen in significantly more subjects with UC and PSC had pouchitis compared to subjects with UC only. Pouchitis was seen earlier in subjects having UC with PSC. Failure due to pouchitis was seen in 12.5% (n=2) of subjects having UC with PSC. More than 4 episodes of pouchitis were seen in 12.90% (n=4) subjects with UC alone and 62.5% (n=10) subjects having UC with PSC. Subjects having pouchitis were 32.25% (n=10) having UC alone and 81.25% (n=13) having UC with PSC. 1st pouchitis episode within 1 year of surgery was seen in 29.03% (n=9) subjects having ulcerative colitis only and in 62.5% (n=10) subjects having UC with concurrent PSC. Proctitis did not show any significance in subjects with UC alone or UC with PSC. For failure, it was seen that the subjects treated with IPAA, the subjects with UC with PSC and UC alone had 15% and 5% failure respectively which was statistically non-significant. However, in subjects treated with IRA, failure in subjects with UC alone and UC with PSC was 21% and 52% respectively. This was statistically significant. These results were comparable to the results by the studies of Joyce MR et al in 2010 and Akbari RP et al in 2009 where comparable complications and failure rates were depicted by the authors in their respective studies.

CONCLUSION

Within its limitations, the present study concludes that the best long-term functional outcomes were seen in K-pouch with stapled anastomosing in subjects with ulcerative colitis with a very low incidence of neoplasia following treatment. High failure rates and compromised functional outcomes are seen in subjects having UC and PSC treated with IRA. However, IPAA showed comparable outcomes in subjects having UC only or UC with PSC. The present study had a few limitations including a small sample size, shorter monitoring period,

retrospective design, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

TABLES

Indefinite for Dysplasia (IFD)	Subgroups	Examiner 1 %(n)	Examiner 2 %(n)
The score for Acute Inflammation	Grade 0	0	0
	Grade 1	0	0
	Grade 2	20.96 (39)	24.73 (46)
	Grade 3	75.80 (141)	51.07 (95)
	Grade 4	79.03 (147)	59.13 (110)
	Grade 5	0	0
	Grade 6	0	0
The score forChronic Inflammation	Grade 1	0	4.83 (9)
	Grade 2	25.80 (48)	23.11 (43)
	Grade 3	53.76 (100)	73.11 (136)
Mucosal Adaptation	Grade 1	25.80 (48)	5.91 (11)
	Grade 2	5.91 (11)	23.11 (43)
	Grade 3	58.06 (108)	59.13 (110)
Chronic inflammation in ATZ	Grade 1	0	3.76 (7)
	Grade 2	16.12 (30)	18.81 (35)
	Grade 3	17.20 (32)	48.92 (91)

Table 1: IFD in pouch and grades of inflammation with chronic inflammation in ATZ in the study subjects

Parameter	Scores	Ulcerative colitis alone % (IRA n=38)	Ulcerative colitis with PSC % (IRA n=7)
Median score ≥8		7.89 (3)	28.57 (2) (NS)
Social Handicap	1	5.26 (2)	42.85 (3)
Urgency	1	2.63 (1)	42.85 (3)
Bowel movement during the night			
None	0	50 (19)	0 (NS)
1or less/week	1	31.57 (12)	28.57 (2) (NS)
2 or more/night	2	13.15 (5)	57.14 (4)
Bowel movement during daytime			
Less than/equal to 4	0	28.94 (11)	28.57 (2) (NS)
5	1	50 (19)	0 (NS)
More than/equal to 6	2	15.78 (6)	71.42 (5)

Table 2: Functional outcomes following IRA in the study subjects

Pouchitis Parameter	Ulcerative colitis alone % (IRA n=31)	Ulcerative colitis with PSC % (IRA n=16)
Failure owing to Pouchitis	0	12.5 (2)
1st episode within 1 year following treatment	29.03 (9)	62.5 (10)
Pouchitis time (years)	3.22 (1)	6.25 (1)
Pouchitis episodes	67.7 (21)	18.75 (3)
1-3 times	19.35 (6)	12.5 (2)

≥4 times	12.90 (4)	62.5 (10)
Subjects with pouchitis	32.25 (10)	81.25 (13)

Table 3: Pouchitis and associated clinicopathologic characteristics in the study subjects

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