

# Current Perspectives on Indications for Ileal Pouch-Anal Anastomosis in Older Patients

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**Abstract:** The population of older patients with inflammatory bowel disease (IBD) is expected to continue to increase in the coming decades, which necessitates and improved understanding of the critical issues faced by patients in this population. Although restorative proctocolectomy with IPAA remains the surgical procedure of choice for the majority of patients with medically refractory ulcerative colitis (UC) and UC-related dysplasia, the evidence surrounding surgery for older patients UC remains sparse. In particular, comparisons of outcomes among older and younger patients undergoing IPAA and comparisons between older patients undergoing IPAA and those undergoing proctocolectomy with end ileostomy remain an understudied and important issue, as evidence in this area will be used to guide patient-centered surgical choices among older patients who require colectomy for UC. In this narrative review, we review the available literature regarding IPAA for older patients, as well as the pre-, peri-, and postoperative factors that may influence outcomes in this population.

**Keywords:** pouchitis, surgery, older age, ulcerative colitis, J-pouch

## Introduction and Epidemiology

Proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the preferred choice of restorative surgery among patients who require colectomy for medically refractory ulcerative colitis (UC) or UC-related dysplasia. As the prevalence of patients with inflammatory bowel disease (IBD) among elderly individuals increase,<sup>1</sup> it is natural that providers will increasingly face complex and multidisciplinary decision-making regarding the need for and timing of restorative proctocolectomy with IPAA in older adults. However, data among older patients undergoing IPAA is limited. In this narrative review, we will discuss the relevant available literature with respect to IPAA among older individuals, with a particular focus on epidemiology, pre-operative and intra-operative planning, and post-operative outcomes among older patients with IBD.

Up to 15% of patients diagnosed with IBD are over 65 years in age, which is generally considered older than the traditional patient with IBD.<sup>2</sup> Additionally, as treatments for IBD improve and the general population life expectancy increases, the proportion of older patients with IBD is expected to increase in the coming years.<sup>1</sup> Even though restorative proctocolectomy with IPAA remains the surgical procedure of choice for most patients with UC, the evidence surrounding surgery for older patients with severe UC remains an understudied and important issue as most studies have been small in size with limited generalizability. In a systematic review of over 5600 publications, a paucity of studies evaluated rates of colectomy for UC in older patients as well as rates of surgery for all older patients with IBD.<sup>1</sup> A multicenter study in Greece showed patients above the age of 60 with UC were less likely to undergo any surgery for UC compared to younger patients (5.9% vs 18.2%).<sup>3</sup> Another small study showed low rates of total colectomy (less than 2%) in the older population but did not comment specifically on the rate of IPAA.<sup>4</sup> Studies looking at surgery for colorectal cancer found patients with IPAA had a mean age of 44 compared to 54 in those with a permanent ileostomy.<sup>5</sup>

A surgeon's preference to reserve IPAA for younger patients may be a result of the extensive pelvic dissection and concern for more postoperative complications in older patients compared to younger, healthier patients. However, several recent publications have demonstrated favorable post-operative outcomes among surgery when preoperative and intra-operative factors are considered.<sup>6,7</sup> Consideration of the patient's comorbidities and goals can allow the provider to create an individualized approach and select among multiple surgical options for the best long-term outcomes.

## Surgical Options

For older patients (defined as age 60 or older)<sup>8,9</sup> with severe or medically refractory UC, several surgical options exist: proctocolectomy with IPAA, total colectomy with end ileostomy, or ileorectal anastomosis. Currently, none of these options are definitively restricted by age. In many cases, an IPAA is the preferred restorative surgical procedure for patients undergoing colectomy for UC in large part due to reported significant improvements in quality of life after IPAA<sup>10,11</sup> (Table 1). In many cases, a major objective of IPAA surgery is to provide a relief from the burden of underlying disease while also maintaining continence.<sup>12</sup> However, it should be noted that there is a paucity of literature demonstrating the superiority of IPAA over total proctocolectomy with end ileostomy, with one systematic review demonstrating equivalence.<sup>13</sup> IPAA surgery also has short- and long-term risks of adverse events that should be considered including immediate postoperative complications such as leaks, hemorrhage, and pelvic sepsis,<sup>12</sup> as well as long-term complications such as pouchitis and other chronic inflammatory conditions of the pouch.<sup>11,12</sup> Given these considerations, shared decision-making is critical for any patient considering surgical options for UC.

Total colectomy with ileorectal anastomosis (IRA) is a rectal sparing surgery that involves removal of the diseased colon with re-anastomosis to the rectum. IRA surgery does not involve an extensive pelvic dissection, thus the risk of sexual dysfunction and incontinence is lower.<sup>14</sup> Potential benefits of IRA include a perceived decreased difficulty or complexity of surgery compared to IPAA, lower complication rates and a similar long-term functional outcome in selected patients.<sup>14</sup> However, patient selection is important as those with extensive rectal disease should be carefully considered for IPAA over IRA given the risk of rectal dysplasia over time, with studies demonstrating dysplasia rates increasing from 9% at 10 years to 25% at 20 years in IRA.<sup>14,15</sup> Additionally, elderly patients without good rectal compliance or adequate anal sphincter tone may be poor surgical candidates.<sup>14</sup> In evaluations not restricted or analyzed by age at the time of surgery, morbidity and mortality after IRA were found to be as high as 28%<sup>16</sup> and 4.2%,<sup>17</sup> respectively.

On average, patients undergoing IRA record 6 bowel movements per day, minimal nighttime seepage, and 1 nocturnal bowel movement.<sup>15</sup> Despite these favorable immediate outcomes, rates of cumulative failure have been reported at 10.1% and 24.1% at 5 and 10 years, with many needing proctectomy with IPAA or continent ileostomy.<sup>18</sup> These data should be interpreted based on each unique clinical scenario; it may be reasonable for an older patient with many comorbidities and shorter life expectancy to undertake these risks compared to a younger patient. However, in the current practice paradigm, IRA remains a choice for a very selected patient population.

**Table 1** Advantages and Disadvantages of Surgical Approaches for Medically Refractory Ulcerative Colitis

	Ileal Pouch-Anal Anastomosis	Ileorectal Anastomosis	End Ileostomy
<b>Advantages</b>	Restorative surgery Low rate of incontinence Low rate of rectal cancer Favorable quality of life	Restorative surgery Lower rates of sexual dysfunction Lower rates of incontinence Favorable functional outcomes	No risk for rectal cancer if proctectomy is performed
<b>Disadvantages</b>	Motility and pelvic floor issues may affect pouch function Inflammatory conditions of the pouch are common	Higher rates of dysplasia and/or rectal cancer Increased risk for recurrent disease and need for maintenance therapy	Non-restorative surgery Decreased quality of life

## Pre-Operative Considerations in Older vs Younger Patients

Patient comorbidities, frailty, and sphincter function are all integral parts of the surgery planning process and can help guide functional assessments to help risk stratify for post-operative adverse outcomes. The American College of Surgeons recommends the use of the National Surgical Quality Improvement Program (NSQIP) risk calculator to estimate risk of adverse outcomes after surgery.<sup>19,20</sup> Important preoperative factors to assess within the calculator include age, functional status, steroid use, disseminated cancer, previous cardiac event, chronic obstructive pulmonary disease (COPD), dialysis and many more.<sup>20</sup> These factors help predict the presence of nonsurgical complications including morbidity, mortality, pneumonia, and cardiac events and should be evaluated in conjunction with data evaluating post-surgical outcomes.<sup>2,20</sup> However, there may be existing limitations to using this generalized calculator in the setting of IBD-related surgeries, particularly IPAA. The American College of Surgeons NSQIP-IBD Collaborative is a disease-specific collaborative focusing on variables specific to IBD-related surgery and outcomes, including IPAA.<sup>21</sup> This may have significant advantages for risk stratification and future research efforts.

Frailty is an emerging factor used to help assess risk of postoperative complications<sup>7</sup> and describes a state of reduced physiologic reserve and includes cognition, functionality, nutrition and comorbidities.<sup>22</sup> Many of the factors involved in determining frailty are similar to those described in the NSQIP risk calculator.<sup>23</sup> One study by Telemi et al showed that higher modified frailty indices correlated with increased rates of morbidity and cardiopulmonary complications.<sup>23</sup>

Similarly, pre-operative sarcopenia is an important factor that may help providers determine risk of non-operative complications. Sarcopenia describes loss of skeletal muscle mass over time and is higher in those with chronic medical conditions and malnourishment such as IBD patients.<sup>24</sup> It could be a surrogate for physiologic reserve; sarcopenia is strongly associated with longer and more difficult post-operative recovery.<sup>24</sup> Some studies have measured sarcopenia through visceral adiposity on abdominal Computed Tomography (CT) imaging and shown a direct correlation between lower visceral adiposity and increased rates of the need for rescue therapy in hospitalized IBD patients.<sup>25</sup> In a retrospective study of 69 patients, sarcopenia was associated with an independent risk factor for surgical site infection after restorative proctocolectomy with IPAA.<sup>26</sup> Similarly, among patients undergoing surgery for colorectal cancer, sarcopenia has been associated with an increased risk for complications such as non-surgical site infections and longer hospital stays.<sup>27</sup> However, standardized definitions and measures of both frailty and sarcopenia in a younger population of adults, such as patients with IBD, are not yet standardized. The combination of frailty, sarcopenia and the NSQIP risk calculators have the potential to serve as valuable tools to determine post-operative risk for non-operative complications.

Sphincter tone and pelvic floor health is another important factor that should be addressed pre-operatively. Increasing age has traditionally been associated with an increased risk for incontinence.<sup>28</sup> Studies using anorectal manometry both pre and post IPAA have demonstrated that patients who experience incontinence after IPAA are more likely to have had incontinence prior to IPAA.<sup>29</sup> A caveat for such an approach would be that assessment of sphincter function in a patient with medically refractory UC is not predictive of the sphincter function in the setting of a pouch with no significant cuff inflammation. Given these potential differences in incontinence and underlying sphincter function, some authors have argued that it is important to assess sphincter function prior to consideration of an IPAA, with a subsequent frank discussion of post-operative expectations particularly among elderly patients.<sup>28</sup> The best method of this assessment is not well defined however. Older literature suggests that although a significant decrease in mean resting pressure may be noted on anorectal manometry in some patients after the initial IPAA creation, this was not associated with worse clinical outcomes after ileostomy takedown. Additionally, there was no correlation between preoperative mean resting pressure and postoperative incontinence score.<sup>30</sup> At a minimum, a digital rectal examination should be performed for evaluation of sphincter tone and dysfunction in lieu of using chronologic age alone as a barrier to determine eligibility for IPAA.

## Intra-Operative Considerations in Older vs Younger Patients

In the current era, IPAA is typically performed in a staged approach, with delayed creation of the pouch being preferred.<sup>11</sup> In a multi-staged approach to IPAA, two forms of ostomy may be used. In a traditional 2-stage IPAA, a total proctocolectomy is performed with a loop ileostomy followed by an ostomy takedown. In a 3-stage approach, a total abdominal colectomy is performed with an end ileostomy, followed by proctectomy and IPAA with a diverting loop ileostomy (second stage), and

ultimately an ostomy takedown. Patients who develop high output in their diverting loop ileostomy (approximately 14% of patients) may require early closure of their ostomy, which increases their risk of morbidity and mortality.<sup>31</sup> Older patients with high output stomas are at greater risk for electrolyte imbalances, dehydration and readmission<sup>32</sup> and elderly patients with underlying sarcopenia or frailty may have even higher susceptibility to these issues.

In an evaluation of prospective data collected through the American College of Surgeons NSQIP, delayed pouch creation was associated with a decreased likelihood of unplanned reoperations and major and minor adverse events.<sup>33</sup> Importantly, this data should be taken in consideration of the need for an additional surgery, which may independently offset these adverse events outlined above in the older patient. Additionally, it may be reasonable to pursue IRA in the right patient to preserve continence and avoid the complicated pelvic dissection in IPAA if the risks of dysplasia are explained and understood, especially in those with a life expectancy of less than 10 years. Additionally, total proctocolectomy with end ileostomy may be considered in this population. For those who choose IPAA, data among rates of postoperative complications comparing one- versus two- or three-stage approaches to IPAA in the older population is limited and therefore should be an individualized decision among providers and patients.

## Post Operative Considerations in Older vs Younger Patients

### Immediate Outcomes

Early complications (within 30 days of surgery)<sup>34</sup> most commonly consist of pelvic sepsis, portal vein thrombosis, hemorrhage, pouch ischemia and anastomotic leak.<sup>12</sup> Late complications (>30 days postoperatively)<sup>34</sup> include but are not limited to chronic pelvic sepsis, pouch fistula, pouch dysfunction, pouchitis, small bowel obstruction, malignancy and pouch failure.<sup>12</sup> Pouchitis is the most common complication after IPAA, affecting 40% of patients within the first year of surgery<sup>35</sup> and more than 80% of patients within their lifetime.<sup>36,37</sup> An additional concern is that the incidence of pouchitis appears to be increasing, as evidenced by a recent evaluation of a population-based prospective cohort study from Denmark.<sup>38</sup>

In a meta-analysis studying postoperative complications among elderly patients undergoing IPAA, increasing age at the time of surgery was not associated with an increase in short- or long-term morbidity and mortality.<sup>39</sup> Immediate outcomes were assessed from 13 studies and found that the rate of surgical site infections, pelvic sepsis and ileus requiring nasogastric tube placement were 8.2%, 9.9% and 18.4%, respectively.<sup>39</sup> Around 8% required reoperation for SBO and 16.3% had an unplanned hospital readmission within 30 days.<sup>39</sup> Further analysis comparing those age 50–65 compared to those over 65 showed no significant difference in rates of SBO, anastomotic leaks, reoperation and readmission among these age groups.<sup>39</sup> Another retrospective study pooling the VA national database of elderly patients with UC found no significant difference in surgical morbidity or 30-day mortality comparing patients who underwent IPAA vs ileo-rectal anastomosis.<sup>40</sup> In a more recent analysis of 601 patients over 50 years of age undergoing IPAA for UC, numerically greater rates of pouchitis were seen in patients 70 and older compared to patients age 60–69 and 50–59 at the time of surgery.<sup>41</sup>

### Natural History

The majority of patients undergoing IPAA experience long-term success, with an estimated pouch failure rate of 6% and 9% at 5–10 years and more than 10 years follow-up, respectively.<sup>42</sup> However, the data on surgery in older patients is lacking as most existing literature consists of evaluations of patients under 45 years without significant co-morbidities or functional limitations who are otherwise healthy and fit for surgery.<sup>43</sup> A meta-analysis found no significant difference in long-term outcomes including incontinence, anastomotic leak, pouchitis, SBO, and chronic fistula/sinus tract development when comparing older and younger patients.<sup>39</sup>

In addition to the risk of acute pouchitis, chronic inflammatory conditions of the pouch place an additional burden on patients. Approximately 17% of patients will develop chronic pouchitis<sup>44</sup> with an additional 10% of patients developing Crohn's-like disease of the pouch despite a pre-operative diagnosis of UC.<sup>45</sup> Although the data are heterogenous, there are some indications that older patients undergoing IPAA may be at risk for chronic inflammatory conditions of the pouch including chronic antibiotic dependent pouchitis (CADP).<sup>46</sup> This is of particular concern given that chronic inflammation is thought to be a potential risk factor for the development of pouch dysplasia<sup>47</sup> and pouch failure.<sup>48</sup>

In more granular comparisons of functional outcomes and patient satisfaction, IPAA appears to be very well tolerated among older patients. One meta-analysis found that patients had an average of 6 daily bowel movements and 1.6 nocturnal bowel movements,<sup>39</sup> both of which are consistent with accepted values postoperatively. In additional assessments, 72% of patients above 60 years with IPAA could differentiate flatus from feces.<sup>39</sup> Another review pooled results from four studies and showed a similar number of daily bowel movements in patients 65 years of age compared to those 45 years old.<sup>1</sup> Other studies demonstrated good quality of life scores in individuals up to 70 years and more than 96% of patients over 65 years said they would recommend the surgery to others after 3 years.<sup>49</sup> Several prior studies have indicated that the average rate of incontinence in patients with IPAA may increase over time after IPAA; however, there may be confounding variables contributing to these findings including increasing age, neuropathy and pharmacologic therapies.<sup>39,50</sup> The assessment of both functional outcomes and specifically patient-reported outcomes among older patients undergoing IPAA is critical, as evidenced by the fact that defecation urge and incomplete evacuation are among the most important factors older patients use to determine whether the surgery was successful.<sup>51</sup>

Although pouch failure rates among elderly patients were similar to the general population, prior studies have shown that pouch failure increases with increasing time, indicating that the time from initial IPAA surgery may be a more important prognostic factor for pouch failure compared to age alone.<sup>28,52</sup> The most common causes of pouch failure include pelvic sepsis and anastomotic leak,<sup>39,41</sup> however the rates of these complications do not seem to differ when comparing age at time of surgery.<sup>39</sup> Rates of dysplasia and/or any neoplasia including pouch lymphoma after IPAA remain low, with estimates generated in a large single center study in the US around 5% at 25 years.<sup>53</sup> Patients undergoing proctocolectomy with IPAA for colonic dysplasia or cancer and individuals with chronic pouch inflammation appear to be at the highest risk for dysplasia complications, with annual pouchoscopy suggested in these patients.<sup>54</sup> Importantly, the impact of aging on pouch and rectal cuff neoplasia is unknown, and thus the evidence to support decisions regarding stopping surveillance pouchoscopy is lacking (Table 2).

## Motility-Related Disorders

Pelvic floor dysfunction and other motility disorders are a feared complication after IPAA in older patients given the extensive pelvic dissection performed in the surgery,<sup>55</sup> however literature surrounding this issue is limited. Moreover, some weakening in pelvic floor and anal sphincter muscles are expected with age, which may predispose patients undergoing IPAA to motility disorders.<sup>55</sup> The mechanism for this is thought to be from anal sphincter atrophy and shortening, and decreased sensation that occurs with age.<sup>56</sup> Furthermore, older patients commonly experience some degree of skeletal muscle loss, which also increase their risk of pelvic floor dyssynergia.<sup>56</sup> In patients undergoing IPAA, rates of incontinence may be even higher due to the association of decreased anal sphincter pressures after pouch creation and impaired relaxation during defecation.<sup>56,57</sup> However, this issue is common, and many patients find some relief from biofeedback therapy, an approach that focuses on improving pelvic and anal muscle relaxation during defecation.<sup>58</sup> A retrospective study by Quinn showed that biofeedback therapy provided improvement in symptoms in 91% of IPAA patients, but this study did not focus on the older patient population.<sup>58</sup> Overall, functional outcomes remain a high priority for elderly patients following IPAA, and surgical techniques should be optimized to preserve sphincter function as much as possible.

**Table 2** Current Knowledge Regarding Ileal Pouch-Anal Anastomosis Surgery in Older Patients and Opportunities for Future Research

<b>What is known</b>	Restorative surgery including IPAA is associated with improved quality of life Risks of short-term morbidity and mortality appear similar between older patients and younger patients undergoing IPAA Rates of pouch failure are similar to younger patients undergoing IPAA Underlying motility disorders may impact pouch function and outcomes
<b>What is unknown/future research questions</b>	How long should surveillance pouchoscopies be performed in older patients with increased risk for colorectal cancer (positive family history or previous colorectal Ca)? What is the impact of aging on neoplasia rates after IPAA? How do frailty and sarcopenia impact short and long-term outcomes after IPAA surgery? What patient preferences drive decisions for end ileostomy versus restorative surgery (IPAA)?

## Conclusion

IPAA has been shown to be safe and well tolerated among elderly patients with IBD. Despite the limitations of a narrative review, we identified no major differences in the literature in both short- and long-term outcomes among patients undergoing IPAA over 60 years compared to younger individuals. Additionally, quality of life indices among this patient population indicate favorable outcomes compared to those receiving an end ileostomy. It is important to note that two patients of the same chronologic age can be significantly different surgical candidates when considering both their comorbidities and functional status, and thus pre-operative screening and individualized counseling regarding all surgical options is critical. Overall, the decisions regarding pursuit of an IPAA should not be based upon age alone but rather a holistic picture taking into consideration the patient's wishes, comorbidities, and preoperative functional status as individualized patient selection likely offers the best opportunity for optimized postoperative outcomes.

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