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To cite this article: Steven Lee-Kong & Ravi Pokala Kiran (2016) Ongoing challenges and controversies in ulcerative colitis surgery, Expert Review of Gastroenterology & Hepatology, 10:2, 187-191, DOI: [10.1586/17474124.2016.1121811](https://doi.org/10.1586/17474124.2016.1121811)

To link to this article: <https://doi.org/10.1586/17474124.2016.1121811>



Published online: 16 Dec 2015.



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SPECIAL REPORT

## Ongoing challenges and controversies in ulcerative colitis surgery

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### ABSTRACT

For patients with ulcerative colitis requiring surgery, surgical options include a total proctocolectomy with an end ileostomy and ileal pouch-anal anastomosis or a continent reservoir, or instead, a subtotal colectomy with an ileorectal anastomosis. The ileal pouch-anal anastomosis is currently considered the gold standard procedure that is employed in the majority of patients. Despite strong data supporting the feasibility, durability and the maintenance of long term functional outcomes and quality of life, certain controversies pertaining to its relative role, method of creation and effects on related pelvic structures remain a matter of debate.

### ARTICLE HISTORY

Received 2 September 2015  
Revised 13 November 2015  
Accepted 16 November 2015  
Published online 17  
December 2015

### KEYWORDS

Ulcerative colitis; surgery;  
ileoanal pouch; ileorectal  
anastomosis; sexual  
function; fertility

### Introduction

Ulcerative colitis (UC) remains a significant medical and surgical problem, with an estimated prevalence of approximately 263 per 100,000 patients in the United States annually.[1] With direct costs estimated to be approximately \$4 billion per year,[2,3] this disease imparts a significant burden on the health care system and economy. While there have been significant advances in the medical management of UC over the past decade, restorative proctocolectomy with ileal pouch–anal anastomosis (IPAA) remains the treatment of choice for patients' disease that is refractory to maximal medical management, steroid-dependent disease, or who develop high-grade dysplasia or cancer.

Consensus recommendations for the escalation of medical therapy help guide the management of patients with UC, particularly those with mild to moderate disease activity.[4] As escalation of therapy from 5-aminosalicylic acid-based medications to topical or systemic corticosteroids, thiopurine, anti-tumor necrosis factor therapy, or methotrexate continues, patients are more strongly considered for, and encouraged to consider, definitive surgical management.

### Surgery for ulcerative colitis

#### *Ileal pouch–anal anastomosis versus ileorectal anastomosis*

Some debate exists as to optimum surgical treatment of patients with UC who are referred for definitive surgical management. The key concept of definitive surgical

treatment includes resection of the entire colon and rectum. In selected patients, a restorative procedure with IPAA is often considered. Patients considered unsuitable for, or unwilling to undergo, IPAA are counseled on end ileostomy or continent ileostomy creation. Prior to the widespread acceptance of IPAA in the 1980s, total colectomy with ileorectal anastomosis (IRA) was often employed.

Interest has resurged in the construction of IRA over IPAA. The advantages of IRA include avoidance (or deference) of pelvic dissection, less frequent bowel movements and theoretically improved functional results, less “complicated” surgery, and improved preservation of fertility. The disadvantages of IRA include the possibility of recurrent or persistent proctitis, fecal urgency related to ongoing proctitis, need for anti-inflammatory medications, and requirement for long-term surveillance and risk of future neoplasia in the retained rectum. On the contrary, total proctocolectomy (TPC) and IPAA removes nearly all remaining at-risk mucosa and offers long-term avoidance of permanent stoma creation. IPAA is, however, a complex operation requiring surgical expertise that may not always be readily available. It is associated with more frequent bowel movements, impaired continence in some patients, and risk of impaired sexual function.[5]

Functional outcomes between IPAA and IRA for UC have been compared. In a single-center study by Andersson et al, the incidence of major complications was similar between groups (12.4% vs 12.8% for IRA and IPAA, respectively). Overall complications, however, were significantly higher in the IPAA group (39.9%

versus 23.8%,  $p < 0.01$ ). Ten-year failure rates were similar between groups (24.1% versus 18.6%). At long-term follow-up, 76.9% of patients with IRA had proctitis and 34.1% of patients with IPAA had pouchitis. Long-term risks of developing cancer were also similar. The authors concluded that IRA can be considered in selected patients, and one can expect similar major complication rates. They recommend considering IRA as an interim procedure specifically in young patients as a way to delay pelvic dissection and help preserve fertility.[6] While avoiding pelvic dissection, potential injury to autonomic nerves and removal of the rectal reservoir, impaired continence after IRA still occurs. This is likely due to ongoing proctitis, causing urgency, frequency, and varying degrees of fecal soiling.

da Luz Moreira et al. also reported on the fate of the rectum in 86 patients who underwent IRA for UC or indeterminate colitis at the Cleveland Clinic Foundation over a 35-year period.[7] Overall 30-day complication rate was 8%. After a median follow-up of 11 years, only 38 patients (44%) had a functional IRA. Fifty-three percent of patients required proctectomy, with a median time of 10 years post-IRA creation. Twenty-four of these patients developed refractory proctitis, 15 developed dysplasia, and 7 developed rectal cancer. The cumulative probability (at 20 years) for having a functional IRA was 46%, the cumulative probability of developing dysplasia was 25%, and the cumulative probability of developing rectal cancer was 14%.

Fazio et al. reported on outcomes from the largest single-institution experience of IPAA. Long-term pouch failure was 5.3%. 3.2% of patients required pouch excision, 0.8% had pouch nonfunction, and 1.2% had redo pouch surgery. Quality of life (QOL) was considered good to excellent in 95% of patients.[8] While IRA can be considered in highly selected patients (and should be discussed with some patients preoperatively as a viable alternative), the excellent long-term functional results of IPAA when performed by experienced surgeons maintain its position as the gold-standard in the surgical management of patients with UC.

### Laparoscopic surgery for ulcerative colitis

Minimally invasive techniques have become more commonplace in the management of colorectal diseases. Numerous prospective, randomized controlled trials and subsequent meta-analyses have demonstrated the safety, efficacy, and benefits of laparoscopic surgery for colon and rectal cancer (COST, COLOR, CLASICC).

Minimally invasive proctocolectomy, particularly rectal dissection in the deep pelvis and division of the anorectal junction with an endoscopic stapler, can be

technically challenging and should be performed by surgeons trained and experienced in minimally invasive colorectal surgery. If difficult, a small lower abdominal incision can be made and division completed with a right-angled stapler.

Studies comparing open and laparoscopic proctocolectomy and IPAA for UC have similarly demonstrated short- and long-term benefits to a minimally invasive approach. Fichera et al. reported on 179 patients undergoing open or laparoscopic IPAA for UC. Patients who had a laparoscopic operation had a faster return of bowel function (first flatus and tolerance of a liquid diet) and less intra-operative blood loss. Hospital stay, narcotic requirement, and procedure length were similar between groups.[9] Post-operative complications were similar between groups (mortality, ileus, small bowel obstruction (SBO) prior to stoma closure, late SBO, anastomotic complications and pouch failure). There was less incisional hernia formation in the laparoscopic group (8.8% vs 0.0%,  $p = 0.011$ ). Overall, bowel function parameters were also similar between groups, as was QOL assessment. These data support the appropriateness of a minimally invasive approach to IPAA for patients with UC. Other studies have supported similar conclusions, including overall equivalent sexual function and improved short-term outcomes.[10–12]

### Fertility and sexual dysfunction

Infertility remains a significant problem for patients after IPAA, with rates of up to 50% in some series. Waljee et al. performed a meta-analysis of studies reporting infertility in women with UC. Infertility in women being medically treated for UC was 15%. For women post IPAA, this rose to 48%.[13]

The decrement in female sexual function after IPAA is likely multifactorial. Autonomic nerve neuropraxia or inadvertent transection of the hypogastric nerves may lead to decreased lubrication and dyspareunia. Post-operative pelvic adhesions may also contribute to dyspareunia and infertility. One study revealed that only one third of women had normal fallopian tubes after IPAA (42% had at least unilateral tube occlusion and 48% had tubes adherent to the pelvic floor).[14] Fecal soiling during intercourse has also been reported in up to 9% of women after IPAA,[14] contributing to decreased desire, arousal, and satisfaction.

Understanding the factors contributing to sexual dysfunction and infertility has allowed us to seek ways to ameliorate the effects of IPAA on them. Laparoscopic approaches have demonstrated a reduction in infertility when compared to open techniques.[15] Also described is a reduction in abdominal and pelvic adhesions after

laparoscopic IPAA.[16] Thus, laparoscopy may minimize the formation troublesome adhesions after restorative proctocolectomy for UC.

### Double-stapled versus hand-sewn anastomosis

Debates still exist as to the optimal method of performing an IPAA. Originally described by Parks and Nicholls in 1978,[17] the anal canal mucosa can be completely stripped prior to performing a hand-sewn pouch–anal anastomosis. Surgeons who routinely employ this technique propose that removal of all remnant distal rectal and anal canal mucosa leads to improved long-term functional outcomes and reduces the risk of persistent inflammation from retained mucosa. It is thought that disturbance of the anal transition zone (ATZ) brought about by mucosal stripping leads to a decrement in functional outcomes. In an attempt to preserve the ATZ, most surgeons employ a “double-stapled” technique for IPAA. During proctectomy, division of the most distal rectum is achieved with a linear stapler, 1–2 cm above the dentate line. A circular stapler is then utilized to perform the IPAA. With this technique, the ATZ is maintained.

Advocates of mucosal stripping and hand-sewn IPAA conjecture that removal of all rectal mucosa is important to prevent development of dysplasia and cancer that can develop in the ATZ. Actual reports of this phenomenon are rare, and this technique does not necessarily eliminate the risk of retained mucosa. In fact, retained mucosa can be hidden “underneath” a hand-sewn IPAA.

A prospective, randomized trial by Reilly et al demonstrated no difference in functional outcomes between a double-stapled and hand-sewn technique.[18] On long-term follow-up, patients undergoing a hand-sewn anastomosis have increased nocturnal seepage when compared to those undergoing a hand-sewn anastomosis with mucosectomy.[19] The risk of neoplasia in the retained anorectal cuff after a stapled IPAA is similar to that after a mucosectomy and hand-sewn anastomosis. Further, the stapled anastomosis allows the endoscopic surveillance of the mucosa at risk for neoplastic transformation. The double-stapled technique is also easier to perform and may result in less tension on the pouch after construction. Given the above factors, most surgeons performing IPAA do so using a double-stapled technique.

### Conclusion

Much has been learned about the surgical management of patients with chronic or fulminant UC since the initial

description of IPAA in 1978. While our understanding continues to evolve regarding the functional and long-term outcomes of surgical interventions, we must continue to strive to resolve the controversies surrounding variations in surgical technique and perioperative management.

### Biologics and surgery – emerging trends

With the approval of infliximab in 2005 came much excitement regarding the treatment of patients with UC. It was originally thought that improved medical management may lead to reduced need for proctocolectomy and improved QOL. Now with over 10 years of experience with the use of various biologic medications in the treatment of UC, we have a better understanding of its efficacy and effect on surgical treatment.

Various reports have suggested an increase in post-operative infectious complications in patients who have recently received infliximab.[20] Geltzeiler et al. reported on the trends of surgical treatment in patients with UC after the introduction of infliximab. Using the nationwide inpatient sample database, they report a 170% increase in UC-related hospital admissions over a 21 year period. There was also a 44% increase in use of total abdominal colectomy during this same time period, with a corresponding decrease in initial TPC. Pouch construction was more often delayed during the study period. An inflexion point can be clearly demonstrated around the time of the approval of infliximab in 2005.[21]

There are numerous reports for and against the notion of increased infectious complications in patients undergoing surgical treatment for UC who have been exposed to biologic medications. A recent meta-analysis by Selvaggi et al. suggest that in patients undergoing primary IPAA, exposure to biologic medications increased the risk of short-term pouch-related infectious complications (odds ratio 4.57). In patients undergoing loop ileostomy closure after IPAA construction, a similar increase in pouch-related infectious complications was also found.[22]

Interestingly, the rate of colectomy has not appeared to decrease since the introduction of biologic treatments.[23] While their use certainly has helped change the management of patients with acute and chronic UC, thought must be given to the timing of surgical intervention in patients for whom biologic medications are contemplated.

### Surgical treatment in children

Unfortunately, UC can manifest in both children and adolescents. If possible, aggressive surgical treatment

can be delayed until the child is older and more emotionally mature. However, in the case of refractory disease or other surgical emergencies (perforation, hemorrhage, growth retardation), colectomy can safely be performed in the pediatric population.

A single-center retrospective review of open versus laparoscopic TPC with ileoanal pouch reconstruction in children found similar complication rates between both groups and less post-operative SBO in patients from the laparoscopic group.[24] Postoperative QOL in children after IPAA can approach that of normal healthy controls.[25]

### Expert commentary

For patients with UC who have failure of medical treatment develop complications of the disease or complications of treatment, or who have persistently poor QOL despite medical management of the disease, TPC allows the elimination of disease, freedom from steroids, and immunosuppression and the prevention of neoplastic change. The ileoanal pouch allows the avoidance of a permanent ostomy while maintaining function and QOL in the majority of patients. For patients with poor sphincter tone, those who wish not to eliminate transanally and those with low rectal cancer complicating colitis, a TPC with end ileostomy is an option. Such patients who wish to avoid an external appliance may choose to have a continent ileostomy. The IRA may be selectively employed in patients with good sphincter function and rectal compliance where there is a need to reduce the risks of an operative insult, which can be achieved by avoiding pelvic dissection. The ileoanal pouch is the procedure of choice for the majority of patients and can be performed laparoscopically with comparable short- and long-term pouch-related outcomes when compared to open surgery, with the added recovery

advantages of the minimally invasive approach. The IPAA is associated with reduced fertility and has the attendant potential negative impact of any pelvic surgery on sexual function. However, there is often improvement in QOL by elimination of disease and improvement in overall health. This likely has an opposing effect in these areas and hence counterbalances any negative results. The stapled anastomosis is the preferable option in the majority of patients.

### Five-year view

With the increasing availability of several biologic medications for colitis, fewer patients may be offered surgery. The potential risk of this dynamic change in management is that patients who are sicker or have developed complications of the disease may only be offered surgery. This may result in patients undergoing IPAA having an increased risk of complications, which is known to be associated with a greater risk for pouch failure or poor pouch function over the short and long term. A judicious approach where the gastroenterologist, surgeon, and patient work as a team to identify patients who will benefit from medical treatment versus those who should promptly be taken for surgery rather than be placed on increasing doses and numbers of potentially harmful and likely unsuccessful medications is hence essential.

### Financial & competing interests disclosure

*The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.*

#### Key issues

- A proportion of patients with ulcerative colitis will require surgery.
- IPAA is the gold standard procedure.
- A stapled IPAA is currently the preferred technique.
- The ileorectal anastomosis has specific indications in selected circumstances.
- Some controversies, particularly relating to the effect of the IPAA or the dissection within the pelvis on sexual function and fertility continue to remain.

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