# Peer Review File

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**REVIEWER A**

Line 76 "minority": Specify proportion with ref.
The text has been changed to show <5% rate. Pappou & Kiran, Clinics in colon & rectal surgery, 2016

Line 79 "increase" Specify proportion with ref.
The text was changed to reflect anecdotal evidence.

Line 88 We use 2x 100 mm linear staple device and aim for 15-20 cm pouch. (As described by Feza Remzi)
Yes, thank you. That is how a J pouch is created, this portion of the text is describing the handsewn S pouch. The J pouch is described later in the text.

Line 91 ref. + rationale for circular stapleing (ref. Lovegrove)
The text was changed to show it preserved the anal transitional zone and is technically easier to perform.

Line 95 add ref.
It has been added.

Line 176 add "conventional" before "laparoscopic" (robotic is also laparoscopic)
It has been changed.

Line 189 ref. to problems with MIS pouches
It has been changed.

Line 209 You state "studies" in plurals but only give one ref.
It has been changed.

Line 214 Ref to IRA in cancer patients. We don't recommend IRA to UC patients CRC...
It has been changed.

Line 234 Define the difference between "total" and "sub-total" in my understanding the 2 terms generally refers to the same operation.
It has been changed to solely be total colectomy as this is more direct to the reader.
The individual surgeon can decide on a total colectomy with the rectum stump in the pelvis or, the *subtotal colectomy- leaving the rectosigmoid and preserving the superior rectal artery so the sigmoid can be tacked to the subcutaneous tissue/superficial to the fascia.*

Line 287 Separate the headlines "Pouch function" " pouch failure" and "redo surgery"

It has been changed.

Line 323 named "after" Nils G Kock
It has been changed.

Define "pouch failure" That term most often refers to a state when the pouch is removed or permanently deviated with a stoma. In such case one does not have "signs and symptoms" of pouch failure. I think I understand what you mean but I think you should consider rephrasing.
It has been changed to define “pouch failure” by its symptoms earlier in the paragraph. Many patients have pouch failure and have not been operated on yet, so I wouldn’t define failure by those who have had their surgery.

Try to avoid mixing abbreviations and full names for the same entity. i.e. you alternate between both "CD" and "Crohn's" referring to the same condition.
It has been changed.

Line 355 I find the word "necessitate" peculiar in that sentence.
Thank you. It has been changed.

Line 356 "most often" not "most oftenly"
It has been changed.

Line 360 "Late complications still... I find that sentence a little hard to understand.
It has been changed.

Line 364 What does "outlet defecation" mean.
Thank you. It has been changed.

Line 378 ref. to "pouch cancer can be very aggressive and look over the following sentence
It has been changed.

Line 386. In my experience anesthesia is really needed for pouch endoscopy.
Thank you.  We are referring to an exam under anesthesia & pouchoscopy.

Line 383 "never felt right" is not very scientific
Thank you. That is what the suffering patient’s say and therefore it is in quotes

Line 392 You describe a number of methods to assess pouch problems but not when to use which it may be understood as all modalities is indicated in every case which does not sound reasonable.
Thank you. It has been changed so that it shows not every patient needs every test, however EUA, pouchoscopy, MRI, GGE and CT are all involved in the work up and are done almost all the time.

For instance, MRI is not at all always necessary.
MRI will show presacral edema/abscess and is always part of the work up for pouch failure.

Line 395 "narrow" what?
It has been changed to narrowing/stricture.

Line 400 describe "afferent limb syndrome"
It was defined under “redo/revisional pouch surgery” as the proximal bowel stuck between the sacrum and pouch causing a bowel obstruction.

Line 451 was the proportion of laparoscopic redo pouches in the different time-periods stated? Was there any specific analysis between laparoscopic and open redo pouches? Did the authors argue any explanation for the decreasing success rate?
It has been changed that other correlations that may be present as well.

**REVIEWER B**
It was a pleasure and honor for me to read this beautiful review paper. I think the work is worthy
of publication. Nevertheless, I have some comment that I would like to ask you to consider.
1. Abstract : largely correct, but in my opinion, the following additions/changes are necessary:

**Comment 1**: There is a lack of reference to conversion to a continent ileostomy in addition to redo surgery for pouch failure. This is mentioned in the main text. However, the reference also belongs in the abstract!
Thank you. The need for permanent ostomy was mentioned in the abstract. Further clarification was added for a continent ileostomy.

**Comment 2**: It does not seem to be true that after redo surgery the results are comparable to those of index operation. On the contrary, many studies show that the results of redo-operation are worse than those of primary IPAA.
Thank you, this was changed to reflect subjective quality of life, rather than objective functional outcomes.

2. introduction: largely accurate, but the following clarifications are necessary in my opinion:

**Comment 3**: Historically, after the failure of direct anastomosis of the ileum with the anus (Ravitch, 1946), the goal was no longer to restore intestinal continuity but to provide control of fecal evacuation.

To do this, it was first necessary to prove that a reservoir could be constructed from the ileum, which came to be used successfully in continent ileostomy (Nils Kock).

It was only after ileum reservoir construction was established that procedures to restore bowel continuity using IPAA could take place in the UK, USA and Japan.

IPAA was thus the successor procedure to continent ileostomy (CI).
Thank you, addressing all comments regarding the introduction. The article has been changed. A remarkable evolution in care and quite a jump from urine to bowel effluent that changed management forever.

3. main text: Largely accurate, but in my opinion the following additions/changes are necessary:

Comment 7: The statements of the chapter "Pouch stages" mainly concern high risk patients. However, it should be added that in the elective situation in low risk patients, one stage operations do not have higher complications, but functionally perform better than staged procedures.
Thank you, the article has been changed

**Comment 8:** In this respect, single stage IPAA is by no means possible only in rare circumstances, but is standard in some institutions. Nonetheless, this standard is often abandoned because of fears of other risks associated with minimally invasive procedures.
Thank you. The article has been changed.

**Comment 9:** MIS IPAA should be considered more critically because of the "risk" of making constructive compromises (length of cuff or residual distal rectal margin and saving of sphincters) with these procedures compared to the partially open approach.
Thank you.

**Comment 10**: Redo IPAA is overrated from the point of view of function restoration in my opinion. Although the references to literature data are correct, in these works one must read critically "between the lines".
Thank you. The outcomes definitely vary from institution to institution.

**Comment 11**: In the same sense, when IPAA fails, conversion to continent ileostomy is mentioned but understated in importance, and current literature on this is suppressed. In addition, the term K- pouch is reserved for the connection of the double folded pouch design of a Kock pouch to the anus!
Thank you. I believe the S-, J-, W-, I- pouches are the pelvic pouch with the K pouch as the sole abdominal pouch.

**REVIEWER C**
Cohen et al. is an overview of restorative pouch surgery following proctocolectomy for colonic IBD, experiences and future direction. They describe the sequential history different pouch types, their construction, the stages of the procedures, the outcomes for ulcerative colitis (UC) and colonic Crohn's disease (CD), the types of operations offered, and the work-up and

treatment for patients who may be suffering from pouch complications and failure. The paper is nicely written and well summarized with interesting history of pouch surgery development. I have some COMMENT/SUGGESTION which I believe will make the paper comprehensive.

Although it is correct that total proctocolectomy with or without IPAA is the standard recommendation to remove all tissue at risk for dysplasia/adenocarcinoma. Authors completely omitted surgery for “indeterminate colitis”. The inability to distinguish between colonic Crohn’s disease namely Crohn’s colitis (CC) and ulcerative colitis (UC) leads to the diagnosis of indeterminate colitis (IC) [PMID: 35629984 & 28817680]. Here, dispersal favors UC, but focal transmural inflammation or inflammation in the ileum is anticipated in blackwash ileitis and no fistulation. IC is seen in about 15% of patients suffering from colonic IBD when features attributable to both UC and CD are inconclusive. Dysplasia on a background of IC warrants surgical resection based on the same principles of management for either CC- or UC-associated dysplasia. The specific surgical approach is based on whether UC or CC is more likely. In such a circumstance, human alpha defensin 5 (DEFA5) testing which is under development, is found to be an accurate candidate biomarker to assist in delineating between IC into authentic CC and UC in the IC patient cohort [PMID: 35629984 & 33690604]. When the disease is more severe, completing the total abdominal colectomy (TAC) first to assist in making a pathological diagnosis may be effective. This can be followed by a proctectomy (in the case of CC) or IPAA (in the case of UC). In cases where UC is suggested, and in a highly select group of patients with a CC-like phenotype without ileal or anal disease, restorative proctocolectomy and ileal pouch-anal anastomosis (RPC-IPAA) may be considered. Overall, treatment is often based on the likely phenotype and patients should be advised that if ileal-pouch CD manifests itself after an RPC-IPAA, conversion to an end ileostomy is likely [PMID: 30059346]. Overall, excision of the entire colon and rectum with or without mucosectomy of the residual anorectal stump is intended to achieve complete removal of all disease-prone mucosa, while maintaining transanal fecal continence. The procedure, however, inadvertently leaves small mucosal residual islands. Indisputably, ileoanal pouch mucosa and the anorectal mucosa below the ileo-anal anastomosis is therefore at potential risk of developing subsequent cancer in the pouch, at the ileal pouch/anal anastomosis, and at the columnar cuff below anastomosis above anal transitional zone. A substantial number of patients, after surgical treatment, even with mucosectomy, will not always be prevented from developing cancer in the pouch and/or from in the remnant anal transition zone (ATZ). Pouch-related carcinomas have recently been reported with increasing frequency since the first report in 1984 [PMID: 21311893].

Thank you for the details here. We have added in a section on pouches for indeterminate colitis