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TOPIC HIGHLIGHT

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Surgical treatment of ulcerative colitis: Ileorectal *vs* ileal pouch-anal anastomosis

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Core tip: Ileal pouch-anal anastomosis (IPAA) is the most commonly performed procedure for treatment of UC patients refractory to medical therapy. However, IPAA carries on its own risks. Recently, some authors have proposed ileorectal anastomosis (IRA) as a valid surgical alternative to IPAA. IRA is an easier operation than IPAA associated with low complication rates and comparable long-term functional results. This manuscript reviews the pros and cons of both procedures and compares results.

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Abstract

Total proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the current gold standard in the surgical treatment of ulcerative colitis (UC) refractory to medical management. A procedure of significant magnitude carries its own risks including anastomotic failure, pelvic sepsis and a low rate of neoplastic degeneration overtime. Recent studies have shown that total colectomy with ileorectal anastomosis (IRA) has been associated with good long-term functional results in a selected group of UC patients amenable to undergo a strict surveillance for the relatively high risk of cancer in the rectum. This manuscript will review and compare the most recent literature on IRA and IPAA as it pertains to postoperative morbidity and mortality, failure rates, functional outcomes and cancer risk.

INTRODUCTION

The main goals of surgical treatment for ulcerative colitis (UC) are not only to alleviate symptoms and minimize cancer risk but also to obtain good functional outcomes and improve quality of life. Until the 1950s total proctocolectomy with end-ileostomy (TPC) was the only available procedure for UC patients failing medical management.

In the 1940s reports of subtotal colectomy with ileorectal anastomosis (IRA) as an alternative to TPC in selected patients were first published[1]. During the 1950s and 1960s, Aylett[2] became the leading proponent of this procedure describing it as a way to avoid a permanent stoma. At that time IRA represented a valid alternative to TPC in high selected patients with minimal rectal inflammation. It was a less invasive operation, performed in one

Table 1 Morbidity and mortality after ileorectal anastomosis

Series	Period	*n*	Anastomotic leak (%)	Proctitis (%)	Need for proctectomy (%)	Overall morbidity (%)	Mortality (%)
da Luz Moreira *et al*[11]	1971-2006	86	2.3	28.0	53	8	0
Leijonmarck *et al*[13]	1955-1984	51	3.9	45.1	57	16	4
Pastore *et al*[15]	1974-1990	48	4.4	10.4	17	22.9	0
Börjesson *et al*[16]	1997-2003	32	3.1	9.3	12	28	0
Grundfest *et al*[17]	1957-1977	89	9.1	11.2	21	16.1	0
Elton *et al*[18]	1990-1999	18	5.6	11.0	17	22.2	0
Andersson *et al*[19]	1992-2006	105	2.8	8.6	13.3	12.4	0
Lepistö *et al*[22]	1978-2000	20	-	45.0	35	-	0
Oakley *et al*[23]	1960-1982	288	-	41.0	55.2	-	4.2

stage and not requiring pelvic dissection with the associated risk of sexual dysfunction[3-5].

In 1978, Parks *et al*[6] described an ileal pouch-anal anastomosis (IPAA). Since then, IPAA has become the procedure of choice for patients affected by UC with excellent long-term functional results, low risk of persistent cuff inflammation or neoplastic degeneration in the retained rectum[7,8]. Consequently, many surgeons have abandoned IRA in favor of IPAA and TPC has remained an option for patients not candidates for IPAA. The counterargument is that IPAA, as a major procedure, carries its own risks including anastomotic failure and pelvic sepsis that could result in poor pouch function, pouchitis and infertility in young women, as well as pelvic nerve damage and portal vein thrombosis[3-5,9,10]. In addition few cases of cancer have been reported arising not only in the anal transitional zone but also in the pouch itself[7,8].

Interestingly, recent series[11-14] of selected UC patients undergoing IRA showed long-term functional results similar to IPAA.

The aim of the current study was to review and compare the most recent literature on IRA and IPAA as it pertains to postoperative morbidity and mortality, failure rates, functional outcomes and cancer risk. It will help surgeons to provide a tailored treatment for UC patients.

ILEORECTAL ANASTOMOSIS

Chronic UC begins in the rectum and extends proximally in a continuous fashion. The severity of the disease also seems to be higher distally with the exception of fulminant pancolitis presentation. However, distal disease is sometimes alleviated by topical treatment and patients with minimal rectal involvement and no dysplastic changes in the rectum could be considered for IRA. Furthermore, an adequate rectal compliance and a normal anal sphincters function are critical for good long-term results. These functions can easily be assessed by digital rectal examination but more accurately by rigid/flexible proctoscopy and manometry. Patients with poor sphincter function, severe rectal disease, and non-distensible rectum should not be offered an IRA. On the contrary, patients with colitis associated colorectal cancer and advanced metastatic disease may benefit from an IRA because of their short life expectancy and the palliative nature of their treatment.

Several studies[11,13,15-17] have shown IRA for UC to be safe, with low postoperative morbidity and mortality. During the years, overall morbidity has been reported between 8% and 28% and mortality between 0% and 4% (Table 1). These studies including the work of Elton *et al*[18] and Andersson *et al*[19], focused their attention on postoperative complications including small bowel obstruction, anastomotic leak and abdominal abscess. The fatal events were due to anastomotic leak and subsequent sepsis and to a pulmonary embolism.

The majority of published data has included mainly primary anastomosis with leak rates ranging from 2% to 9%[11,13,15-20]. Diverting ileostomies have been utilized in selective cases at the surgeon discretion. Turnbull[21] suggested that preservation of grossly involved rectosigmoid colon was the main cause of IRA failure. In his opinion an anastomosis at 6 cm or less above peritoneal reflexion improved rectal inflammation during the first months and reduced the likelihood of IRA failure.

IRA does not involve extensive pelvic dissection, unlike IPAA or TPC, minimizing the risk of sexual and urinary dysfunction. Hence, higher fertility rates may be expected in IRA patients compared to IPAA although definitive studies providing evidence for better fertility rates in UC patients are lacking. Thus, colectomy with IRA could be considered when treating women in their reproductive age[20].

Some authors[2,11,13,15,18,22] have shown acceptable long-term success rate after IRA. Aylett[2] in 1966 reported on a total of 300 cases operated on over a ten-year period with only 7% failure rates. Lepistö *et al*[22] and Pastore *et al*[15] reported a cumulative probability of having a functioning IRA at five years of 84%. Elton *et al*[18] had 88% success in their 18 patients, but the follow-up in that study was shorter. Ten year cumulative success (69%) in Lepistö's series[22] was higher than reported by Leijonmarck *et al*[13] (51%) in 1990. At 20-years the current probability of having a functioning IRA has ranged between 46% and 69 %[20]. One recent study proposed by da Luz Moreira *et al*[11], from Cleveland Clinic, compared 22 IRA with 66 IPAA patients matched for age, gender, and follow-up time, including IRAs performed in the past 25 years showed a cumulative probability of having a functioning IRA at 5, 10, 15 and 20 years of 81, 74, 56

and 46 percent respectively in accordance with previously published work.

In terms of functional results, the da Luz Moreira's series[11] reported six bowel movements per day (range 2-11), 1/22 (5%) night-time seepage and 15/22 (68%) reporting frequent urgency. Leijonmarck *et al*[13] showed four bowel movements per day and none during the night, with 100% of continence (25% of patients are on antidiarrheal medication), after a mean follow-up of 13 years. Elton *et al*[18] had no significant difference between preoperative and 1-year postoperative stool frequency, 11/12 patients had no problems with continence, and three were using antidiarrheal medication. Pastore *et al*[15] described a median number of six bowel movements per day (range 2-20). The median number of nocturnal bowel movements was one (range 0-10) and three patients had more than eight daily stools with frequent soiling and urgency. At the time of follow-up, antidiarrheal medications were taken by 53.3% of patients, whereas 31.3% required low doses of systemic or topical steroids. More than 90% of patients considered that their health status had improved after the operation. Quality of life was improved in 84%.

All the studies above showed that IRA is a safe procedure with an acceptable function and quality of life but unfortunately it is not necessarily a definitive operation, especially for young patients. Specifically, Andersson and colleagues[19] reported an estimated cumulative failure rate of 10.1% and 24.1% respectively at 5 and 10 years. In his series Leijonmarck *et al*[13] had 57% of failure after 13-year follow-up. Pastore *et al*[15] suggested that time between IRA and additional surgery in his series was 3.9 ± 4.7 years. In da Luz Moreira's series[11], 38 patients (44%) continued to have a functioned IRA after a median follow-up of 11 years (range 1-30 years). The rectum was resected in 46 (53%) of 86 patients and the median follow-up between IRA and completion proctectomy was 10 years (range 1-33 years).

The main indication for proctectomy is recurrent proctitis refractory to medical management[11,13,15-19,22,23], followed by dysplasia or cancer, and the development of Crohn's disease. The options for these patients include IPAA, Brooke ileostomy, or a continent ileostomy (Kock pouch). Very Often IPAA can be safely performed in the majority of these patients thus preserving bowel continuity and avoiding permanent fecal diversion[11].

Cancer risk

Mucosal dysplasia is a premalignant pathological state associated with long standing UC[24]. Dysplasia in general is considered an indication for surgery in UC, even though this paradigm is rapidly changing. Epithelial dysplasia of the colon and rectum was graded as mild, moderate, or severe depending on whether the upper one-third, upper two-thirds, or entire glands displayed nuclear anisocytosis and hyperchromatism, as well as loss of nuclear polarity and the normal goblet cell configuration of colonic mucosa. Since dysplastic changes were often patchy, only the highest degree of dysplasia was considered. Johnson *et al*[25] had shown in 1983 that the probability of developing rectal adenocarcinoma after a diagnosis of mild or severe dysplasia in IRA patients reached 42% at nine years from diagnosis. The rate of dysplasia and cancer, in patients with UC, increases with time and leaving the rectum in place contributes to the increased risk. The overall cumulative probability of rectal dysplasia in the retained rectum increases from 9% at 10 years to 25% at 20 years[11]. The overall incidence of rectal cancer after an IRA varies in the literature based on length of follow-up, ranging from 0% to 18%. Grundfest *et al*[17] reported on four patients who developed carcinoma of the rectum during their study period (4.8% at 8-year follow-up), although he estimated the risk of rectal cancer to be 13% at more than 25 years of follow-up. Oakley *et al*[23] found nine patients with rectal cancer in the stump (3.1%) at an 8-year follow-up while Andersson *et al*[19] showed an overall risk of cancer of 1.9% at a 5.4-year follow-up. However, some series reported higher rates of degeneration as Baker *et al*[26] who described, in 1978, a cumulative cancer risk of 6% after 20 years rising to 18% after 35 years in a series of 374 unselected patients. In da Luz Moreira's series[11], the cumulative probability of developing dysplasia and cancer was 7%, 9%, 20% and 25% and 0%, 2%, 5% and 14% at 5, 10, 15 and 20 years respectively. On the other hand, Leijonmarck *et al*[13] and Lepistö *et al*[22] had reported no case of cancer in more recent series at 13 and 18-year follow-up, respectively. Pastore *et al*[15] showed a cumulative probability of remaining free of cancer around 85.5% at 12 years (95%CI: 57.7%-100%).

Most patients who develop rectal cancer in the retained rectum presented at an advanced stage (stage III-IV) suggesting the possibility of a more aggressive biology and making close surveillance imperative[11,27]. For instance, in Baker's study 62% of patients who had developed rectal cancer died within three years of diagnosis. Johnson *et al*[27] reported a total of 10 rectal cancers, 8 of which had either nodal or distant metastases. The patients in the series reported by Oakley *et al*[23] fared better, with just 2 of 9 patients with rectal cancer dying over a 22-year time period. Rectal biopsies taken from multiple sites every 6 to 12 mo are advised following IRA in UC patients. If dysplasia is found, completion proctectomy is indicated. Patients with long standing UC who are not able or willing to undergo surveillance should not be offered an IRA. It is also important to emphasize that colectomy with IRA should not be offered to patients with preexisting dysplasia or cancer due to the increased risk of further neoplastic degeneration[28]. In addiction, the presence of dysplasia or cancer in the resected colon should cause particular concern about the fate of the remaining rectum suggesting that a completion proctectomy would be indicated in these cases. In fact, Oakley *et al*[12] reported on five surviving patients who had cancer in their colonic specimens; three of the five were found on follow-up to have cancer or severe dysplasia in the rectal remnant. Grundfest *et al*[17] described nine patients

Table 2 Morbidity and mortality after ileal pouch-anal anastomosis

Period	No. of studies	No. of patients	Pelvic sepsis (%, 95%CI)	Pouch failure (%, 95%CI)	Pouchitis (%, 95%CI)	Mortality (%, range)
Meta-analysis studies < 2000[32]	43	9317	9.5 (8.2-10.9)	6.8 (5.8-8.4)	18.8 (15.7-22.4)	-
Meta-analysis studies ⩾ 2000[33]	53	14966	7.5 (6.1-9.1)	4.3 (3.5-5.3)	26.8 (21.0-33.5)	0 (0-2.9)

with a colitis-associated colon cancer or severe dysplasia who underwent subtotal colectomy, eight of whom survived; of the eight, five developed severe dysplasia or cancer in the retained rectum.

ILEAL POUCH-ANAL ANASTOMOSIS

Restorative proctocolectomy with IPAA is currently the procedure of choice for the surgical treatment of UC. The main reason for its popularity is its avoidance of a permanent stoma with stable functional results and good quality of life. In over 30 years of its existence, the IPAA has undergone several refinements in the quest of achieving optimal results. Examples include different shapes of the pouch, different anastomotic techniques, use of defunctioning ileostomy and various dissection methods[29-31]. Surgeons have also obtained greater experience and familiarity with the technique, which has also benefited outcomes.

A large body of literature exists on the outcomes of IPAA. Most studies, however, are retrospective cohorts reporting outcomes from a single institution. Due to large variations between studies, an overview is needed for reliably assessment of the IPAA outcomes. A meta-analysis of 43 observational studies, all published before 2000, has provided pooled estimates of complications and functional outcomes after IPAA[32]. This meta-analysis showed a pouch failure risk of 6.8% (95%CI: 5.4%-8.4%), increasing to 8.5% (95%CI: 5.4%-13.2%) when only patients with a minimal follow-up of 5 years were considered[32]. Other pouch related complications were also studied. Pelvic sepsis and pouch fistulas, both major postoperative complications, were observed in 9.5% (95%CI: 8.2%-10.9%) and 5.5% (95%CI: 4.3%-7.0%), respectively. Sexual dysfunction was present in 3.4% (95%CI: 2.7%-4.7%), while pouchitis was reported in 18.8% (95%CI: 15.7%-22.4%).

A recent meta-analysis, including 53 studies published after 2000, showed significant improvements in these results[33]. The overall rate of pouch failure was significantly reduced to 4.3% (95%CI: 3.5%-5.3%), and pouch failure after at least 5 years of follow-up was 4.7% (95%CI: 3.4%-6.4%). An improvement was also seen in most other complications. Pelvic sepsis, pouch fistula and sexual dysfunction were reported in 7.5% (95%CI: 6.1%-9.1%), 4.5% (95%CI: 3.5%-5.7%) and 3.0% (95%CI: 1.7%-5.2%) of patients. The only complication showing a substantial increase was pouchitis, with a rate of 26.8% (95%CI: 21.0%-33.5%).

Thus it seems that the rate of complications after IPAA has declined over time (Table 2). The authors of the meta-analyses have noticed that the decline was largest in the earlier period of the IPAA, but seems to have continued over time. Nonetheless, IPAA remains a complex surgery with substantial risk of morbidity. The high rate of pouchitis is also worrisome, since this complication can affect functional outcomes, quality of life and might also increase risk of dysplasia in the pouch. It should be noted that the meta-analyses discussed above did not distinguish between acute and chronic pouchitis, which is an important distinction in terms of course and health implications[34-36].

Functional outcomes after IPAA were similar in studies published before and after 2000[33]. Average frequency of bowel movements per 24 h was 5.9 (95%CI: 5.0-6.9), of which 1.5 (95%CI: 1.0-2.1) overnight. Mild and severe faecal incontinence were reported in 14.3% (7.3%-25.9%) and 6.1% (2.9%-12.3%) of patients, respectively. The authors conclude that functional outcomes of IPAA may be determined by an intrinsic limitation of the IPAA procedure, rather than growing expertise or technical refinement. This is in line with other studies showing no improvement in functional outcomes based on technical developments, such as type of anastomosis or laparoscopic approach[36,37]. However, most patients consider the functional outcome after IPAA to be highly satisfactory, with good quality of life and social functionality that are comparable to those in a healthy reference population[38,39]. As expected, achieving these adequate quality of life scores was highly correlated with achieving of good functional outcomes[40].

Cancer risk

The IPAA has as an important advantage the removal of the whole colon and virtually the entire rectum as part of the procedure. This minimizes chances of colon and rectal cancer in this high-risk population. A proctocolectomy should be considered almost mandatory when dysplasia is present. Even when only low-grade dysplasia has been identified by colonoscopy, the risk remains substantial. In such patients, studies show a risk of concomitant cancer or high-grade dysplasia of 15% and a 5-year progression rate of up to 54% if not operated on[28,41].

When a double-stapled approach for IPAA is used, a mucosal remnant at the anal transition zone (ATZ) is left in place. The risk of cancer in this area is a matter of controversy. In three series with long-term follow-up focused on this outcome, dysplasia and cancer in the anal transitional zone after stapled pouch surgery was found to be infrequent[7,42,43]. Dysplasia was observed in 8/178

Table 3 Main advantages and disadvantages of ileorectal anastomosis and ileal pouch-anal anastomosis

	IRA	IPAA
Advantages	Easier operation	Lower risk of cancer
	Lower infertility rate	No need for medical therapy
	Lower risk of urinary and sexual dysfunction	Less urgency
	Fewer bowel movements per day	
	Better continence	
Disadvantages	Need for maintenance therapy	Major operation
	Risk of recurrent/persistent disease	Risk of postoperative complications (pelvic nerves damage, pelvic sepsis, portal vein thrombosis)
	Higher risk of neoplastic degeneration	Pouchitis
	Need for strict surveillance	
	More dietary and work restrictions	

IRA: Ileorectal anastomosis; IPAA: Ileal pouch-anal anastomosis.

(4.4%), 7/210 (3.3%) and 0/135 (0%) after at least 10 years of follow-up. In most of these cases, dysplasia developed in the first 2 to 3 years and often disappeared on repeated biopsies. None of the series found cancer in the ATZ after such prolonged follow-up. These data strongly emphasize the extent to which IPAA minimizes the risk of cancer.

The best evidence regarding the development of dysplasia and adenocarcinoma after IPAA can be obtained from a recent study from the Cleveland Clinic[44], in which 3203 patients undergoing an IPAA from 1984 to 2009 were analyzed. Cumulative incidences for pouch neoplasia at 5, 10, 15, 20, and 25 years were 0.9%, 1.3%, 1.9%, 4.2%, and 5.1%, respectively. Overall, 23 patients (0.72%) developed dysplasia, while 11 (0.36%) developed adenocarcinoma of the pouch and/or the ATZ. Risk factors for pouch neoplasia were also evaluated. Preoperative established cancer [hazard ratios (HR) = 13.43, 95%CI: 3.96-45.53, $P < 0.001$] or dysplasia (HR = 3.62, 95%CI: 1.59-8.23, $P = 0.002$) were the only independent factors associated with increased risk of pouch neoplasia. Mucosectomy did not protect against this risk, and the rate of pouch cancer was actually higher after mucosectomy with a rate of 1.3% (6/451) compared to 0.3% (9/2734) after the double-stapled approach. The authors[44] concluded that the risk for neoplasia in patients with UC and IPAA is small, and that it is mainly determined by the presence of preoperative dysplasia or cancer.

Additionally, in a review of literature, 26 published case reports were identified between 1984 and 2008[45]. Certain observations from this review are noteworthy. First, of the 26 carcinomas, 14 (52%) arose from rectal mucosa or from the anal transition zone, while 6 (23%) were from ileal pouch mucosa. Second, adenocarcinomas developed after mucosectomy in 17 patients, and after a double-stapled approach in 8 patients (1 case not reported). Also worth noting, the indication for the IPAA was due to neoplasia in 19 patients (9 cancers and 10 dysplasia) and non-neoplasia in 6 patients. The median time for development of pouch lesions was the shortest in patients operated on for cancer (median 3 years), compared to a median of 6.5 in the other patients. This review is in line with results from the above mentioned study, and further establishes the following conclusions: (1) the low number of reported cases; (2) cancer can develop both after mucosectomy or double-stapled approach; and (3) the close relationship between surgery for neoplasia and development of cancer. The review was not able to estimate the incidence of cancer after IPAA, since the total number of IPAA cases was not stated in most case reports. Branco *et al*[45] did publish their own case as part of this review, which was the first case they observed in a cohort of 520 patients (0.2%) from 1978 to 2008. This percentage is also in line with the Cleveland study[44].

Despite this seemingly small risk, surveillance of selected patients has been recommended by some authors[46,47]. This approach might especially be important in UC patients with dysplasia or cancer present at time of surgery, or patients with retained rectal mucosa and active inflammation (*i.e.*, cuffitis). Also the presence of chronic pouchitis might be a valid indication for surveillance, since this has been associated with increased risk of low-grade dysplasia (odds ratio 13.48, $P < 0.02$), as well as high-grade dysplasia (3/66 *vs* 0/210, $P = 0.01$)[35].

CONCLUSION

In the current era IPAA is the preferred approach for patients with UC requiring surgical treatment. The removal of all diseased mucosa and the lower risk of cancer after IPAA compared to IRA are the main advantages of this technique (Table 3). Therefore, IPAA should certainly be performed when the rectum is actively involved in the disease or when dysplasia or cancer are present in any part of the colon or rectum. Nonetheless, there is still a role for IRA and TPC for selected patients and for patients not candidates for IPAA.

Total abdominal colectomy with IRA is justified in UC patients with normal anal sphincters tone without severe perineal disease, and spared and distensible rectum with no evidence of dysplasia or cancer at the time of intervention. It can be also proposed to young women as a possible interim procedure based on concerns for infertility after IPAA.

The risk of cancer is of particular concern in the comparison between these two techniques. Current evi-

Table 4 Risk of cancer after ileorectal *vs* ileal pouch-anal anastomosis in ulcerative colitis

	Period	*n*	Follow-up average (yr)	Overall cancer rate (%)	Estimated cumulative risk after 20 years (%)
Ileorectal anastomosis					
da Luz Moreira *et al*[11]	1971-2006	86	9	8	14
Leijonmarck *et al*[13]	1955-1984	51	13	0	-
Pastore *et al*[15]	1974-1990	48	6.3	2	14.3[1]
Börjesson *et al*[16]	1997-2003	32	3.5	0	-
Grundfest *et al*[17]	1957-1977	89	8	4.8	5 ± 3.5
Elton *et al*[18]	1990-1999	18	2.6	-	-
Andersson *et al*[19]	1992-2006	105	5.4	-	2.1
Lepistö *et al*[22]	1978-2000	20	18	0	-
Oakley *et al*[23]	1960-1982	288	8.2	3.1	-
Baker *et al*[26]	1952-1976	374	> 10	5.9	6 ± 2
Ileo-pouch anal anastomosis					
Kariv *et al*[44]	1984-2009	3203	± 12	0.4	4
Branco *et al*[45]	1978-2008	520	± 15	0.2	-

[1]Cumulative risk at 12 years (rather than 20).

dence shows a large variation in the reported rates of cancer after IRA from 0% to 8%. For IPAA, this risk is much smaller, and two large series have shown a rate of cancer of about 0.3%. Few studies have calculated the cumulative risk of cancer as well. Similarly, estimated cumulative risk of cancer after 20 years was higher after IRA (6% to 14%) compared to IPAA (4.2%) (Table 4).

Therefore, every patient undergoing IRA should be informed about the risk of recurrent proctitis and cancer in long standing disease. They have to fully understand the need for meticulous surveillance and agree to comply with at least yearly endoscopy with rectal biopsies. Unless these conditions are met, patients should not be offered an IRA. Also, patients with widely metastatic colorectal cancer may benefit from an IRA as a palliative procedure.

Functional results seem to be better after IRA with lower frequency of bowel movements and less night-time seepage but with more urgency compared to patients with an IPAA. The overall quality of life is similar, although the IRA group has significantly more dietary and work restrictions[11].

Finally, TPC still remains the procedure of choice in patients with impaired anal sphincter function and high-risk of pouch failure.

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