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# Systematic Review: The Burden of Post-operative Complications Following Colectomy for Ulcerative Colitis

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## ABSTRACT

**Background:** Ulcerative colitis (UC) patients failing medical management require colectomy.

**Methods:**Literature search in MEDLINE , CINAHL andEmbase, targeting studies reporting the outcomes of colorectal procedures (from 2002 to 2016 with total and subtotal colectomy postoperative complications in adults with ulcerative colitis as an endpoint. Texts and authoritative Web sites were also reviewed then identification of papers according to the inclusion and exclusion criteria and data extraction were performed by two independent researchers.

**Results:**Following data extraction and synthesis,we identified 24 articles for review. Reporting outcomes from procedures conducted from 2002–2016. Most frequent short-term complications: infectious complications and ileus (mean incidence 21% and 19%), while most frequent long-term complications: pouchitis, fecal incontinence and small bowel obstruction (mean incidence 31%, 22% and 18%). Post-operative early complications (≤30 days) occurred in 18–63% of patients with ulcerative colitis while late complications (>30 days) occurred in 19–58% of patients. Rates of early infection and late pouch failure decreased significantly from 2002 to 2015 (22% to 2% respectively).

**Conclusion:**although Colectomy remains an appropriate therapeutic strategy for specific groups of patients- it is not the optimal cure for UC. Clinicians need to fully understand the various postoperative complications and comorbidities that are highly prevalent with over a third of patients expected to experience long-term or late arising post-operative complications. Thus, while surgical procedures are recommended as an appropriate therapeutic strategy for a specific group of patients, the post-operative complications associated with these surgical procedures should not be underestimated.

**Keywords:**Ulcerative Colitis, post-operative complications, colectomy ,pouchitis, colon surgery.

## INTRODUCTION

The global burden of Ulcerative Colitis(UC) is significant and continues to rise, even in western countries where historical prevalence was already high[1].The natural history of UC suggests that in the years following diagnosis, only half of all patients achieve remission, with the remainder continuing to experience disease burden; this results in an increasing proportion requiring colectomy. After 10 years of treatment, over one-third of patients still have active disease and 20% will undergo colectomy.[2]

Even for patients who initially present with a limited extent of disease, such as those with proctitis or proctosigmoiditis, UC will progress to a greater extent of disease extension in about one-third of patients, with 10–20% developing extensive colitis.[3]

Colectomy for UC is a technically demanding operation associated with morbidity and mortality [4,5] .Patients undergoing elective procedures have lower risk of postoperative mortality, ranging from 0.0% to 1.0%[6]. In contrast, mortality in those requiring emergent colectomy was as high as 6.9% [7] .Other factors that have been shown to



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influence postoperative outcomes include older age and comorbidities [8] .

Several types of colorectal procedure may be performed, depending on patient characteristics and the precipitating indication for surgery. Subtotal colectomy with subsequent ileal pouch-anal anastomosis (IPAA) is the most common procedure[9].Historically, a restorative proctocolectomy has been viewed as a cure for UC [10]as it provides good functional outcomes and quality of life to the vast majority of the patients with UC[11].However, this surgical procedure is associated with a number of short- and long-term complications and comorbidities, such as pouchitis, faecal incontinence, irritable pouch syndrome, anastomotic ulcer and stenosis, cuffitis, missed or de-novo Crohn's disease and, in young females, reduced fecundity [12].Thus, varying rates of failure of this procedure, defined as the necessity to remove the pouch or produce a permanent ileostomy, have been reported[9].

Assessing the reported absolute rates of short- and long-term complications and comorbidities associated with colectomy for UC is important to help clinicians estimate the risks and benefits of colectomy vs. continued medical therapy, and consequently in making informed decisions on indications and timing of colectomy. In addition, there is a need for healthcare budget holders to appreciate the prevalence of these complications and comorbidities, as it has been demonstrated that patients experiencing complications incur greater costs for several years post-operatively, compared with patients who do not experience complications [13,14] .

## METHODS

### *Literature search*

**The present systematic review (SR) is reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.**

**Data Sources**: electronic databases were searched: MEDLINE (including MEDLINE in-process, from 1946); Embase (from 1980); The Cochrane Library (Evidence-based medicine reviews in OVID) including: the NHS Economic Evaluation Database (NHS EED) and Health technology assessment (HTA); Econlit (from 1886).**Search terms**included colectomy , colorectal surgery , +/complications

### *Data extraction*

Search results were screened by scanning abstracts for the following ***Inclusion Criteria***

- Randomized clinical trials (RCTs) and observational studies (prospective or retrospective non-RCTs) reporting colorectal surgical procedures for UC.
- Participants were to be aged 18 years or older, to be diagnosed with UC, and to have received a specified surgical procedure for UC, in any country.
- Randomized controlled trials (RCTs), controlled clinical trials (RCTs), comparative studies, studies with irrelevant endpoints were excluded.
- Relevant publications reporting colorectal surgical procedures for UC performed between 2002 and 2015 (2002 onwards is the date from which biological drugs began to be administered in clinical practice and these agents may have had an impact upon surgical complication rates.
- Surgical operation of concern : total and subtotal colectomy, ileal pouch-anal anastomosis (IPAA) with J pouch, S pouch or W pouch.

Independent reviewers reviewedthe studies, abstracted data, and resolved disagreements by consensus. Studies were evaluated for quality. A review protocol was followed throughout. A total of 24 studies were reviewed.

**The study was done after approval of ethical board of King AbdulazizUniversity**.

## RESULTS

Searches identified 1123 publications in addition to another 36 publications that were found through manual research. After removal of duplicates, abstracts and titles 768publications were assessed as identified from title and abstract, and 340 papers were excluded. There were 56 papers full text could not be retrieved , also 297 papers excluded because they did not discuss the present study's relevant endpoint (complications, risk factors and burden of UC colectomy) and another 59 papers excluded for having the same cohort. We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in reporting the results (**Figure 1).**

Finally, 24 publications were selected to be studied in the presentsystematic review.

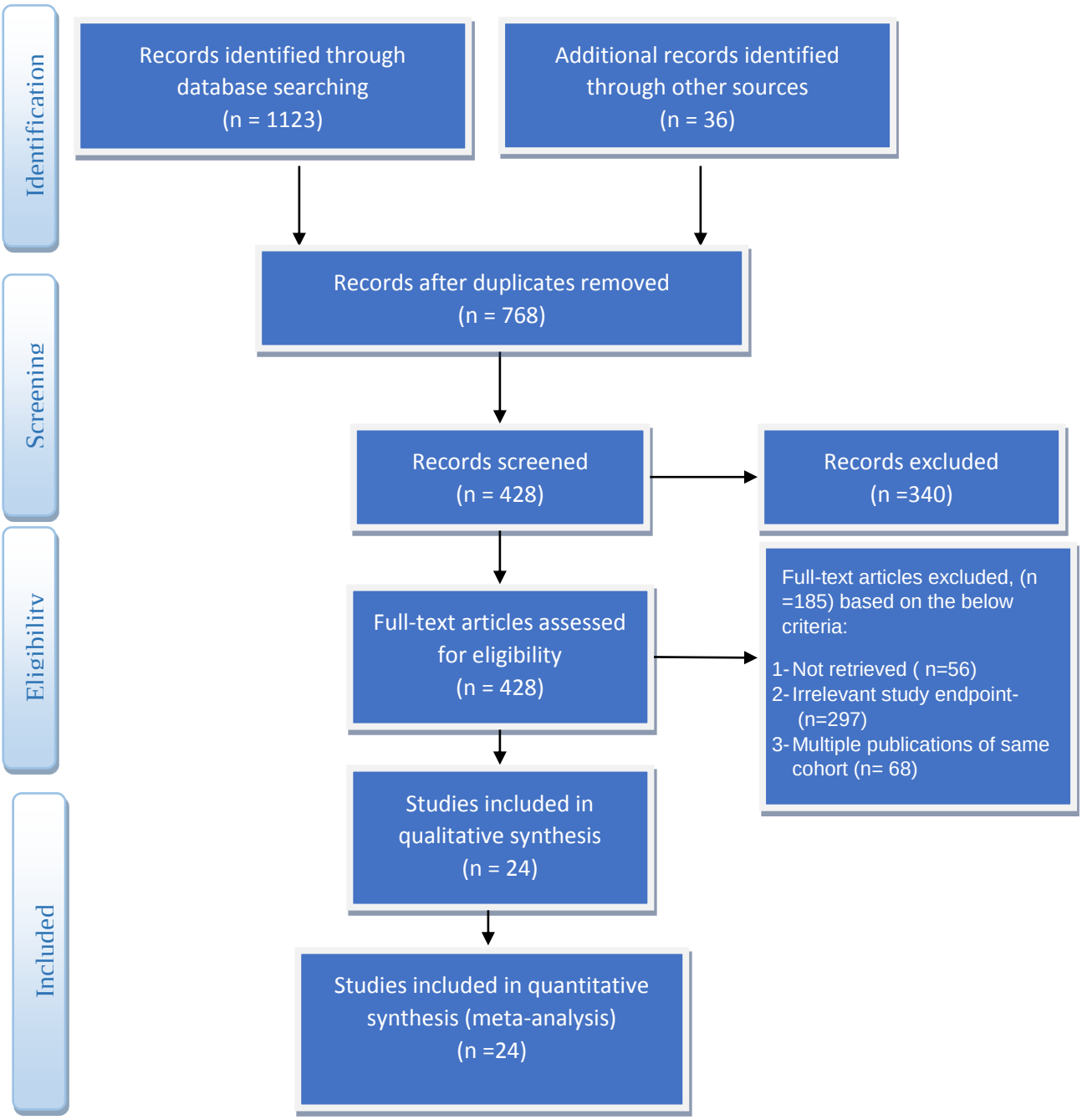


**Figure 1: PRISMA flow diagram showing the selection process and steps of the literature search**

***Risk factors for postoperative complications***

A validation study conducted by Christopher Ma *et al.*concluded thatage ≥ 65 increased the risk of postoperative complications by approximately 2-fold (**Table 1**). Although emergent admission status was a risk factor for postoperative complication, the odds ratio for emergent admission was higher in the administrative database (OR 2.52 [1.80–3.52]) than that in the chart review (OR 1.49 [1.06–2.09]). The odds ratio for presence of ≥1 Charlson comorbidity was also higher in administrative data (OR 2.91 [1.86–4.56]) as compared to chart data (OR 1.50 [1.05–2.15]) [39].

**Table (1):** shows the relation between age and type of admission and incidence of complications

| Risk Factor | (95%CI) n = 697* |
|---|---|
| **Age** | |
| **18–34** | 1.0 |
| **35–64** | 0.83 (0.58–1.19) |
| **65+** | 2.04 (1.18–3.52) |
| **Admission Type** | |
| **Elective** | 1.0 |
| **Emergent** | 2.52 (1.80–3.52) |
| **Charlson Comorbidity** | |
| **0** | 1.0 |
| **≥ 1** | 2.91 1.86–4.56) |

OR - odds ratios; CI - confidence interval.

1. ***Quantitative analysis for short and long term complications***

A quantitative analysis was done across all studies for Short- and long-term surgical complications and comorbidities summarized and illustrated in Figures 1 and 2, respectively

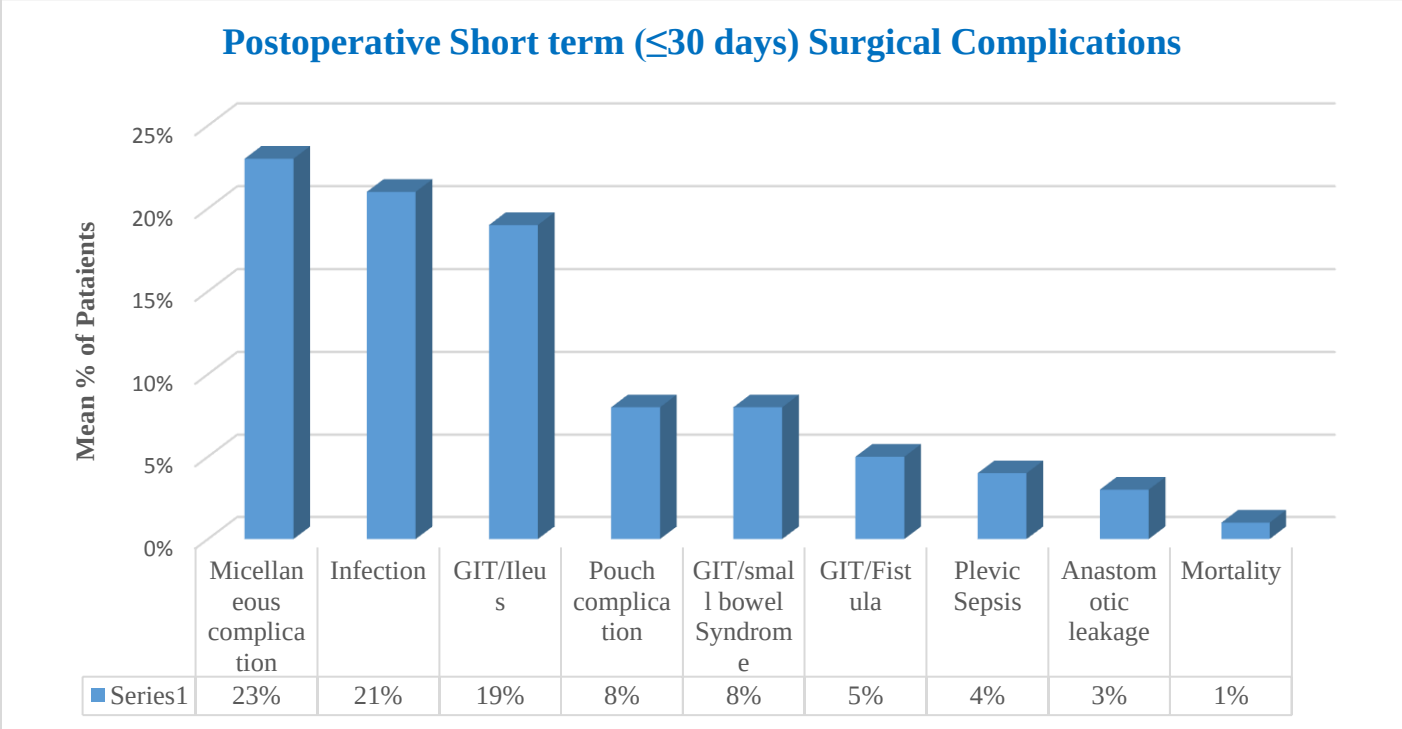


**Figure 2**: mean % of patients with complications of post-operative short-term (≤30 days) surgical complications across all studies

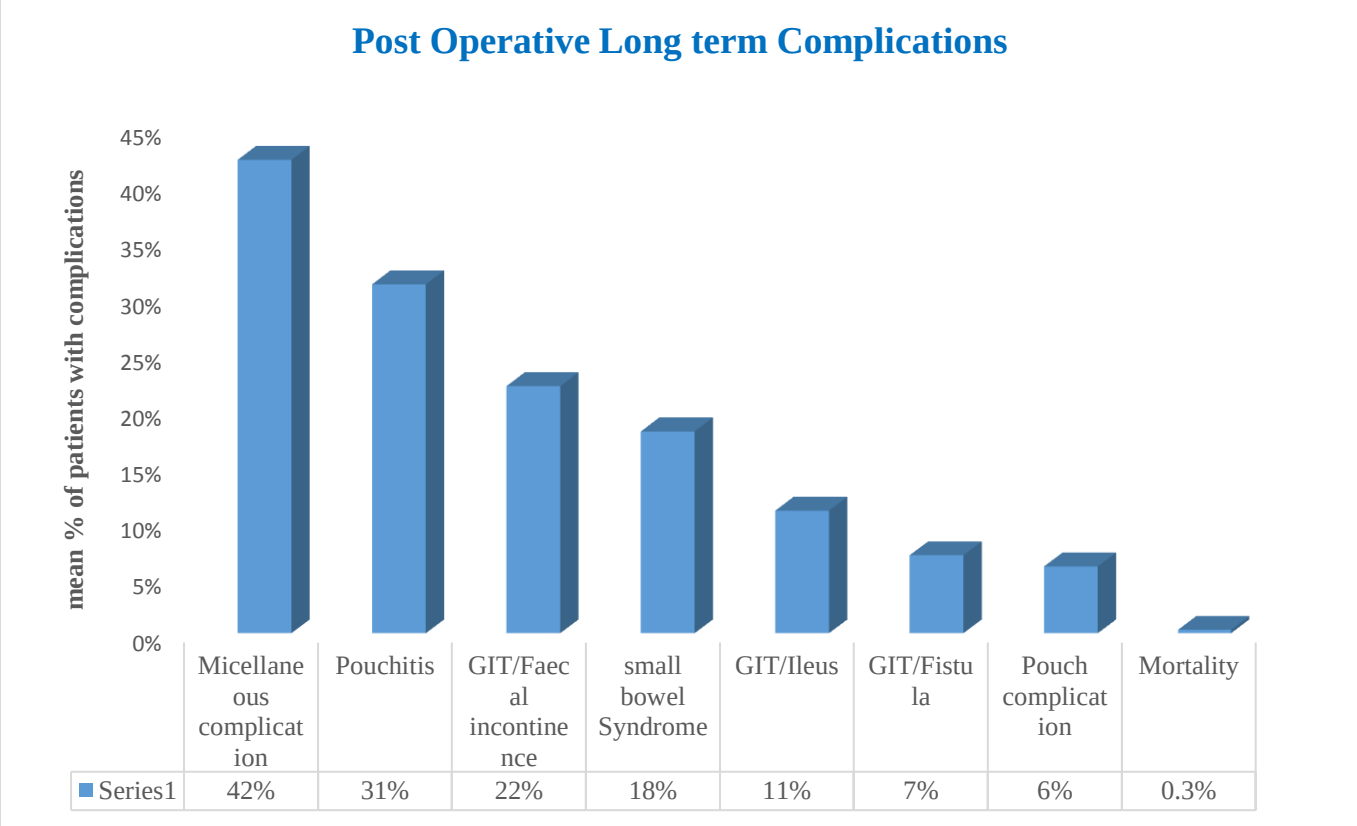


**Figure 3**: mean % of patients with complications) of post-operative long-term (>30 days) surgical complications across all studies.

## 2. Type of complications in patients undergoing colorectal procedures for UC

### 1. *Mortality*

Eleven studies analysing 5196 patients with UC[15, 16, 17,18, 22,24, 48] reported post-operative mortality data. Of the eleven studies, eight reported the incidence of mortality within 30 days from the colorectal procedure, [15,17,19,20,28]two reported mortality post-operatively (one reported mortality as in-hospital complication), [15,22] one as a long-term complication – within 60 days after first operation, [28] and one study did not report details on time of patients' death[24] Mortality rates ranged from 0 (0%) [18,20] to 16/559 (2.9%),[15,28] with a mean incidence of 1.0% across all included studies.

### 2. *Infection*

#### *2.1. General Infectious complication*

Eight retrospective studies analysing 1,134 patients with UC [17, 18,19,26,27,30,31, 32]reported the outcome of 'any infectious' complication (defined as the occurrence of ≥1 infectious complications in an individual patient during the study follow-up period) as an early complication. The frequency of 'any infectious' complication ranged from 25/254 (10%) to 44/98 (45%) [27]; in neither of these particular control arms had patients received infliximab prior to surgery.

#### *2.2. Common infectious complication: Pelvic sepsis or pelvic abscess*

Five retrospective studies analyzing 1941 patients with UC,[17, 2328, 31, 32]reported pelvic sepsis or pelvic abscess as a complication of surgery. In three studies reporting pelvic sepsis as an early complication,[31, 23, 28] the frequency ranged from 0/27, 0/19 and 0/199 (0%) respectively, to 9/48 (19%) [23] Of note, the 0% frequency of pelvic sepsis or pelvic abscess was reported in sub-groups of patients who underwent partial colectomy [23] having been treated with different combinations of cyclosporine A, intravenous corticosteroids and infliximab, [31] or with anti-TNF-alpha 12 weeks prior to surgery[28] None of the included studies reported pelvic sepsis as late complication.

## *2.* GIT complications

### *2.1. Small bowel obstruction*

Six studies analysing 943 patients with UC, two of which were prospective [22,24]and four were retrospective,[20, 21,26] reported the rates of small bowel obstruction (SBO). The frequency of early SBO ranged from 1/61 (2%) to 8/68 (12%) in two-stage procedure patients. [24] The frequency of late SBO in two studies was 17% (58/332 and 30/179 respectively) [21,22] .

### *2.2. Faecal incontinence*

One prospective study analysing 179 patients with UC, [22] reported faecal incontinence following surgery, defined as major or minor leakage; the long-term incontinence was reported as 23/106 (22%) in a group of patients who underwent open IPAA, and 15/73 (21%) in a group of patients who underwent laparoscopic IPAA.

### *2.3.* Fistula

One retrospective studyanalysing 430 patients with UC [23] reported the outcome of fistula. In this study, the frequency of early fistula ranged from 0 (0%), in patients who underwent partial colectomy or total proctocolectomy with ileostomy, to 3/48 (6%) in patients who underwent subtotal colectomy with ileostomy and Hartmann's procedure. The frequency of long-term fistula ranged from 0 (0%), in patients who underwent partial colectomy or total proctocolectomy with ileostomy to 4/48 (8%) in patients who underwent subtotal colectomy with ileostomy and Hartmann's procedure[23].

### *2.4.* Ileus

Postoperative ileus has long been considered an inevitable consequence of gastrointestinal surgery. The frequency of ileus ranged from 7/51 (14%) in a group of patients who had not been receiving infliximab prior to surgery to 6/20 (30%) in a group of patients who had been receiving infliximab prior to surgery. [17] The long-term complications ranged from 3/106 (3%) [24] in open IPAA patients to 17/68 (25%) in a group of patients who underwent two-stage laparoscopic IPAA [24]

## *3.* General pouch-related complications

Two retrospective studies analysing 382 patients with UC, [18,32] reported the outcome of 'general' pouch-related complications, the definition of which was study-specific. In all studies reporting 'general' pouch-related complications, data referred to early post-operative outcomes. The frequency of these complications ranged from 0 (0%) in one study reporting outcomes of patients who had previously received infliximab, [18,34] to 9/47 (19%) in patients who underwent IPAA and had also received infliximab prior to surgery [32] .

### *3.1. Pouchitis*

Four studies analysing 946 patients with UC [35,36] reported pouchitis in a long-term follow-up (>30 days post-operatively). The frequency of pouchitis ranged from 1/12 (8%) [36] to 237/576 (41%). [35]None of the included studies reported pouchitis as an early complication.

### *3.2. Pouch loss/pouch failure/pouch excision performed*

Two studies [22,36]analysing 239 patients with UC, one prospective and one retrospective, reported severe pouch problems as a long-term outcome, with a frequency in a range of 0 (0%) [22] to 2/12 (17%). [36]Severe pouch problems lead to outcomes described as any of pouch loss, pouch excision or pouch failure. Pouch failure was defined as dysfunctional pouch requiring pouch excision or a permanent diversion by Moore *et al*., [36] and as pouch failure requiring excision by Fichera *et al*. [22]

## *4.* Anastomotic leakage

Anastomotic leaks may be divided into those which are clinically significant and those which are not. Subclinical leaks are more benign in their natural history compared with clinical leaks although quality of life and bowel function does not differ in these groups. 3 studies analyzing 1608 patients with UC, [18, 28,32]reported the association of an anastomotic leak with the pouch construction. The frequency range of anastomotic leakage reported as an early complication was from 1/199 (0.5%), [28] to 5/52 (10%) [33]. Neither study included patients who had received anti-TNF therapy. Similarly, no evidence of anastomotic leakage as a late complication.

**The observations and results of the present study concurred with a systematic review done by Peyrin-Biroulet*et al.*(2016) [34]**

# DISCUSSION

In this systematic review, we summarized studies that assessed the he outcomes of colectomy and ileal pouch surgery for ulcerative colitis (UC). It was crucial to restrict this analysis patients who

underwent surgery after 2002, when biological therapy was widely available for ulcerative colitis.

The most frequent postoperative surgical complications after colorectal resections are surgical site infection, anastomotic leakage, intraabdominal abscess, ileus and bleeding .These complications have different influences on outcome and have to be diagnosed accurately. In order to meet certain quality standards it is essential to assess postoperative complications [36]

Risk factors in emergency, in elective open and laparoscopic colorectal surgery should be recognized prior to surgery in order to reduce complications and to initialize individualized treatment as soon as possible. However, some risk factors such as age, gender and prior abdominal surgery can obviously not be influenced before surgery[37]

Most profound outcome:

- 9–65% of patients with UC undergoing surgical procedures had early complications
- 31–55% of patients with UC undergoing surgical procedures experienced late complications
- 8–41% of patients with UC undergoing surgical procedures experienced pouchitis.

A meta-analysis published in 2012, which included 16 studies, reported the central estimate of the prevalence of nonchronicpouchitis (≤3 episodes per year) as 28%, chronic pouchitis (≥4 episodes per year) as 11% and small bowel obstruction as 18%. [35]

Time trends analysis showed that the majority of early and late complications were not reported between 2010 and 2015 in the included studies. The paucity of reported data on post-operative complications during this time range might be due to the impact of the use of biologics in clinical practice upon the proportion of patients undergoing surgical procedures for UC and hence on the number of published studies. Alternatively, the lag time in publications may mean that the studies covering these years have yet to reach publication. Nonetheless, we found that the incidence rates of early infectious complication and pouch failure/pouch loss/pouch excision as late complication have decreased from 22% and 13% in 2002–2009 to 11% and 2% in 2010–2015 respectively. However, these findings should be interpreted cautiously as duration of follow-up and surgical management of these patients may vary across studies- however the present study had not the impact of medications such as anti-TNF in the scope of the study [38] .

***Limitation of the study***

The heterogeneity encountered in the UC patient populations analysed, procedures received, duration of follow-up, approaches of procedures used (open vs. laparoscopic) and definitions of outcomes reported in the included studies.

## CONCLUSION

UC has a major impact on quality of life, and clinicians need to fully understand the various postoperative complications and comorbidities that are highly prevalent with over a third of patients expected to experience long-term or late arising post-operative complications. Thus, while surgical procedures are recommended as an appropriate therapeutic strategy for a specific group of patients, the post-operative complications associated with these surgical procedures should not be underestimated.

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