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**Restorative proctocolectomy with ileal pouch-anal anastomosis for ulcerative colitis: a narrative review**

Sofo L *et al*. Surgery for ulcerative colitis

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**Abstract**

Restorative proctocolectomy with ileal pouch-anal anastomosis (RP-IPAA) is the gold standard surgical treatment for ulcerative colitis. However, despite the widespread use of RP-IPAA, many aspects of this treatment still remain controversial, such as the approach (open or laparoscopic), number of stages in the surgery, type of pouch, and construction type (hand-sewn or stapled ileal pouch-anal anastomosis). The present narrative review aims to discuss current evidence on the short-, mid-, and long-term results of each of these technical alternatives as well as their benefits and disadvantages. A review of the MEDLINE, EMBASE, and Ovid databases was performed to identify studies published through March 2016. Few large, randomized, controlled studies have been conducted, which limits the conclusions that can be drawn regarding controversial issues. The available data from retrospective studies suggest that laparoscopic surgery has no clear advantages compared with open surgery and that one-stage RP-IPAA may be indicated in selected cases. Regarding 2- and 3-stage RP-IPAA, patients who underwent these surgeries differed significantly with respect to clinical and laboratoryvariables, making any comparisons extremely difficult. The long-term results regarding the pouch type show that theW- and J-reservoirs do not differ significantly, although the J pouch is generally preferred by surgeons. Hand-sewn and stapled ileal pouch-anal anastomoses have their own advantages, and there is no clear benefit of one technique over the other.

**Key words:** ulcerative colitis; total proctocolectomy; ileal pouch; anal anastomosis; surgery; laparoscopic

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**Core tip**: Restorative proctocolectomy with ileal pouch-anal anastomosis (RP-IPAA) is the preferred surgical treatment for ulcerative colitis. However, despite the widespread use of RP-IPAA, many aspects of this treatment still remain controversial, such as the approach (open or laparoscopic), number of stages of surgery, type of pouch, and type of construction (*e.g.*, hand-sewn or stapled ileal pouch-anal anastomosis). Few large, randomized, controlled studies have been conducted, which limits the conclusions that can be drawn regarding controversial issues associated with RP-IPAA. It is suggested that prospective, randomized studies should be conducted in the futureto compare the frequency of post-operative complications, cosmetic results, short- and long-term functional outcomes, and quality of life associated with the available techniques of RT-IPAA for the treatment of ulcerative colitis.

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**Introduction**

Ulcerative colitis is an inflammatory disease of the colon and rectum that affects millions of adults and children worldwide. Despite the progress of medical therapy, which has broadened the possible treatments after failure of corticosteroids, surgery is still required in 15%-35% of patients affected by ulcerative colitis[1,2]. Surgery is indicated in the elective setting when dysplasia or cancer is present, the patient has a refractory disease, the side effects significantly impair the patient’s quality of life, the patient develops steroid-dependence, or the patient is not compliant[3,4]. In the acute setting, surgery is recommended in cases with hemorrhage, perforation, toxic megacolon, acute severe colitis,and a lack of improvement with second-line therapy. Surgeries are performed before these conditions worsen to avoid increased surgical morbidity and potential mortality[3,4].

Since its introduction in 1978 by Nicholls *et al*[5], the new gold standard surgical treatment of ulcerative colitis is restorative proctocolectomy with ileal pouch-anal anastomosis (RP-IPAA), which offers patients an unchanged body image with no stoma and a preserved anal route of defecation. It has been shown that RP-IPAA is common among older patients; one study revealed that the likelihood of requiring an end ileostomy decreased by 12% per year between 2005 and 2012 in patients aged 61 to 70 years compared with patients ≤ 50 years of age [adjusted odds ratio (OR), 0.88 per year; *P* = 0.021][6].

However, despite the widespread use of RP-IPAA, many aspects of this treatment still remain controversial, including the type of approach (*i.e.*, open or laparoscopic), number of stages of surgery, type of pouch, and construction type (*i.e.*, hand-sewn or stapled ileal pouch-anal anastomosis) because few prospective, randomized studies have been designed and performed.

The present narrative review aimed to define the controversies associated with the use of RP-IPAA in patients affected by ulcerative colitis. An electronic literature search of PubMed, MEDLINE, EMBASE, and the Cochrane Database of Collected Reviews was performed for the dates from January 1978 to March 2016. The search included the following terms: "inflammatory bowel disease," "colitis," "colectomy," and "ileal pouch-anal anastomosis."

**Open or laparoscopic RP-IPAA**

Laparoscopic surgery in the treatment of ulcerative colitis has become very popular in the last decade. An analysis of the American College of Surgeons National Surgical Quality Improvement Program database (ACS-NSQIP, 2005-2008) for all ulcerative colitis patients who underwent a colectomy showed that the laparoscopic approach was used in 29.2% of cases, with rates increasing 8.5% each year (18.5% in 2005 to 41.3% in 2008, *P* < 0.001)[7].

Recently, three meta-analyses[7-9] compared open and laparoscopic RP-IPAA conducted for ulcerative colitis and familial adenomatous polyposis with respect to operative (duration of surgery, blood loss) and short-term (intraoperative mortality and post-operative complications) outcomes. One meta-analysis also compared functional outcomes (number of bowel movements in 24 h and per night, use of pads during the day and during the night, incontinence, and use of anti-diarrheal medications). As shown in Table 1, all of the meta-analyses reported that laparoscopic surgery requires a longer operative time and produces significantly less blood loss. The post-operative complications were also similar between the two procedures (with the exception of the incidence of wound infection, which was shown to be lower with laparoscopic surgery in the meta-analysis conducted by Singh *et al*[7]). Functional outcomes were also similar between laparoscopic and open RP-IPAA in the meta-analysis of Singh e*t al*[7].

It should be noted that these meta-analyses were conducted on studies that were published many years ago (with the most recent study dated March 2012), included numerous types of interventions, and were essentially executed during the ascending phase of the learning curve of laparoscopic surgery. However, there are several more recent studies highlighted in Table 2. One of these studies showed that there was no significant difference between laparoscopic and open IPAA with respect to estimated blood loss, blood transfusions, postoperative narcotic usage, total complications, return of bowel function, length of stay, and hospital readmission rates[10]. However, this study also reported that patients in the laparoscopic IPAA group underwent ileostomy closure an average of 24.1 d sooner than patients in the open group (*P* = 0.045). The study by Fleming *et al*[11], which included 339 laparoscopic and 337 open IPAA procedures, showed that the laparoscopic approach was associated with a lower rate of major (OR = 0.67, 95%CI: 0.45-0.99, *P* = 0.04) and minor (OR = 0.44, 95% CI: 0.27-0.70, P = 0.01) complications. Accordingly, results from the American College of Surgeons National Surgical Quality Improvement Program database (ACS-NSQIP, 2005-2008) for all ulcerative colitis patients who underwent colectomy demonstrated that a laparoscopic approach was associated with lower morbidity and mortality (IPAA complication rate: laparoscopic = 18.2% and open =29.9%, *P* = 0.008)[12]. Interestingly, a prospective, randomized study comparing laparoscopic and open IPAA for the treatment of ulcerative colitis and familial adenomatous polyposis was recently conducted by German researchers[13]. Unfortunately, the study was stopped prematurely due to insufficient patient recruitment, and data for only 21 patients in each arm were reported. The available results revealed that there was no difference in the amount of blood loss between the two groups, as well as that laparoscopic surgery was superior with respect to the length of skin incision, whereas the open approach was superior in the operative duration. However, there were no discrepancies in the length of hospital stay, postoperative pain, bowel function, and quality of life between the approaches. The retrospective cohort study (conducted from January 1992 through December 2007) by Benlice *et al*[14] examined 238 open and 119 laparoscopic IPAAs and showed that open and laparoscopic operations were associated with similar incidences of incisional hernia (8.4% *vs* 5.9%; *P* = 0.40), small-bowel obstruction requiring hospital admission (26.1% *vs* 29.4%; *P* = 0.50), and small-bowel obstruction requiring surgery (8.4% *vs* 11.8%; *P* = 0.31). The small study by Tajti *et al*[15] showed that there was no difference between laparoscopic and open IPAA regarding the rate of early postoperative complications, whereas the rates of intestinal obstruction (8.7% *vs* 45%) and sepsis (0% *vs* 27%) were significantly lower in the laparoscopic group. Conversely, the study by Inada *et al*[16], which included only 24 patients, revealed that the percentage of patients requiring a transfusion and having postoperative complications was lower in the laparoscopic group.

A cross-sectional study carried out in 3 university hospitals in the Netherlands and Belgium compared the time to first spontaneous pregnancy between 23 young patients who had undergone open RP-IPAA and 27 young patients who had undergone laparoscopic RP-IPAA. Patient characteristics were similar in both groups. Indications for surgery were ulcerative colitis in 37 patients, familial adenomatous polyposis (FAP) in 12 patients, and colonic ischemia in 1 patient. A Kaplan-Meier survival analysis was conducted to assess the time to first spontaneous pregnancy and revealed a higher pregnancy rate after laparoscopic IPAA (log-rank test, *P* = 0.023). Similarly, a subsequent survival analysis of all the patients with ulcerative colitis showed an increased pregnancy rate in the laparoscopic group (log-rank test, *P* = 0.033)[16]. This result is probably due to the reduced formation of adhesions after laparoscopic colectomy[17].

Finally, a recent systematic review showed that the incidence of wound infection and intra-abdominal abscess is significantly lower in laparoscopy than in open emergency subtotal colectomy performed in patients with severe acute colitis[18].

Overall, it appears that there is no clear evidence that laparoscopic RP-IPAA offers significant advantages over open surgery. Nevertheless, more recent studies indicate that laparoscopic surgery is associated with fewer complications than open surgery. However, the scarcity of randomized, controlled trials makes any definitive conclusions impossible to draw.

**One- *vs* two-stage RP-IPAA**

One-stage surgery consists of RP-IPAA without ileostomy and aims to reduce the potential impact of surgery on a patient’s quality of life. Many surgeons prefer to perform the entire RP-IPAA operation without the ileostomy[19-21]. However, other surgeons consider the ileostomy to be useful and mandatory because the rate of complications and number of subsequent laparotomies is higher when diversion is not performed[22-24].

The large retrospective study by Remzi *et al*[25] compared data from patients at a single institution who underwent RP-IPAA either with (*n* = 1725) or without (*n* = 277) a diverting ileostomy. They observed that there were no differences between the two groups with respect to septic complications, quality of life, and functional outcomes and concluded that in patients with stapled anastomosis, tension-free anastomosis, intact tissue rings, normal hemostasis, absence of air leaks, malnutrition, toxicity, anemia, or prolonged consumption of steroids should be considered for one-stage RP-IPAA because the one-stage procedure is safe for these patients and is associated with similar results to those of the 2-stage RP-IPAA. Conversely, a meta-analysis reviewing 17 independent studies and including a total of 1486 patients yielded different results[26]. Essentially, the study showed that the incidence of anastomotic leakage and pouch-related sepsis was significantly greater in the group without a protective ileostomy. According to the authors of this review, the exclusion of a protective stoma may only be appropriate for specific patients undergoing RP-IPAA, such as those in whom a pouch may be technically easier to perform (*e.g.*, young women not taking corticosteroids and without comorbidities).

It appears that one-stage RP-IPAA may be safe in selected patients and that adequate, randomized studies are necessary to clarify whether protective ileostomy is needed in patients undergoing RP-IPAA.

**Two- *vs* three-stage RP-IPAA**

Two-stage surgery consists of RP-IPAA and ileostomy during the initial operation, followed by ileostomy closure, whereas the three-stage surgery consists of a subtotal colectomy and ileostomy, proctectomy and pouch creation, and ileostomy closure. The usage rate of a 3-stage RP-IPAA is extremely variable, ranging from 19% to 69%[27-29]. Data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) have shown that the usage rate of a 3-stage approach remained stable in the USA between 2007 and 2011, with approximately 25% of patients affected by ulcerative colitis in a non-emergent setting undergoing a 3-stage RP-IPAA[28].

The two-stage RP-IPAA has the advantages of avoiding an additional operation, a shorter hospital stay, administration of less anesthetic, and a shorter time with a stoma compared with the three-stage procedure. The three-stage procedure allows the patients to improve their nutritional status, withdraw from immunosuppressive medications, and resolve any anemia before the pelvic dissection for pouch construction and IPAA, as well as avoid a complex pelvic dissection in the setting of systemic inflammation.

All of the studies that compared 2- and 3-stage RP-IPAA are retrospective (Table 3)[27-30].Usually, in these studies, patients who underwent either 2- or 3-stage surgery differed significantly with respect to clinical and laboratory variables as well as the use of steroids and anti-TNF agents[27-30]. In 1989, Nicholls *et al*[25] reviewed data from 152 consecutive patients undergoing RP-IPAA (57 two-stage and 95 three-stage) and showed that the anastomotic leakage rate was 10.3% in the 2-stage group and 3.6% in the 3-stage group, with long-term pouch failure rates of 2% and 9%, respectively (*P* < 0.05). The frequency of defecation, frequency of night evacuation, and need for anti-diarrheal medication were reduced in patients who underwent the 3-stage procedure compared with those who underwent the 2-stage procedure. Although a higher proportion of patients in the 3-stage group had emergency surgery compared with the 2-stage group (32% *vs* 2.6%; *P* < 0.01), there was no advantage to the 3-stage procedure except when urgent surgery was required for the following: (1) a patient had complications of ulcerative colitis; (2) malignancy or Crohn's disease could not be ruled out; and (3) a patient taking oral steroids with active colitis had a combination of a low hemoglobin value and low serum albumin levels. In the study by Pandley *et al*[28], 68 ulcerative colitis patients were in the 2-stage group and 50 were in the 3-stage group. The patients in the 3-stage group were more likely to have received aggressive medical therapy, antitumor necrosis factor therapy, and systemic corticosteroids. The overall complication rates were similar between the groups, but infectious complications were significantly higher in the 2-stage group.

Conversely, in the study by Bikhchandani *et al*[29], the records of 2002 patients (2-stage = 1452 and 3-stage = 550) from the ACS-NSQIP were reviewed, and the 30-d morbidity and mortality rates were found to be similar between the two approaches. Unfortunately, the incidence of anastomotic leakage was not reported. However, the authors reported that the rate of deep organ space infections (which were presumed to be due to a postoperative leak) did not differ between the two approaches. Interestingly, the patients who underwent a 3-stage surgery in this study had more favorable clinical features at the time of IPAA, including decreased preoperative sepsis, corticosteroid use, weight loss, and hypoalbuminemia. Finally, the study by Hicks *et al*[29] revealed that the 3-stage procedure was associated with a higher frequency of emergency status, greater intraoperative hemodynamic instability, and a lower use of immunomodulators compared with the 2-stage procedure, but the two procedure types were similar with regard to the number of comorbidities and use of either steroids or anti-TNF agents. The patients who underwent the 2-stage surgery had a lower risk of anal stricture but a comparable risk of fistula or abscess formation or pouch failure over the long term compared with the patients who underwent the 3-stage procedure.

One recent retrospective study showed that a modified 2-stage RP-IPAA (subtotal colectomy with end ileostomy, followed by completion proctectomy and IPAA without diverting ileostomy) compared with the conventional 2-stage RP-IPAA was associated with a significantly lower rate of anastomotic leakage following pouch creation (4.6% *vs* 15.7%, *P* < 0.01; multivariate analysis: OR = 0.27, 95%CI: 0.12-0.57)[31].

**Type of pouch**

An IPAA can be constructed with an S-reservoir, a J-reservoir, or a W-reservoir. The J-pouch, unlike the S-pouch and W-pouch, can be formed by stapling and requires less time; for this reason, the J-pouch is generally preferred by surgeons.

The meta-analysis conducted by Lovegrove *et al*[32] compared the short- and long-term outcomes of J, W, and S ileal reservoirs using data from 18 studies published between 1985 and 2000, with a total of 1519 patients with ulcerative colitis and familial adenomatous polyposis (689 J-pouch, 306 W-pouch, and 524 S-pouch). There were no significant differences between the groups with regard to total postoperative complications, anastomotic leakage, anastomotic stricture, wound infection, pelvic sepsis, pouchitis, and pouch failure. However, the patients with either an S- or W-pouch had a lower frequency of defecation and a reduced need for antidiarrheal medications compared with the patients with a J-pouch, whereas patients with a J-pouch were significantly less likely to require intubation than patients with either an S- or a W-pouch.

However, two recent studies demonstrated that the J- and W-pouches have the same long-term functional results[32,33]. In the study by Rokke *et al*[33], which only included patients with ulcerative colitis, the functional results of the W- and J-reservoir were similar in the middle (2.5 years) and long (11.5 years) term. Similarly, McCormick *et al*[34] reported that 24-h bowel movement frequency, daytime frequency, and nocturnal function did not differ between the W- and J-pouch groups at the 9-year follow-up appointments.

Some surgeons prefer the S-pouch because the efferent limb fits well into the anal canal and the body lies on the levators, whereas the blunt end of a J-pouch may be distorted because it is forced into the muscular tube of the stripped anus. In this regard, the retrospective study by Wu *et al*[35] showed that patients with an S-pouch, compared with patients with a J-pouch, had fewer bowel movements, less frequent pad use, and a lower fecal incontinence severity index, suggesting that, when constructing the IPAA with the hand-sewn technique, the S-pouch is preferable.

**Hand-sewn or stapled ileal pouch-anal anastomosis**

Two types of pouch-anal anastomoses can be performed in RP-IPAA: a hand-sewn IPAA (with or without a mucosectomy) of the rectal stump and a stapled pouch-anal anastomosis with conservation of the rectal mucosa.

In 2006, two different meta-analyses were published that compared these two techniques[36,37]. The meta-analysis by Lovegrove *et al*[36] included 4183 patients with ulcerative colitis and familial adenomatous polyposis who underwent formation of an ileal pouch reservoir (2699 patients with a hand-sewn pouch and 1484 patients with a stapled pouch) between 1983 and 2000. Patients with hand-sewn and stapled anastomoses showed similar early postoperative outcomes (anastomotic leak: 8.8% *vs* 5.2%, *P* = 0.42; pelvic sepsis: 7.2% *vs* 4.7%, *P* = 0.21; pouch-related fistula: 5.9% *vs* 2.2%, *P* = 0.31; pouchitis: 2.2% *vs* 5%, *P* = 0.81; stricture of the anastomosis: 18.2% *vs* 12.5%, *P* = 0.20; pouch failure: 5.3% *vs* 2.3%, *P* = 0.06). In addition, the two techniques were similar with regard to stool frequency per 24 hours, defecation at night, use of antidiarrheal medication, seepage during the daytime, and daytime pad usage. However, in the hand-sewn group, seepage at night and incontinence of liquid stool occurred more frequently, and the use of pads overnight was more common. The improved nocturnal continence observed in the hand-sewn group was correlated with higher anorectal physiological measurements. Unfortunately, there were insufficient data from the included studies to perform a quantitative and comparative analysis on the incidence of dysplasia in the anal transition zone.

The meta-analysis by Schluender *et al*[37], which included four prospective, randomized trials published between 1994 and 2006 that included 180 ulcerative colitis and familial adenomatous polyposis patients, clearly demonstrated that there were no significant differences in functional outcomes between hand-sewn and stapled IPAA, as well as in the resting and contracting sphincter pressures. Based on these results, the authors concluded that, given the potential for persistent cuffitis and/or dysplasia/cancer development in the incompletely removed rectal mucosa after stapled IPAA, the hand-sewn IPAA appears to be preferable.

The large, retrospective study by Kirat *et al*[38], which included patients affected by ulcerative colitis and familial adenomatous polyposis, compared 474 hand-sewn and 2270 stapled ileal pouch-anal anastomoses performed at a single institution. Overall, patients with a stapled IPAA had better outcomes and quality of life compared with those with a hand-sewn IPAA. The frequencies of anastomotic stricture, septic complications, bowel obstruction, and pouch failure were significantly lower among the patients who received a stapled anastomosis. In addition, stapled anastomosis was associated with a lower frequency of incontinence, seepage, and pad usage, as well as reduced dietary, social, and work restrictions. Kirat *et al*[38] concluded that as long as there are no contraindications (dysplasia, presence of cancer in the rectum or colon), stapled anastomosis is the superior technique with respect to short-, mid-, and long-term outcomes. Nevertheless, the same study analysis demonstrated that preservation of the anal transitional zone did not lead to the development of cancer in patients monitored for a minimum of ten years[39].

More recently, a small retrospective study that included patients only affected by ulcerative colitis showed that postoperative complications did not differ significantly between the two pouch groups, with the exception of a greater incidence of postoperative anal fistula in the stapled group (*P* = 0.03). Functional outcomes and long-term quality of life were similar between patients who had received either hand-sewn or stapled IPAA[40].

**Conclusion**

Regarding the use of RT-IPAA for the treatment of ulcerative colitis, there are few large, randomized, controlled studies, which makes it impossible to draw definitive conclusions regarding controversial issues such as the use of either theopen or laparoscopic approach, number of stages of surgery, type of pouch, and pouch construction (*i.e.*, hand-sewn or stapled pouch). The available data from retrospective studies suggest that laparoscopic surgery has no clear advantages over open surgery and that one-stage RP-IPAA may be indicated in qualifying cases. With regard to the 2- and 3-stage RP-IPAA, the fact thatpatients who underwent 2- and 3-stage surgeries differed significantly with regard to their clinical and laboratoryvariables makes any comparison extremely difficult. Regarding pouch type, the long-term results show that W- and J-reservoirs do not differ significantly. Finally, the hand-sewn and stapled ileal pouch-anal anastomoses have their own advantages, but there is no clear benefit of one technique over the other. It is suggested that adequate prospective, randomized studies should be conducted in the near futureto compare the frequency of post-operative complications, cosmetic results, short- and long-term functional outcomes, and quality of life between the available RT-IPAA techniques for the treatment of ulcerative colitis.

Currently, it is important to emphasize that the choice of the type of surgery should be based on the experience and skills of the performing surgeons in the hospital as well as on each individual case.

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**Table 1 Meta-analyses comparing the intra-operative, short-term, and functional outcomes of open *vs* laparoscopic restorative proctocolectomy with ileal pouch-anal anastomosis**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Authors** | **Number of studies included/N of RCTs** | **Number of patients** | **Operative time** | **Blood loss** | **Intra-operative mortality** | **Hospital stay** | **Post-operative complications** | **Functional outcomes** |
| Tilney *et al*[9], 2007 | 10/1 | Open: 178  LS: 175 | Higher in LS by 86 mine | Lower in LS by 84 mle | Not reported | No significant differences | No significant differences | No significant differences1 |
| Ali *et al*[8], 2009 | 11/1 | Open: 354  LS: 253 | Higher in LS by 92 mine | Lower in LS by 138 ml | No significant differences | Shorter in LS by 2.12 d | Total  Open: 41.5  LS: 37.6  Severe  Open: 7.8  LS: 5.1 | LS: shorter time to bowel movement (-1.96 d); no  significant difference  in daytime and overnight continence, soiling, or urge incontinence |
| Singh *et al*[7], 2013 | 27/1 | Open: 1331  LS: 1097 | Higher in LS by 70.1 mine | Lower in LS by 89.1 mle | Not reported | Shorter in LS by 1 d | No significant differences with the exception of wound infection (lower in LS) | LS led to fewer nocturnal bowel movements and reduced pad usage during the day |

1data based on only 2 studies; e*P* < 0.001. RCT: randomized controlled trial; LS: laparoscopic surgery.

**Table 2 Studies comparing the intra-operative, short-term, and functional outcomes of open *vs* laparoscopic restorative proctocolectomy with ileal pouch-anal anastomosis**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Type of study** | **Number of patients** | **Operative time (min)** | **Blood loss (ml)** | **Mortality (%)** | **Hospital stay (d)** | **Post-operative complications (%)** | **Functional outcomes** |
| Fajardo *et al*[10], 2010 | retrospective | Open: 69  LS: 55 | Open:  187 ± 52  LS:  266 ± 55e | Open:  284 ± 146  LS:  294 ± 274 | Open: 0  LS: 0 | Open: 7.8 ± 4.9  LS: 8.4 ± 6.0 | Open: 59.4  LS: 50.1 | Open:  5.1 ± 2.8  LS:  4.9 ± 4.92 |
| Fleming *et al*[11], 2011 | retrospective | Open: 339  LS: 337 | Patients with an operative time > 336 min  Open: 13.7%e  LS: 36.6%e | Patients with transfusion  Open: 8%a  LS: 3.9a | Open: 0.6  LS: 0.5 | Open: 7.9 ± 4.8  LS: 7.3 ± 4.3 | Major  Open: 29.74  LS: 16.84  Minor  Open: 18.43  LS: 10.63 | not reported |
| Causey *et al*[12], 2013 | retrospective | Open: 148  LS: 299 | not reported | not reported | Open: 0  LS: 0 | not reported | Open: 18.2b  LS: 29.8b | not reported |
| Schiessling *et al*[13], 2013 | PRT1 | Open: 21  LS: 21 | Open: 200 ± 53  LS: 313 ± 52e | Open: 228 ± 119  LS:  261 ± 195 | Open: 0  LS: 0 | Open: 19.6 ± 20.5  LS:  12.3 ± 5.8 | Open: 5  LS: 9.5 | Open:  3. 5 ± 2.5  LS:  3.4 ± 2.52 |
| Tajti *et al*[15], 2015 | retrospective | Open: 22  LS: 23 | Open: 185 ± 171,c  LS: 245 ± 511,c | Units of blood transfusion  Open: 3 ± 1.9  LS: 2 ± 1.7 | Open:  LS: | Open:  11.6 ± 3.4  LS:  11.5 ± 3.8 | Sepsis  Open: 27d  LS: 0d | Open:  7.83 ± 3.285 LS:  7.81 ± 3.315 |
| Benlice *et al*[14], 2015 | retrospective | Open: 238  LS: 119 | Higher in LS |  | Not evaluated |  | Similar incidence of incisional hernia and small bowel obstruction |  |

1included patients with ulcerative colitis and familial adenomatous polyposis; 2days to first ingestion; 3based on a multivariate analysis: OR = 0.44 [0.27-0.70] (P = 0.01); 4based on a multivariate analysis: OR = 0.67 [0.45–0.99] (*P* = 0.04); 5number of stools per day. a*P* = 0.02; b*P* = 0.008; c*P* = 0.040; d*P* = 0.007; e*P* < 0.0001. LS: laparoscopic surgery; PRT: prospective randomized trial.

**Table 3 Studies comparing the mortality and morbidity of 2-stage and 3-stage restorative proctocolectomy with ileal pouch-anal anastomosis**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Author** | **Type of study** | **Number of patients**  **2- *vs* 3-stage** | **Mortality (%)** | **Post-operative complications (%)** | **Sepsis/**  **Septic shock (%)** | **Pouch leak (%)** | **Wound infection (%)** | **Intra-abdominal abscess (%)** | **Bowel obstruction**  **(%)** | **Pouch failure (%)** |
| Nicholls *et al*[27], 19892 | retrospective | 2-stage: 57  3-stage: 95 | 2-stage: 2  3-stage: 0 | 2-stage: 49  3-stage: 51 | 2-stage: 20  3-stage: 17 | 2-stage:  10.3  3-stage:  3.6 | 2-stage: 9  3-stage: 12 | 2-stage: 2  3-stage: 1 | 2-stage: 9  3-stage: 15 | 2-stage: 2a  3-stage: 9a |
| Pandey *et al*[28], 2011 | retrospective | 2-stage: 68  3-stage: 50 | 2-stage:  1.47  3-stage:  0 | 2-stage: 55.2%  3-stage: 52.2% | unknown | 2-stage:  13.2  3-stage:  8 | 2-stage:  8.8  3-stage:  7 | 2-stage:  16.2  3-stage:  6 | 2-stage:  11.8  3-stage:  9 | unknown |
| Hicks *et al*[29], 2013 | retrospective | 2-stage:  116  3-stage:  28 | 2-stage: 0  3-stage: 0 | Mean number of complications: 1.18 *vs* 1.29 | unknown | 2-stage:  10.3  3-stage: 3.6 | unknown | 2-stage:  21.6  3-stage:  21.4 | 2-stage:  20.8  3-stage:  3.6g | 2-stage:  6.7  3-stage:  3.6 |
| Bikhchandani *et al*[29], 2015 | retrospective | 2-stage:  1452  3-stage:  550 | 2-stage:  0.4  3-stage:  0 | 2-stage: 11.5%  3-stage: 9.4% | 2-stage:  9.1  3-stage:  7.4 | 2-stage:  9.4  3-stage:  6.71 | 2-stage:  10.5  3-stage:  13.11 | unknown | unknown | unknown |

Differences are not significantly different. 1reported as deep organ space infection; 2studies including patients affected by ulcerative colitis and familial adenomatous polyposis; a*P* < 0.05; g*P* = 0.03