



SAHLGRENKA ACADEMY

**Ulcerative Colitis: Rate of Complications Following Open
Respective Laparoscopic Colectomy and Extent of Reconstructive
Surgery at Sahlgrenska University Hospital in Gothenburg,
Sweden– A Retrospective Cohort Study.**

Degree Project in Medicine

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List of Abbreviations

Abbreviation	Definition
CI	Confidence interval
CRC	Colorectal cancer
CRF	Case report form
IBD	Inflammatory bowel disease
IPAA	Ileal pouch-anal anastomosis
IRA	Ileorectal anastomosis
OR	Odds ratio
RCT	Randomized controlled trial
UC	Ulcerative colitis

1. ABSTRACT

Degree Project, Programme in Medicine

TITLE: Ulcerative Colitis; Rate of Complications Following Open Respective Laparoscopic Colectomy and Extent of Reconstructive Surgery at Sahlgrenska University Hospital, Gothenburg, Sweden– A Retrospective Cohort Study.

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BACKGROUND: Ulcerative colitis is an inflammatory bowel disease commonly treated with medical therapy. However up to 20% of patients need surgical treatment with colectomy, after which reconstructive surgery may be performed as an ileorectal anastomosis (IRA) or an ileal pouch-anal anastomosis (IPAA).

OBJECTIVE: The aim of this study was to examine the rate of postoperative complications after open versus laparoscopic colectomy in patients with ulcerative colitis as well as to assess to which extent they were offered reconstructive surgery.

METHODS: Four hundred and thirty-six patients with ulcerative colitis underwent colectomy due to ulcerative colitis between January 2000 and December 2019, at Sahlgrenska University Hospital, and included in the study. Postoperative complications within 90 days were classified according to Clavien-Dindo, where \geq IIIb was considered as a major

complication. It was noted whether the patients were reconstructed with an ileal pouch-anal anastomosis (IPAA), ileorectal anastomosis (IRA) or remained with an ileostomy.

RESULTS: Major complications, occurred in 13.3% of patients that underwent colectomy and in total, 67.6% of patients had reconstructive surgery. No difference in complication rate was found between open and laparoscopic colectomies. Age was found to be associated with chance of reconstructive surgery after colectomy.

CONCLUSION: In the above study we did not find a difference in risk of complication after open vs laparoscopic colectomy. Nearly 68% of colectomies were followed with reconstructive surgery, which is higher than in the rest of Sweden.

KEY WORDS: Ulcerative colitis, colectomy, reconstructive surgery, postoperative complications

2. BACKGROUND

2.1 Introduction

2.1.1 Ulcerative colitis

Ulcerative colitis (UC) is an inflammatory bowel disease (IBD) (1) characterized by a chronically remitting-relapsing course with symptoms such as diarrhea mixed with blood, stomach pains, frequent bowel movements as well as generalized fatigue due to the inflammatory response. Each year 12-14/100 000 individuals are diagnosed and with a prevalence of 250/100 000, some 25 000 individuals suffer from ulcerative colitis in Sweden (2). The majority of patients are diagnosed in early age, 15–45 years but debut of ulcerative colitis is seen in all ages (3). Ulcerative colitis is generally said to affect both men and women equally (4), however recent studies suggest that there may be a male predominance (5).

Ulcerative colitis affects the colon and rectum with an inflammation of the colorectal mucosa (4), as opposed to Crohn's disease which is characterized by skip lesion with a transmural inflammation that can occur throughout the gastrointestinal tract (6). Ulcerative colitis can have a varying distribution – affecting only the rectum, reaching the sigmoid colon, left sided colitis involving the descending and sigmoid colon or reaching beyond the left colic flexure as an extensive colitis (4), as can be seen in Figure 1.

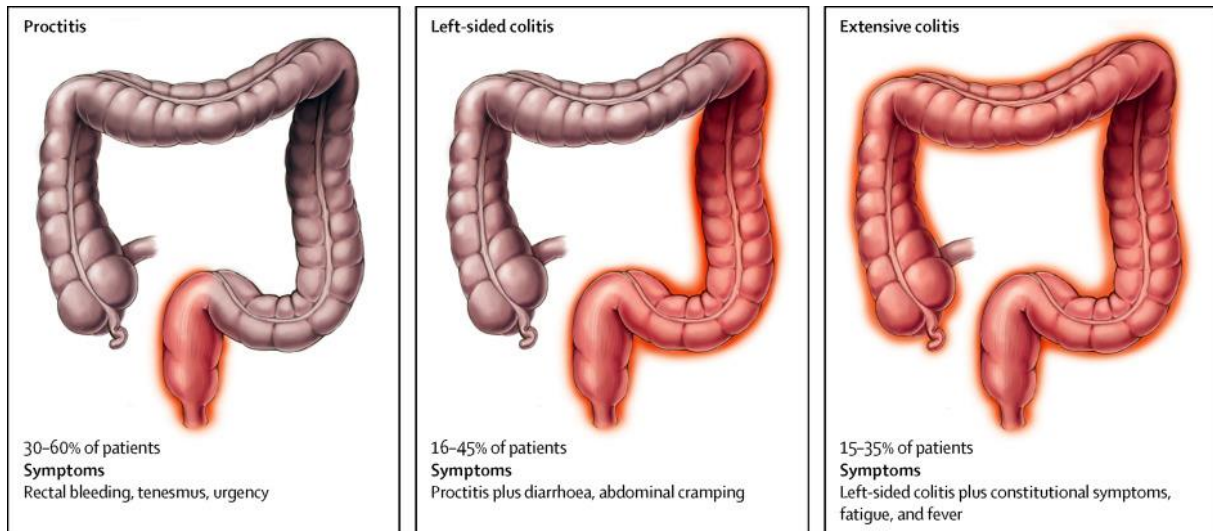


Figure 1. Illustration of the varying distribution of ulcerative colitis in the colon (7).

Today, individuals suffering from UC are commonly managed with immunosuppressive medication where the first-line therapy is 5-ASA drugs, then moving on to thiopurines, biological therapy and corticosteroids (2, 4, 7).

Patients with ulcerative colitis have an increased risk of developing colorectal cancer (CRC) (8). This risk of developing cancer increases with the duration of the disease and is between four to ten times greater than the risk of sporadic CRC in non-UC patients (9). As well as an increased risk, the age of onset is on average 20 years earlier for individuals with UC-associated colorectal cancer (9). The increased risk of cancer development is attributable both to the chronic inflammation and/or to the carcinogenic effect of immunosuppressing drugs (8). Other risk factors for developing UC-related colorectal cancer include diagnosis at young age, long disease duration, primary sclerosing cholangitis (PSC), the extent of the disease and family history of CRC (8-10).

2.1.2 Colectomy

Surgical treatment for ulcerative colitis, colectomy, is relevant when a patient has a therapy-refractory illness. For example, when a patient requires corticosteroids to keep the inflammation under control or simply not responding well enough to medical treatment, with impaired bowel function due to an extensive inflammation. Colectomy is also indicated when a patient with UC is suspected to have dysplasia or a malignant tumor (2). Acute severe ulcerative colitis can be life-threatening and requires intensive treatment at hospital, often with intravenous steroids and salvage therapy with immunosuppressants. Acute colitis, which comes with a risk of toxic colonic dilation or even perforation, that does not respond to salvage therapy is the most common indication for emergency colectomy (11, 12). During the course of the disease approximately 20% of UC patients will suffer from a flare of acute severe ulcerative colitis (3). The risk of needing surgical treatment for ulcerative colitis is about 20% 10 years after diagnosis and 30% after 25 years (2). Due to progress in biological therapy these numbers are decreasing (13).

2.1.3 Reconstructive Surgery

After the initial colectomy, where the colon is removed, patients may be offered reconstruction in order to achieve intestinal continuity. For many years ileal pouch-anal anastomosis (IPAA) has been the most common type of reconstructive surgery (7, 12, 14), but besides the IPAA there is also the choice of ileorectal anastomosis (IRA) (2, 15, 16). An IPAA is created by forming a reservoir of the distal ileum and connecting it to the anal canal (2). IPAA has a good functional outcome and offers patients a better sense of control of bowel movements (2, 11). However, up to 50% of patients with an IPAA will experience an

inflammation in the reservoir, pouchitis, at some time and 10-15% will have more chronic pouchitis with increased number of stool passages, as well as increased risk of leakage (7, 14, 17). Further, due to the extensive surgery IPAA is associated with reduced fertility, impotence and retrograde ejaculation (12, 14). In the case of IRA the distal ileum is reconnected with the rectum (2). Patients selected for this type of reconstructive surgery usually have a rectum with minimal signs of inflammation and respond well to local medical treatment and a good sphincter tonus (11). However, the construction of an IRA is a less complex procedure with a lower risk of damage to pelvic structures, sparing patients of the risk of sexual dysfunction (18). With this in mind, IRA might be a good option for women of reproductive age or for patients willing to undergo close surveillance of the rectum instead of facing potential complications of an IPAA (14, 18, 19). However, the remaining rectum retains the risk of cancer development and the patients need to be under annual surveillance. This is of course a great concern and a reason why many surgeons advocate in favor of IPAA (19).

2.1.4 Laparoscopic Surgery

During the 1900s colectomies were almost exclusively performed by open laparotomy.

However, since the progression of the laparoscopic technique in the late 20th century, it is a procedure commonly used today (20).

Colectomy performed as laparoscopy is a minimally invasive technique (20). It may result in positive cosmetic results as well, and studies suggest a lower complication rate (21). It has been reported that patients experiences a reduction in postoperative pain, shorter hospital stays with faster recovery and therefore potentially improved quality of life compared to open

surgery (20). Theoretically, with less adhesions after laparoscopic surgery (20), minimally invasive surgery may facilitate future laparoscopic reconstructive surgery for the patient.

At Sahlgrenska University Hospital, the laparoscopic surgical technique for colectomies was put to practice during the later part of this study.

2.2 Hypothesis

The hypothesis of this study is that the patients operated on with open surgical approach will have an increased risk of postoperative complications after colectomy compared to those operated on with the laparoscopic technique. In regard to reconstructive surgery, it is our belief that patients of a younger age have a higher chance of receiving reconstructive surgery compared to those of older age.

2.3 Aim of study

The aim of this study was to examine the rate of postoperative complications after open versus laparoscopic colectomy in patients with ulcerative colitis. More specifically if there were any difference in risk of having postoperative complications between open surgery and laparoscopic approach, within 90 days of the operation.

Secondly, our aim was to examine the number of patients that received reconstructive surgery and what type of reconstruction (IPAA or IRA), and to study whether there were factors affecting the chance of having reconstructive surgery.

3. METHOD

3.1 Patient cohort

Patients included in the study had been diagnosed with ulcerative colitis and received surgical treatment with colectomy at Sahlgrenska University Hospital.

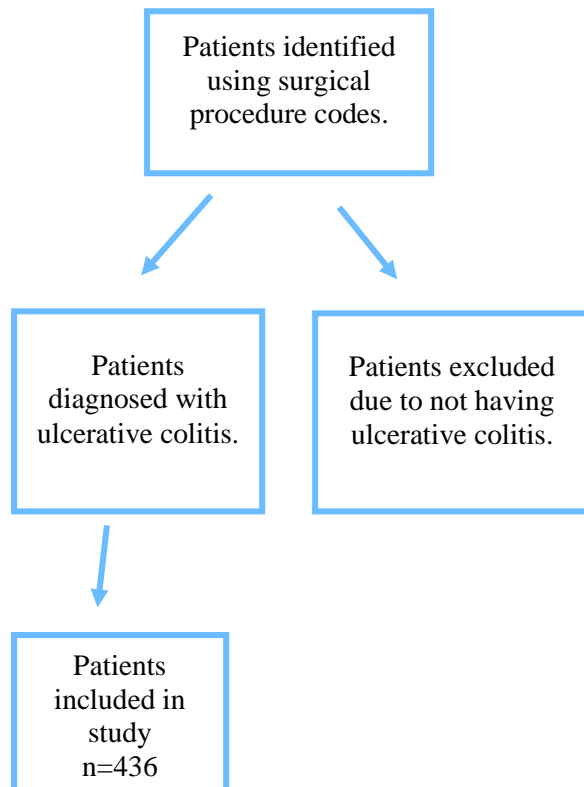


Figure 1. Flow chart for inclusion of patients

The study was set to include patients who had received a colectomy during the period January 1st 2000 and December 31st 2019. Patients who underwent a colectomy within this timeframe were identified using surgical procedure codes; JFH00, JFH01, JFH10, JFH11, JFH20, JFH30, JFH31, JFH33, JFH40 and JFH96.

Excluded were patients with no UC diagnosis, who had a colectomy for other reasons.

3.2 Data collection procedures

Surgical procedure codes were put into databases Operett and Orbit and a list of patients treated with colectomy at Sahlgrenska University Hospital between January 1st 2000 and December 31st 2019 was identified. Further information and data - such as date of colectomy,

open/laparoscopic surgery, complications classified according to the Clavien-Dindo classification (22), whether the patients received reconstructive surgery, as well as patients' age and gender were collected from medical records obtained in the database Melior and put into a case report form (CRF).

3.3 Definition of endpoints

The primary endpoint of this study was to assess the rate of 90-days postoperative complications according to Clavien-Dindo classification (22), and to compare the risk of complications after open versus laparoscopic colectomy. Secondary endpoint was to assess whether the patients had received reconstructive surgery within the time of follow-up of the study. Patients included in the study were considered to be in the postoperative period for 90 days after surgery, with the day of surgery as index. All complications within this time were noted. Patients were followed from date of admission until the date of reconstructive surgery, death, or December 31st 2019.

The Clavien-Dindo scale is a grading system for postoperative complications, that can be used for documenting morbidity and mortality after surgery (23). The scale consists of 5 different severity grades, with grade I being minor deviations from the normal postoperative course and grade V being the death of a patient (22). In this study the complications were graded as minor I-IIIa meaning that patients could need surgical or endoscopic intervention without general anesthesia, and major meaning grade IIIb, - where there is need for general anesthesia, or higher (22).

When defining minor postoperative complications, it was decided that pain complications was receiving at least two pain relieving drugs in 24 hours, in addition to the basic pain management plan. Nausea was considered a complication if the patient vomited more than one time or needed antiemetic drugs more than once within 24 hours. In the case of more severe nausea where the patient needed a nasogastric tube as treatment, it was considered to be a Clavien-Dindo grade II.

Concerning reconstructive surgery, patients were categorized into subgroups regarding if they received reconstructive surgery or not as well as if they had IRA, IPAA or remained with an ileostomy.

3.4 Statistical methods

Statistical analyses were made in SPSS 27. The characteristics of the cohort was summarized descriptively based on reconstructive surgery in order to create table 1. Variables included in the multivariate analysis were chosen based on knowledge of factors that may affect the outcome of surgery or suspected to play a role in the risk of having postoperative complications as well as the chance of receiving reconstructive surgery. In order to include the variables, they needed to be accessible through medical journals.

The chosen variables were first included in a univariate logistic regression analysis, and those which received $p < 0.2$ were further included in the multivariate logistic regression analysis. Considered a significant result after the multivariate analysis was $p < 0.05$.

The results were presented as odds ratio (OR), with 95% confidence intervals (CI) and p-values. Odds can be used to represent the probability for an event to occur to the probability

that it does not (24). For example, the odds for something to occur will be estimated by taking a group exposed to a factor divided by a group not exposed to that factor, which will be considered a reference group. The result, OR, will be presented as a ratio to denominator 1. When an OR is <1 , it means that the exposure to a factor reduces the risk of an event. Similarly, an OR that is >1 indicates that the exposure to a factor will increase the risk (25).

3.6 Ethical considerations

Ethical considerations have been central throughout the course of this study. All patients included in this project have been anonymized and cannot be identified by characteristics in the study. Since it is a retrospective study, no patients were at risk of receiving different treatment. However, none of the patients were asked before inclusion and could not give informed consent to be included in the study and there is always a risk of intrusion into an individual's privacy by going through medical records without their knowledge. Obtaining data by going through medical records may also come with a risk of unintentional distribution of classified material and is a risk which must be put into perspective and compared to the benefit of the study. Approval to conduct this study was given by the Regional Ethics Board in Gothenburg, dnr 2021-00380.

4. RESULTS

As demonstrated in Table 1, the study included a total of 436 patients, among which 148 (34%) were women and 288 (66%) were men. The median age of all patients that underwent a colectomy was 39 years. Median ages for those who received an IPAA, IRA or permanent ileostomy was 37, 31 and 54 years, respectively. Patients were rather equally divided, with 34.9% having received an IPAA, 32.8% an IRA and 32.3% remaining with an ileostomy. In total, 295 patients received reconstructive surgery, while 141 remained with a permanent ileostomy.

The majority of patients (85%) had their colectomy performed with open surgery, and 63% of the operations were elective surgeries. The reason for colectomy was refractory disease in 82,3% and suspected malignancy in 17.7%.

About 12% (n= 55) of the individuals included in this cohort were diagnosed with PSC, compared to 1-5% of ulcerative colitis patients in general (26).

The frequency of reconstructive surgery after colectomy were equal for men and women (69% and 64% respectively), especially within the younger age groups.

Table 1. Descriptive characteristics of the cohort divided into groups based on reconstructive surgery. All ages listed in Table 1 are in years and refer to age at time of colectomy.

	All, n (%)	IPAA	IRA	Ileostomy (no reconstruction)
All	436	152 (34.9%)	143 (32.8%)	141 (32.3%)
Median age (years)	39	37	31	54
Women ¹	148 (34.0%)	49 (33.1%)	46 (31.1%)	53 (35.8%)
15-29 ²	39 (26.4%)	14 (36.0%)	21 (53.8%)	4 (10.2%)
30-43 ²	48 (32.4%)	18 (37.5%)	16 (33.3%)	14 (29.2%)
44-58 ²	37 (25.0%)	15 (40.5%)	5 (13.5%)	17 (46.0%)
≥59 ²	24 (16.2%)	2 (8.3%)	4 (16.7%)	18 (75.0%)
Men ¹	288 (66.0%)	103 (35.8%)	97 (33.7%)	88 (30.5%)
15-29 ³	73 (25.3%)	28 (38.3%)	37 (50.7%)	8 (11.0%)
30-43 ³	94 (32.6%)	41 (43.6%)	32 (34.0%)	21 (22.4%)
44-58 ³	67 (23.3%)	29 (43.2%)	16 (24.0%)	22 (32.8%)
≥59 ³	54 (18.8%)	5 (9.3%)	12 (22.2%)	37 (68.5%)
Type of surgery				
Laparoscopic	66 (15.1%)	26 (39.4%)	24 (36.4%)	16 (24.2%)
Open	362 (83.0%)	126 (34.8%)	118 (32.6%)	118 (32.6%)
Converted to open	8 (1.9%)	0 (0%)	1 (12.5%)	7 (87.5%)
Emergency	161 (36.9%)	56 (34.8%)	61 (37.9%)	44 (27.3%)
Planned	275 (63.1%)	96 (34.9%)	82 (29.8%)	97 (35.3%)
Reason for surgery *				
Therapy-refractory disease	359 (82.3%)	120 (33.4%)	133 (37.1%)	106 (29.5%)
Suspected malignancy	77 (17.7%)	32 (41.6%)	10 (12.9%)	35 (45.5%)
Primary sclerosing cholangitis **				
Yes	55 (12.6%)	20 (36.4%)	14 (25.4%)	21 (38.2%)
No	381 (87.4%)	132 (34.6%)	129 (33.9%)	120 (31.5%)

Abbreviations: IPAA – Ileal pouch-anal anastomosis, IRA – Ileorectal anastomosis

¹: All women/men included in the study, per centage calculated from total amount of patients in study.

²: Age groups divided from all women in the study. Per centages based on all women in age group.

³: Age groups divided from all men in the study. Per centages based on all men in age group.

*: Reason stated in medical records, if no reason was stated “therapy-refractory disease” was assumed.

** : Defined as PSC diagnosis at time of colectomy or reconstructive surgery.

As seen in table 2, there was no statistically significant association with increased risk of complications after open compared to laparoscopic colectomy. Neither was there any association between any of the other variables chosen and extent of complications after colectomy.

Table 2. Univariate and multivariate logistic regression analysis for having postoperative complications \geq Clavien-Dindo IIIb, regarded as severe complications. Results are presented as Odds ratios.

Variable	Univariate analysis			Multivariate analysis		
	Odds Ratio	p-value	(95% CI)	Odds ratio	p-value	(95% CI)
Gender						
Male	1 (ref)					
Female	1.122	0.696	0.630-1.996			
Age at colectomy						
15-29	1 (ref)					
30-43	1.176	0.673	0.554-2.499			
44-58	1.088	0.840	0.479-2.470			
\geq 59	1.523	0.320	0.664-3.493			
Type of surgery						
Open	0.835	0.632	0.399-1.746			
Laparoscopy	1 (ref)					
Emergency	1.242	0.451	0.707-2.181			
Planned	1 (ref)					
Reason for surgery¹						
Therapy-refractory disease	1 (ref)					
Suspected malignancy	1.778	0.082	0.930-3.398			
Primary sclerosing cholangitis²						
Yes	0.775	0.577	0.316-1.899			
No	1 (ref)					

¹: Reason stated in medical records, if no reason was stated “therapy-refractory disease” was assumed.

²: Defined as PSC diagnosis at time of colectomy or reconstructive surgery

Using the backward stepwise regression model, the only variable significant enough to be included in the multivariate analysis was “reason for surgery” were suspected malignancy presented an OR of 1.778 (CI= 0.930-3.398) and a p-value of 0.082 – which in the end is not considered a significant result, and one variable is not enough to be included in a multivariate analysis.

Table 3. Table comparing postoperative complications in patients with open and laparoscopic surgery.

Postoperative complications:	Type of surgery		
	Open surgery (%)	Laparoscopic surgery (%)	Total (%)
Clavien-Dindo ≥IIIb	48 (82.8%)*	10 (17.2%)*	58 (13.3%)**
Clavien-Dindo <IIIb	264 (87.1%)*	39 (12.9%)*	303 (69.5%)**
No complications	58 (77.3%)*	17 (22.7%)*	75 (17.2%)**

* Calculated as a per centage of the total amount of patients displayed in the same row of this table.

** Calculated as a per centage of the total amount of patients included in this study (n=436).

Table 3 demonstrates the amount of patients who had either major, minor or no complications among those who had open colectomy as well as laparoscopic colectomy.

Among the patients who underwent colectomy, 13.3% (n=58) suffered from major complications. Out of the 58, 44.8% (n=26) ended up with a permanent ileostomy, 29.3% (n=17) had an IPAA and 25.9% (n=15) an IRA. In comparison to those with grade IIIa or less (86.7%, n=378) where 30.4% (n=115) received a permanent ileostomy, 35.7% (n=135) an IPAA and 33.9% (n=128) an IRA. These results suggest that a larger population who experience complications of Clavien-Dindo grade IIIb or more end up with a permanent ileostomy.

Table 4. Univariate and multivariate logistic regression analysis for having reconstructive surgery after colectomy. Results are presented as Odds ratios.

Variable	Univariate analysis			Multivariate analysis		
	Odds Ratio	p-value	(95% CI)	Odds ratio	p-value	(95% CI)
Gender						
Male	1 (ref)					
Female	1.268	0.267	0.834-1.928			
Age at colectomy						
15-29	1 (ref)			1 (ref)		
30-43	2.726	0.006	1.340-5.545	2.574	0.01	1.252-5.291
44-58	5.000	0.001	2.438-10.256	4.512	0.001	2.137-9.528
≥59	19.928	0.001	9.212-43.109	18.176	0.001	8.263-39.984
Type of surgery						
Open	1.594	0.129	0.873-2.913	1.238	0.530	0.635-2.412
Laparoscopy	1 (ref)			1 (ref)		
Emergency	0.690	0.088	0.451-1.056	0.904	0.701	0.540-1.513
Planned	1 (ref)			1 (ref)		
Reason for surgery¹						
Therapy-refractory disease	1 (ref)			1 (ref)		
Suspected malignancy	1.989	0.007	1.203-3.288	1.263	0.441	0.697-2.289
Primary sclerosing cholangitis²						
Yes	1.343	0.323	0.748-2.412			
No	1 (ref)					
Postoperative complications						
Clavien-Dindo <IIIb	1 (ref)			1 (ref)		
Clavien-Dindo ≥IIIb	1.858	0.031	1.059-3.259	1.848	0.057	0.981-3.479

¹: Reason stated in medical records, if no reason was stated “therapy-refractory disease” was assumed.

²: Defined as PSC diagnosis at time of colectomy or reconstructive surgery

In total, 200 out of 288 men had reconstructive surgery (69.4%) and 95 out of 148 women (64.2%). As seen in table 4, gender was not statistically significant when it comes to receiving reconstructive surgery after colectomy. However, age was a significantly associated with the

chance of having reconstruction or not. As demonstrated in the multivariate analysis (in Table 4) the risk of having a permanent ileostomy increased with age, 15-29 compared to 59 or older, OR 18.176 (CI=8.263-39.984), p=0.001.

The univariate analysis (Table 4) show a significant difference between refractory disease and suspected malignancy. The odds were higher for having reconstructive surgery in patients with suspected malignancy, - OR 1.989 (CI=1.203-3.288), p=0.007. However, when included in the multivariate analysis with other variables this significance diminished.

Similarly, patients who experienced major complications had a decreased chance of having reconstructive surgery, OR 1.858 (CI=1.059-3.259), p=0.031.

Nonetheless, when included in the multivariate analysis no significant difference was found, OR 1.848 (CI=0.981-3.479), p=0.057, which is just on the verge of still being considered a significant result. When looking at type of surgery, it can be observed that both surgical technique (open or laparoscopic) and whether it was planned or emergent were significant enough to be included in the multivariate analysis.

5. DISCUSSION

Four hundred and thirty-six individuals were found to have had colectomy due to ulcerative colitis between the years 2000-2019 at Sahlgrenska University Hospital. Although the incidence of ulcerative colitis among men and women is almost equal, near two thirds of the operated patients were men. Open colectomy occurred in 85% of cases, compared to laparoscopy in 15%. The most common indication for colectomy was therapy-refractory disease (82%). No increased risk for major complications was seen between open surgery compared to laparoscopic surgery as hypothesized. Increased age was significantly associated with a decreased chance of having reconstructive surgery after colectomy.

As previously stated, a hypothesis for this study was that open surgical technique would present a higher risk for developing postoperative complications. Our study could not verify this hypothesis. In this study, 13% of patients were observed to have suffered from major complications. Schineis et al. reported Clavien-Dindo III complications in 8% of patients, however over 87% of these operations were performed laparoscopically (27) compared to 15% here. Additionally, there was no distinction made between Clavien-Dindo IIIa and IIIb in their study. Furthermore, other studies have also shown that open surgery has an increased morbidity rate compared to laparoscopy (28). In our study there was a higher percentage of patients undergoing open surgery (85%), rendering a comparison to laparoscopy difficult.

As this is a retrospective study ranging from 2000-2019 and laparoscopic surgery was introduced as a technique for colectomy at Sahlgrenska University Hospital during the later years of this study, the surgeons' learning curve could be a reason for there not being a difference. Besides from complications there are other advantages of laparoscopic colectomy

such as formation of fewer adhesions (20), making it easier to reconstruct bowel continuity.

Other advantages is shorter hospital stay and faster recovery (20).

Among the findings, older age contributes as a risk factor for not having reconstructive surgery, as previously reported (13). In this study we found a total of 295 patients who received restorative surgery, which is equal to 67.6%. In a Swedish study from 2015, Nordenvall et al. found that 43% of patients underwent reconstructive surgery (13). Similarly, a study comparing reconstruction rates in England and Sweden, showed that only about one third of patients received reconstructive surgery in England compared to nearly 50% in Sweden (16). Our study was conducted at a university hospital and earlier reports show that reconstructive rates are higher in high-volume hospitals (13, 16). Furthermore, there are plans to conduct a larger-scale study in the whole Västra Götaland to assess whether there is a difference in receiving reconstructive surgery after having colectomy in a larger city compared to rural areas.

It has to be noted that the study population consisted of 66% men and 34% women, not representable to the ulcerative colitis population where men and women are more equally afflicted (4, 7). Similar numbers can be seen in a study by Nordenvall et al., where 39% were women and 61% men (13) and in a Swiss study where 64% of those who underwent colectomy were men and 36% women (29). This could potentially mean that less women than men are operated on, and if so, why is that?

5.1 Strengths and limitations

The strength of this study is that it is a large retrospective cohort study including more than 400 individuals. The retrospective design makes it easy and time-effective to collect all the data needed as it was available in the medical records. By using surgical procedure codes in the databases Operett and Orbit, patients were identified consecutively within the set time frame and all patients were included with no other inclusion criteria than being diagnosed with UC.

As this is a retrospective cohort study, there is a risk of bias when selecting patients for open versus laparoscopic colectomy. In cases where the operation was considered challenging it was likely planned as an open laparotomy ahead of time. This differs from randomized controlled trial (RCT) studies, where the only difference among the cohorts is the factor you wish to examine. A retrospective design can be beneficial when analyzing multiple outcomes, as well as more time and cost-effective compared to prospective cohort studies. However, RCT studies offers more control over exposures in the cohorts producing a reliable result.

The retrospective design can also be considered as a weakness. Some data may not be available for all patients, and therefore certain statistics cannot be measured. Further, it is not possible to control exposures or assess different outcomes of the patients included.

Consequently, you have to rely on medical documentation that is produced by a variety of people, and therefore documentation may vary. This could possibly lead to misinterpretations and a risk of discrepancies when going back and searching for information in medical journals.

In comparison to collecting data from questionnaire's where the patients themselves have to estimate their answers, medical records provide more objective information without bias. This could on the other hand, also be regarded as a weakness considering that we have no data representing the patients' experiences.

To be considered, this study included patients who had their colectomy between the years 2000 and 2019. During these years we can expect many changes in the areas of surgical techniques and treatments, as could be seen in this study where for example the majority of laparoscopic operations occurred in the later years.

The variables included in our multivariate analysis for the study were variables thought to be of importance. We could however not find any significance between the variables and risk of complications. Although, this could mean that the cohort is not large enough to detect a potentially significant result. As could be in the case of type-II errors where the null hypothesis fails to be rejected even though it is not true (30). This could indicate that there is a difference in the risk of having complications when comparing open and laparoscopic colectomy, as previous studies have implied, only the study population was not large enough to find it. There are also type-I statistical errors to be considered, when the null hypothesis is rejected even though it is false (30). Both these errors may occur in this study and can not be entirely avoided. However, including a larger amount of individuals will decrease the risk as it is more likely to resemble the population (30).

When studying outcomes there is also a possibility that one may appear significant simply by chance and not because it is genuinely significant. Performing a large number of statistical

test will increase the risk (31). False negative or positive outcomes may also occur due to bias, though these are very difficult to detect (30).

We made no corrections for multiple testing in this study.

5.2 Conclusion

In conclusion, a patient's age plays a large roll on the chance of having reconstructive surgery after colectomy. Some factors alone may influence the likelihood of restorative surgery, but when included with several commonly occurring factors, significance was not found.

Nonetheless, this study found a greater overall reconstruction rate when compared to the general results in Sweden.

Unlike previous studies, we found no increased risk of postoperative complications in patients who had open surgery.

6. POPULÄR VETENSKAPLIG SAMMANFATTNING

Examensarbete 30 hp, Läkarprogrammet

Ulcerös kolit: komplikationer och omfattning av rekonstruktiv kirurgi efter öppen respektive laparoskopisk kolektomi på Sahlgrenska Universitetssjukhuset – en retrospektiv kohortstudie.

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Varje år drabbas ca 12–14/100 000 individer av ulcerös kolit, en inflammatorisk tarmsjukdom som karaktäriseras av ett kroniskt recidiverande förlopp med symtom såsom blodiga diarréer, buksmärta, frekventa tarmtömningar och generaliserad trötthet som en följd av den inflammatoriska reaktionen. Generellt behandlas ulcerös kolit i första hand med medicinsk behandling, men för upp till 20% kan det bli aktuellt med kirurgisk behandling i form av kolektomi. Kirurgi är oftast indicerat då patienten inte längre svarar adekvat på medicinsk behandling, blivit beroende av steroid-behandling eller har en hotande cancer.

Efter kolektomi kan patienterna erbjudas rekonstruktiv kirurgi i två varianter – bäckenreservoar (IPAA), där rektum tas bort och man skapar en reservoar av den sista delen av tunntarmsslyngan som sedan passas in där rektum tagits bort. Alternativ nummer två är en ileorektal anastomos (IRA) där ändtarmen sparas för att kopplas ihop med resterande tunntarm för att uppnå tarmkontinuitet.

Målet med denna studie har varit att undersöka komplikationer som uppstår inom 90 dagar efter öppen respektive laparoskopisk kolektomi och i vilken omfattning dessa patienter erhåller rekonstruktiv kirurgi.

Totalt 436 patienter inkluderades i studien och dessa hade diagnosticerats med ulcerös kolit samt opererats med kolektomi mellan januari 2000 och december 2019 på Sahlgrenska Universitetssjukhuset. Komplikationerna klassificerades enligt Clavien-Dindo, där IIIb ansågs vara en allvarlig komplikation samt relevant för studien. Patienterna grupperades utefter om de fått rekonstruktion, om den var i form av bäckenreservoar, ileorektal anastomos eller om de hade kvar sin ileostomi.

Vi fann ingen statistiskt signifikant skillnad i risken för komplikationer mellan öppen och laparoskopisk kolektomi, som var hypotesen. Däremot har tidigare studier visat en ökad morbiditet efter öppen kolektomi jämfört med laparoskopisk. Åldern var en signifikant faktor associerad till minskad risk för rekonstruktiv kirurgi efter kolektomi. Andra studier har visat en rekonstruktionsgrad på ca 50% efter kolektomi i Sverige. I denna studie fann vi att 295 patienter fick antingen en IRA eller IPAA efter sin kolektomi, vilket motsvarar ca 67%.

Studien genomfördes på ett universitetssjukhus och som tidigare studier visat så är rekonstruktionsgraden högre på sjukhus med stor volym av dessa operationer. Vidare fann vi ingen koppling mellan de förutbestämda faktorerna och en ökad risk att utveckla postoperativa komplikationer.

Det skulle kunna förklaras av det faktum att det är en retrospektiv kohortstudie som sträcker sig mellan åren 2000–2019, där den laparoskopiska tekniken främst började användas för kolektomi på Sahlgrenska Universitetssjukhuset vid slutet av studieperioden.

Vidare så innehöll studien 66% män och 34% kvinnor, vilket inte representerar den generella utbredningen som är mer jämn. Detta skulle kunna tala för att fler män än kvinnor blir kolektoerade, om så är fallet, varför?

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References

1. Ludvigsson JF, Andersson M, Bengtsson J, Eberhardson M, Fagerberg UL, Grip O, et al. Swedish Inflammatory Bowel Disease Register (SWIBREG) – a nationwide quality register. *Scandinavian Journal of Gastroenterology*. 2019;54(9):1089-101.
2. Pålman L, Dabrosin Söderholm J. Kirurgi. In: Bertil H, Ulf H, editors. 8th ed. Stockholm: Liber; 2013. p. 311-6.
3. Hindryckx P, Jairath V, D'Haens G. Acute severe ulcerative colitis: from pathophysiology to clinical management. *Nature Reviews Gastroenterology & Hepatology*. 2016;13(11):654-64.
4. Simrén M, Lindgren S. Medicin. In: Lindgren S, Engström-Laurent A, Karason K, Tiensuu Janson E, editors. *Medicin*. 2nd ed. Lund: Studentlitteratur; 2017. p. 498-520.
5. Silva BCD, Lyra AC, Rocha R, Santana GO. Epidemiology, demographic characteristics and prognostic predictors of ulcerative colitis. *World Journal of Gastroenterology*. 2014;20(28):9458-67.
6. Feuerstein JD, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. *Mayo Clinic Proceedings*. 2017;92(7):1088-103.
7. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel J-F. Ulcerative colitis. *The Lancet*. 2017;389(10080):1756-70.
8. Annese V, Beaugerie L, Egan L, Biancone L, Bolling C, Brandts C, et al. European Evidence-based Consensus: Inflammatory Bowel Disease and Malignancies. *J Crohns Colitis*. 2015;9(11):945-65.
9. Yashiro M. Ulcerative colitis-associated colorectal cancer. *World Journal of Gastroenterology*. 2014;20(44):16389.
10. Fumery M, Singh S, Dulai PS, Gower-Rousseau C, Peyrin-Biroulet L, Sandborn WJ. Natural History of Adult Ulcerative Colitis in Population-based Cohorts: A Systematic Review. *Clinical Gastroenterology and Hepatology*. 2018;16(3):343-56.e3.
11. Øresland T, Bemelman WA, Sampietro GM, Spinelli A, Windsor A, Ferrante M, et al. European evidence based consensus on surgery for ulcerative colitis. *J Crohns Colitis*. 2015;9(1):4-25.
12. Peyrin-Biroulet L, Germain A, Patel AS, Lindsay JO. Systematic review: outcomes and post-operative complications following colectomy for ulcerative colitis. *Alimentary Pharmacology & Therapeutics*. 2016;44(8):807-16.
13. Nordenvall C, Myrelid P, Ekbom A, Bottai M, Smedby KE, Olén O, et al. Probability, rate and timing of reconstructive surgery following colectomy for inflammatory bowel disease in Sweden: a population-based cohort study. *Colorectal Disease*. 2015;17(10):882-90.
14. Andersson P, Ouml, Derholm JD. Surgery in Ulcerative Colitis: Indication and Timing. *Digestive Diseases*. 2009;27(3):335-40.
15. Nordenvall C, Olén O, Nilsson PJ, Ekbom A, Bottai M, Myrelid P. The Fate of Reconstructive Surgery Following Colectomy for Inflammatory Bowel Disease in Sweden: A Population-based Cohort Study. *Journal of Crohn's and Colitis*. 2016;10(10):1165-71.
16. Worley G, Nordenvall C, Askari A, Pinkney T, Burns E, Akbar A, et al. Restorative surgery after colectomy for ulcerative colitis in England and Sweden: observations from a comparison of nationwide cohorts. *Colorectal Disease*. 2018;20(9):804-12.
17. Ng K-S, Gonsalves SJ, Sagar PM. Ileal-anal pouches: A review of its history, indications, and complications. *World Journal of Gastroenterology*. 2019;25(31):4320-42.

18. Scoglio D. Surgical treatment of ulcerative colitis: Ileorectalvsileal pouch-anal anastomosis. *World Journal of Gastroenterology*. 2014;20(37):13211.
19. Andersson P, Norblad R, Söderholm JD, Myrelid P. Ileorectal anastomosis in comparison with ileal pouch anal anastomosis in reconstructive surgery for ulcerative colitis — a single institution experience. *Journal of Crohn's and Colitis*. 2014;8(7):582-9.
20. Chang GJ, Nelson H. Laparoscopic colectomy. *Current Gastroenterology Reports*. 2005;7(5):396-403.
21. Hata K, Kazama S, Nozawa H, Kawai K, Kiyomatsu T, Tanaka J, et al. Laparoscopic surgery for ulcerative colitis: a review of the literature. *Surgery Today*. 2015;45(8):933-8.
22. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240(2):205-13.
23. Bolliger M, Kroehnert JA, Molineus F, Kandioler D, Schindl M, Riss P. Experiences with the standardized classification of surgical complications (Clavien-Dindo) in general surgery patients. *European Surgery*. 2018;50(6):256-61.
24. Bland JM. Statistics Notes: The odds ratio. *BMJ*. 2000;320(7247):1468-.
25. Andrade C. Understanding Relative Risk, Odds Ratio, and Related Terms: As Simple as It Can Get. *The Journal of Clinical Psychiatry*. 2015;76(07):e857-e61.
26. Nordenvall C, Olén O, Johan Nilsson P, Ekbohm A, Bottai M, Myrelid P, et al. Restorative Surgery in Patients With Primary Sclerosing Cholangitis and Ulcerative Colitis Following a Colectomy. *Inflammatory Bowel Diseases*. 2018;24(3):624-32.
27. Schineis C, Lehmann KS, Lauscher JC, Beyer K, Hartmann L, Margonis GA, et al. Colectomy with ileostomy for severe ulcerative colitis-postoperative complications and risk factors. *International Journal of Colorectal Disease*. 2020;35(3):387-94.
28. Kothari P, Congiusta DV, Merchant AM. Laparoscopic versus open colectomy: the impact of frailty on outcomes. *Updates in Surgery*. 2019;71(1):89-96.
29. Parragi L, Fournier N, Zeitz J, Scharl M, Greuter T, Schreiner P, et al. Colectomy Rates in Ulcerative Colitis are Low and Decreasing: 10-year Follow-up Data From the Swiss IBD Cohort Study. *Journal of Crohn's and Colitis*. 2018;12(7):811-8.
30. Banerjee A, Chitnis UB, Jadhav SL, Bhawalkar JS, Chaudhury S. Hypothesis testing, type I and type II errors. *Ind Psychiatry J*. 2009;18(2):127-31.
31. Andrade C. Multiple Testing and Protection Against a Type 1 (False Positive) Error Using the Bonferroni and Hochberg Corrections. *Indian Journal of Psychological Medicine*. 2019;41(1):99-100.