Postoperative Morbidity After Iterative Ileocolonic Resection for Crohn's Disease: Should we be Worried? A Prospective Multicentric Cohort Study of the GETAID Chirurgie

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ABSTRACT

Background and Aims

To compare perioperative characteristics and outcomes between primary ileocolonic resection (PICR) and iterative ileocolonic resection (IICR) for Crohn's disease.

Methods

From 2013 to 2015, 567 patients undergoing ileocolonic resection were prospectively included in 19 centers of the GETAID chirurgie group. Perioperative characteristics and postoperative results of both groups (431 PICR, 136 IICR) were compared. Uni- and multivariate analyses of the risk factors of overall 30-days postoperative morbidity was carried out in the IICR group.

Results

IICR patients were less likely to be malnourished (27.2% vs 39.9%, p=0.007), had more stricturing forms (69.1% vs 54.3% p=0.002) and less perforating disease (19.9% vs 39.2%, p<0.001). Laparoscopy was less commonly used in IICR (45.6% vs 84.5%, p<0.01) and associated with increased conversion rates (27.4% vs 14.6%, p=0.012). Overall postoperative morbidity was 36.8% in the IICR group and 26.7% in the PICR (p=0.024). There was no significant difference between IICR and PICR regarding septic intraabdominal complications, anastomotic leakage (8.8% vs 8.4%) and temporary stoma requirement. IICR patients more likely presented with non-infectious complications and ileus (11.8% vs 3.7%, p<0.001). Uni- and multivariate analyses did not identify specific risk factors of overall postoperative morbidity in the IICR group.

Conclusions

Surgery for recurrent CD is associated with a slight increase of non-infectious morbidity (postoperative ileus) that mainly reflects the technical difficulties of these procedures. However, iterative ileocolonic resection remains a safe therapeutic option in patient with

recurrent Crohn disease since severe morbidity including anastomotic complications is similar to patients undergoing primary resection.

Keywords: Crohn's disease; recurrent disease; ileo-colic resection; morbidity

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INTRODUCTION

Despite increased use of immunosuppressive and anti-tumour necrosis factor (anti-TNF) treatments, approximately half of the patients presenting with Crohn's Disease (CD) will require surgery within 10 years after diagnosis. [1] The main location of CD is terminal ileum with or without involvement of the proximal colon. Thus, up to 75% of patients requiring abdominal surgery for CD will have ileal or ileocolic resection (ICR), among which 20 to 40% are performed within the first year after the diagnosis. [2,3] Operative indications include failed medical therapy, complicated CD (perforation, obstruction, hemorrhage) and neoplasia, as expressed in the 2018 ECCO-ESCP guidelines. [4] In some specific indications, surgical resection has been proved to be an effective alternative to medical treatment. Indeed, Ponsioen et al. showed that laparoscopic resection in patients with limited (< 40 cm), non-stricturing ileocecal CD is a reasonable alternative to infliximab therapy in terms of health-related quality of life. [5] However, surgical resection of the diseased bowel is not curative and postoperative recurrence remains a significant problem. [6] After ileocolic resection, endoscopic recurrence of CD arises in the neoterminal ileum in 30% of patients after 3 months and in up to 80% of patients after 1 year. Clinical recurrence has been reported to be as high as 20-30% at 1 year with a 10% increase in each of the subsequent years. [7] The probability of a second resection for recurrent disease is 7-25% at 5 years and 19-35% at 10 years. [8,9] Data of the literature are scarce concerning surgery for recurrent CD after previous intestinal resection and are mainly based on retrospective data. In a comparative study, surgery for recurrent CD showed higher morbidity rate, greater risk of postoperative intra-abdominal abscess and longer postoperative hospital stay. [10] Comparing to primary ileocolic resections for CD, laparoscopy for iterative ileocolic resection has also been proved to be a safe and feasible approach without differences in stoma creation, early postoperative morbidity and mortality, reoperation rates and inhospital stay. [11-14] However, no multicentric prospective study designed to specifically compare operative and

postoperative outcome between primary and iterative ileocolic resection for CD is currently available.

Thus, the aim of our study was to compare perioperative characteristics and outcomes between primary and iterative ileocolic resection in patients operated for ileocolic CD.

METHODS

Patients and data collection

This study was based on the previously published data of the GETAID chirurgie group cohort. [15] Briefly, all patients undergoing surgery for ileocolic CD at 19 French academic centers were prospectively included from September 2013, to September 2015. To summarize, the inclusion criteria were: age >18 years, ileocolic CD and elective or emergency intestinal resection. The patients who had surgery for CD limited to a perianal or a colonic location were excluded. For the present work, we also excluded patients who underwent isolated stricturoplasty or small bowel resections. Variables including demographics, disease type and severity, previous treatment of CD, number and type of previous resections for CD, intraoperative findings and surgical procedures were prospectively collected. This study was conducted according to the ethical standards of the institutional committee on human experimentation and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. [16]

Surgical procedure and postoperative outcome

The description of surgical procedures has been given in the previously published paper. [15] Briefly, a laparoscopic approach was proposed as the favored option whenever possible at all participating centers. The bowel planned for resection was extracted through a 5 to 6 cm incision in a right lower quadrant or midline incision. Conversion to open surgery was defined

as any unplanned incision or a planned incision that was made longer than necessary to extract the resected specimen and fashion of the anastomosis. The decision to fashion primary anastomosis or temporary ileocolostomy was made on a per-patient basis and left to the discretion of the surgeon, according to the preoperative clinical data and intraoperative findings. The in-hospital or 30-day postoperative morbidity and mortality were recorded prospectively starting from the date of the surgery. Postoperative morbidity was defined as any deviation from the normal postoperative course, graded according to the Dindo-Clavien classification. [17] Intraabdominal septic morbidity included anastomotic leakage with or without peritonitis, intraabdominal abscess and postoperative peritonitis. Moreover, the reoperation rate, length of hospital stay, and readmission rate were prospectively recorded.

Statistical analysis

Patients were divided into two groups, namely "primary ileocolic resection" (PICR) and "iterative ileocolic resection" (IICR). The quantitative and qualitative variables were expressed as the mean ± the standard deviation (SD), median (interquartile range), and frequency. For univariate comparisons between the PICR and IICR groups, the chi-squared test was used for categorical variables, while the Mann–Whitney U test was applied for continuous variables. The primary endpoint was the overall 30-day postoperative morbidity. To identify the risk factors of the overall postoperative morbidity, univariate and multivariate analyses were used to examine the relationship between the occurrence of postoperative morbidity and 49 variables related to the patient characteristics and comorbidities, the type and severity of the CD, preoperative treatment targeting CD, preoperative biological parameters, and intraoperative findings and surgical procedures. Denutrition was defined as BMI<18 kg/m^2, and/or weight loss> 10% of the body weight within 6 months before surgery and/or preoperative serum albumin <30 g/dL. The association of baseline parameters with postoperative morbidity was

first assessed using univariable Cox analyses, and then parameters with P values of less than 0.1 or clinically relevant variables known for their impact of postoperative morbidity were entered into a final multivariable Cox regression model.

A P value <0.05 was considered statistically significant. Statistics were performed using SPSS (Statistical Package for Social Science, IBM SPSS Statistics, Version 23 for Macintosh; IBM Corp., Armonk, NY, USA).

RESULTS

Preoperative characteristics and previous medical treatment (Table 1).

From September 1, 2013 to September 1, 2015, 567 patients underwent ICR. Four hundred and thirty-one underwent PICR (76%) and 136 (24%) underwent IICR. Denutrition was more frequent in the PICR group than in the IIRC group (39.9% vs. 27.2%, p=0.007). Thus, the proportion of patients receiving preoperative nutritional support was higher in the PICR group compared to the IICR patients (36.0% vs 25.7% respectively, p=0.028). The phenotype of CD according to Montreal/Vienna classification significantly differed between both groups (p<0.001). Indeed, perforating CD was more frequent in the PICR group (39.2% vs 19.9%) whereas stricturing CD was more frequent in the IICR group (69.1% vs 54.3%). Previous medical exposure within 6 and 3 months were similar in both groups.

Surgical procedures and intraoperative findings (Table 2).

Laparoscopic approach was less frequently used in the IICR group (45.6% vs 84.5, p<0.01) and the conversion rate was significantly higher (27.4% vs. 14.6%, p=0.012). As expected, internal fistula (25% vs. 37.6%, p=0.007) and abscesses (11% vs. 20.2%, p=0.013) were less frequent in the IICR group. Primary anastomosis was performed in 449 patients (79.2%) with a majority of stapled ileocolic anastomosis (59.2%, n=266), without statistical difference between both

groups. Mean operative time was statistically longer in the IICR group (155.9 ± 53.3 min vs. 138.9 ± 49.9 min, p=0.002).

Postoperative outcome (Table 2).

Overall postoperative morbidity (36.8% vs. 26.7%, p=0.024), non-infectious morbidity (20.6% vs 13.7%, p=0.052) and ileus (11.8%. vs. 3.7%, p<0.001) were significantly higher in the IICR group. However, postoperative length of stay was similar between both groups (10.2±23.0 in the PICR vs. 9.3±6.9 days in the IICR, p=0.499). There were no significant differences between intraabdominal septic complications, anastomotic leakage rate, severe postoperative complications and reoperation with or without stoma confection between both groups (table 2).

Four hundred and forty-nine patients underwent ICR with primary anastomosis.

We then compared postoperative outcomes in the subgroup with primary anastomosis between PICR (n=337, 75.1%) and IICR (n=112, 24.9%). Overall postoperative morbidity (38.4% vs. 25.8%, p = 0.011) and non-infectious morbidity (21.4% vs. 11.9%, p=0.012) were significantly higher in the IICR group. There were no significant differences in infectious morbidity, surgical site infections, intraabdominal septic complications, anastomotic leakage, severe postoperative complications and reoperation rate for complications between both groups.

We also conducted a subgroup analysis on patients with elective procedures (PICR n=385 & IICR n=130). We found the same differences in patients' characteristics. Laparoscopic approach was less frequently used for IICR (46.9% vs. 90.4%, p<0.001) with more conversions (27.9% vs. 13.8%, p=0.006). Again, overall morbidity was significantly increased in the IICR group (37.7% vs. 17.4%, p=0.015) but only the postoperative ileus was significantly increased in the IICR (11.5% vs. 2.4%, p<0.001).

Patients undergoing multiple IICR (Table 3).

Primary anastomosis was performed in the vast majority of the patients (82.4%) and its rate was not correlated with the number of previous resections (p=0.578). Concerning the postoperative outcome, there was a tendency for more frequent intraabdominal septic complications in patients undergoing a third ICR or more (6.2% vs. 15.4%, p=0.087). Overall postoperative morbidity, severe complications, reoperation rate for complications and length of stay were not different depending on the number of previous ICR.

Impact of case-volume on operative and postoperative outcomes (Table 4)

Mean ICR per center per year was 15.9 (±12.9), with 11.9 (±9.3) PICR per center per year and 4.0 (±4.1) IICR per center per year. There were no significant differences in terms of laparoscopic approach (p=0.282), overall postoperative morbidity (p=0.829) and length of hospital stay (p=0.297) according to the yearly case-volume of the centers (Table 4). However, there was a trend toward a lower conversion rate in high volume centers (22.0% vs. 46.2%, p=0.080).

Analyses of the risk factors of overall postoperative morbidity (Table 5)

The results of the univariate and multivariate analyses of the risk factors for overall postoperative morbidity in 136 patients undergoing iterative ileocolic resection for ileocolic CD are reported in Table 5. In the univariate analysis, previous ICR (p=0.041) and intraoperative bowel injury (p=0.062) were associated with a higher risk of overall postoperative morbidity. However, none of these parameters were statistically significant in the multivariate analysis (p=0.138 and p=0.999 respectively).

DISCUSSION

Our results confirm that surgery for recurrent CD slightly increases the risk of overall postoperative morbidity. This is explained by a more technically difficult procedure that usually lasts longer than primary surgery. This translates into a higher risk of non-infectious complications, especially ileus, whereas the risk of infectious complications and major morbidity is equivalent to primary surgery. Consequently, iterative ileocolonic resection remains a safe therapeutic option in patient with recurrent Crohn disease. However, although laparoscopy was feasible in 50% of the cases, IICR was technically more difficult. In this series, overall postoperative morbidity was increased in the IICR group but linked only to the postoperative ileus explained by the necessity of longer dissections and longer intraoperative durations. Indeed, the rate of AL and duration of hospitalization stay were similar in both groups.

In this prospective multicentric study, we included 136 IICR to 431 PICR within 3 years, which is, to our knowledge, the largest series in the literature. Only few previous studies focused on specific comparison between IICR and PICR. There were all retrospectives, unicentric with less than 80 patients undergoing iterative resections.[13,18,19] In their meta-analysis, Shigeta et al. evaluated the perioperative results of laparoscopy in 413 primary CD vs. 214 recurrent CD.[11] More specifically, this last study involved 350 PICR and 164 IICR, mostly included retrospectively, in monocentric studies, over a period of 19 years, meanwhile our patients were prospectively included in a shorter range of time which limited more efficiently several biases.

The patients of the IICR group were less frequently malnourished, necessitated less preoperative nutritional support but had more favorable preoperative biological parameters (CRP<10 g/L). This better preoperative nutritional status may reflect a less aggressive behavior of the CD. Indeed, the patients of the IICR group presented more frequently a stricturing behavior of CD, whereas the patients of the PICR group presented with penetrating CD. Previous series comparing digestive resection surgery for primary vs recurrent CD were similar

to ours. Indeed, except for Manser et al. [19] stricturing behavior of CD was more frequent in recurrent CD and obstructive bowel syndrome was the main indication for surgery in this group. [14,18,20,21] Stricturing behavior of CD has also been identified as an independent risk factor of surgical recurrence. [4] These differences reflect a better selection of patients before surgical resection and may explain the favorable results observed in this series.

The patients of the IICR group were older, with more patients > 65 years old. As in other studies, this difference is explained by a younger age at the diagnosis and a longer duration of the CD. [19,22]

As expert centers, the participating centers of this study performed laparoscopy as often as possible, according to the 2018 ECCO-ESCP recommendations. [4] In this study, laparoscopy was feasible in 45.6% of the IICR, which is comparable with the data of the literature. [10] However, laparoscopy in IICR was technically more difficult than in PICR, as evidenced by the higher conversion rate and the prolonged operative duration than in the PICR group. Moreover, we showed that feasibility of a laparoscopic approach was also hampered with the number of previous resections. Other studies showed similar results, as Goyer et al. who showed that laparoscopy for complex and recurrent CD was associated with longer operative time and increased risk of conversion. [14] We did not have the data concerning the surgical approach of the first resection and therefore it was impossible to identify the probability of being operated through a laparoscopic approach after an open surgery.

Overall morbidity was significantly higher in the IICR group (36.8% vs. 26.7%, p=0.024). Studies comparing IICR vs. PICR showed similar results. [18] This higher morbidity rate was explained by a higher rate of postoperative ileus related to intraoperative adherences, longer dissections and thus longer operative duration and conversion rate. Our 3.7% rate of postoperative ileus in the PICR group was similar in the LIRIC trial (4%). [5] On the other hand, if the overall morbidity was increased in the IICR group due to ileus, it can be noted that specific

surgical morbidity and anastomotic leakage were not different in both groups, and this also in the subgroup of primary anastomoses. This increased postoperative ileus is of importance in the current management of such patients in whom the enhanced recovery programs will fail more frequently.

Enhanced recovery for colorectal surgery (ERAS) programs is associated with shorter time to restoration of bowel movement and shorter length of hospital stay (LHS) in patients undergoing ICR for CD. [23,24] In our study, mean LHS was relatively long (9-10 days) but median was 7 days, similar in both group (PICR: 7 days (IQR=6-9), IICR : 7 days (IQR=6-10). Indeed, the 19 participating centers had diverse ERAS protocols with different inclusion criteria. However, data in the literature is in accordance with our findings. In a RCT, Zhou and al. compared 16 laparoscopic PICR for CD with ERAS vs 16 PICR with conventional management for CD: mean postoperative DHS was 9.94 +/-3.3 days. [24] Brouquet and al. compared 57 PICR (52.6% through laparoscopic approach) with 54 IICR (48% through laparoscopic approach). [18] The median LHS was 7 days (4-18) versus 9 days (6-63) in the PICR and IICR group respectively. In the TRUE trial comparing single port versus conventional multiport conventional laparoscopy for colonic resection, including 47 (75%) conventional laparoscopic right colectomies for cancer, and 53 (42%) PICR for CD, the mean LHS was 6 +/-2 days in the conventional laparoscopic group. [25]Finally, in a randomized controlled trial, Maggiori and al. evaluated full vs limited ERAS programs in colorectal resections for cancer. [26] Mean DHS was 9.4+/-3.3 days (range, 6-24) in the limited fast track program vs 8.6 +/- 3.5 days in the full fast track program. Only Spinelli and al , who evaluated ERAS programs in primary ileocolonic resections for CD found a shorter DHS of 6.8 +/-3.1 days in the patients undergoing laparoscopic primary ICR without ERAS. [23]

In this series, we could not identify risk factors of postoperative overall morbidity in the IICR group and we did not demonstrate a negative impact of preoperative treatment targeting

CD as recently reported. [15] This could be related to a lack of statistical power. Indeed, only 29 patients were treated previously with anti-TNF alpha in the IICR group which is insufficient to individualize an independent effect. Of this parameter, preoperative hemoglobin < 10g/dL was also not identified as a predictive factor of overall morbidity in our study. Indeed, patients in the IICR group were in a better general and nutritional condition, with a less inflammatory type of CD, which explains the low prevalence of anemia in this group. Operative duration > 180 min was not individualized as a risk factor of postoperative morbidity. Indeed, the IICR group was characterized by longer operative duration.

In conclusion, this large prospective multicentric study on IICR showed only an increase of post-operative ileus. Major surgical morbidity is similar to primary ileo-colic resection and iterative procedures should not push to creation of stoma and be performed in expert center through laparoscopy. This therapeutic option could thus be discussed in patients with recurrent disease and should not be denied on the basis of risk of increased morbidity.

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Table 1. Preoperative characteristics and previous medical treatments of patients undergoing IICR and PICR

	Total n=567	IICR n=136	PICR n=431	p
Age > 65 years	33 (5.8)	15 (11.0)	18 (4.2)	0.030
Male gender	247 (43.6)	57 (41.9)	190 (44.1)	0.656
BMI <18	92 (16.2)	17 (12.5)	75 (17.4)	0.164
BMI > 30	27 (4.8)	8 (5.9)	19 (4.4)	0.495
Denutrition	209 (36.9)	37 (27.2)	172 (39.9)	0.007
Current smoker	161 (28.4)	37 (27.2)	124 (28.8)	0.777
ASA score > 2	29 (5.1)	13 (9.6)	16 (3.7)	0.011
Duration of CD > 2 years	435 (76.7)	132 (97.1)	303 (70.3)	<0.001
Previous acute episode > 3	80 (14.1)	28 (20.6)	52 (12.1)	0.013
Disease behavior				
Stricturing CD	328 (57.8)	94 (69.1)	234 (54.3)	<0.001
Inflammatory CD	43 (7.6)	15 (11.0)	28 (6.5)	
Perforating CD	196 (34.6)	27 (19.9)	169 (39.2)	
Multifocal intestinal CD	94 (16.6)	21 (15.4)	73 (16.9)	0.642
Associated colorectal CD	102 (18.0)	21 (15.4)	81 (18.8)	0.363
Associated perianal CD	82 (14.5)	24 (17.6)	58 (13.5)	0.221
Associated extradigestive CD	57 (10.1)	14 (10.3)	43 (10.0)	0.940
Previous isolated small bowel resection	127 (22.4)	103 (75.7)	24 (5.6)	<0.001
Previous colorectal resection	63 (11.1)	54 (39.7)	9 (2.1)	<0.001
Preoperative biologic parameters				
Hemoglobin level < 10 g/Dl	18 (3.2)	3 (2.2)	15 (3.5)	0.448
Albumin serum level < 30 g/L	67 (15.5)	15 (11.0)	52 (12.1)	0.845
C reactive protein serum level > 10 mg/L	240 (42.3)	45 (33.1)	195 (45.2)	0.028
Preoperative nutritional support	190 (33.5)	35 (25.7)	155 (36.0)	0.028
Previous medical treatment exposure	436(76.9)	105 (77.2)	331 (76.8)	0.950
Steroids	59 (10.4)	12 (8.8)	47 (10.8)	0.488
Thiopurin and/or Methotrexate	53 (9.3)	13 (9.6)	40 (9.3)	0.923
All anti-TNF	146 (25.7)	31 (22.8)	115 (26.7)	0.411
Number of lines of medical treatment ≥ 2	190(33.5)	51 (37.5)	139 (32.3)	0.280
Medical treatment < 3 months before surgery	243 (42.9)	55 (40.4)	188 (43.6)	0.514
Steroids	45 (7.9)	10 (7.4)	35 (8.1)	0.773
Thiopurin and/or Methotrexate	47 (8.3)	10 (7.4)	37 (8.6)	0.650
All anti-TNF	133 (23.5)	29 (21.3)	104 (30.9)	0.554

ASA American Society of Anesthesiologists, BMI body mass index, CD Crohn's Disease, IICR: iterative ileocolonic resection, PICR: primary ileocolonic resection

Table 2. Surgical procedures and postoperative outcome in patients undergoing IICR and PICR

Variables	Total n=567	IICR n=136	PICR n=431	p
Emergency surgery	52 (9.2)	6 (4.4)	46 (10.7)	0.027
Surgical approach				
Laparoscopy	426 (75.1)	62 (45.6)	364 (84.5)	<0.001
Conversion	70 (16.4)	17 (27.4)	53 (14.6)	0.012
Associated procedures				
Strictureplasty	13 (2.3)	3 (2.2)	10 (2.3)	0.938
Additional intestinal resection	40 (7.1)	9 (6.6)	31 (7.2)	0.819
Intraoperative findings				
Internal fistula	196 (34.6)	34 (25)	162 (37.6)	0.007
Abscess	102 (18.0)	15 (11.0)	87 (20.2)	0.013
Intraoperative CD length > 50 cm	61 (10.8)	5 (3.7)	56 (13.0)	0.002
Length of resected bowel > 50 cm	79 (13.9)	14 (10.3)	65 (15.1)	0.140
Intraoperative complication				
Bowel injury	2 (0.4)	2 (1.5)	0	-
Bleeding	2 (0.4)	0	2 (0.5)	-
Primary anastomosis	449 (79.2)	112 (82.4)	337 (78.2)	0.297
Type of anastomosis				
End to side	86(15.2)	19 (14.0)	67 (19.9)	
End to end	49(8.6)	13 (9.6)	6 (10.7)	0.457
Side to side	304(53.6)	77 (56.6)	227 (67.4)	
Hand-sewn/stapled	183 (40.8) /266 (59.2)	38(33.9)/74(66.1)	145 (43)/192 (57)	0.100
Operative time, min	143.1 (+/- 51.2)	155.9 (+/- 53.3)	138.9 (+/-49.9)	0.002
Operative time > 180 min	121 (21.3)	42 (30.9)	79 (18.3)	0.002
Postoperative mortality	0	0	0	-
Overall postoperative morbidity	165 (29.1)	50 (36.8)	115 (26.7)	0.024
Infectious morbidity	101 (17.8)	27 (19.9)	74 (17.2)	0.476
Non infectious morbidity	87 (15.3)	28 (20.6)	59 (13.7)	0.052
Morbidity surgical site infection	78 (13.8)	19 (14.0)	59 (13.7)	0.934
Intraabdominal septic complications	48 (8.5)	12 (8.8)	36 (8.4)	0.863
Anastomotic leakage with peritonitis	14/449 (3.1)	3/112 (2.7)	11/337 (3.3)	0.757
Anastomotic leakage without peritonitis	11/449 (2.4)	2/112 (1.8)	9/337 (2.7)	0.600
Intraabdominal abscess	23/567 (4.1)	7/136 (5.1)	16/436 (3.7)	0.460
Other complications				
Intraabdominal bleeding	12 (2.1)	1 (0.7)	11 (2.6)	0.199
Ileus	32 (5.6)	16 (11. 8)	16 (3.7)	<0.001
Wound infection	22 (3.9)	8 (5.9)	14 (3.2)	0.165
Urinary tract infection	11 (1.9)	4 (2.9)	7 (1.6)	0.332
Pneumonia	2 (0.3)	0	2	-
Pulmonary embolism	1 (0.2)	0	1	-
Catheter infection	9 (1.6)	3 (2.2)	6 (1.4)	0.504
Urinary retention	4 (0.7)	1 (0.7)	3 (0.7)	0.962
Acute renal failure	6 (1.1)	0	6 (1.4)	-
Severe complications (Dindo-Clavien III,IV)	49 (8.6)	11 (8.1)	38 (8.8)	0.792
Reoperation for complications	24 (4.2)	4 (2.9)	20 (4.6)	0.391
Reoperation with stoma for complications	19 (3.4)	4 (2.9)	15 (3.5)	0.761
Drainage for complications	14 (2.5)	2 (1.5)	12 (2.9)	0.389

Length of stay mean±SD, median (IQR)	9.9±2.3; 7(6-9)	9.3±6.9; 7(6-10)	10.2±23.0); 7(6-9)	0.499

Table 3. Surgical procedures and post-operative outcomes in 136 patients undergoing iterative ileocolonic resection (IICR) depending on the number of previous ileocolonic resections

	Iterative ICR n = 136	**2nd ICR n = 97**	**3rd ICR or more n = 39**	**p**
Laparoscopy	62 (45.6)	48 (49.5)	14 (35.9)	0.150
Conversion	17 (27.4)	14 (14.4)	3 (7.7)	0.568
Primary anastomosis	112 (82.4)	81 (83.5)	31 (79.5)	0.578
Operative duration	155.9 (+/- 53.3)	153.2 (+/-52.4)	162.9 (+/-55.6)	0.747
Operative duration > 180 min	42 (30.9)	28 (28.9)	14 (35.9)	0.372
Overall postoperative morbidity	50 (36.8)	34 (35.1)	16 (41.0)	0.513
Intra-abdominal septic complications	12 (8.8)	6 (6.2)	6 (15.4)	0.087
Severe postoperative complications	11 (8.1)	7 (7.2)	4 (10.3)	0.557
Reoperation for complications	4 (2.9)	2 (2.1)	2 (5.1)	0.338
Length of stay mean±SD, median (IQR)	9.3±6.9; 7(6-10)	8.5±4.7; 7(6-9)	11.2±10.4; 7.5(6-13)	0.181

% are in parentheses

Table 4. Operative and postoperative outcome by yearly case volume in the IICR group.

	Volume ≤ 15 patients / year*	Volume > 15 patients / year	p
IICR/total	23/130 (17.7)	113/434 (26.0)	0.051
Laparoscopy	13/23 (56.5)	50/113 (44.2)	0.282
Conversion	6/13 (46.2)	11/50 (22.0)	0.080
Operative duration > 180 min	6/23 (26.1)	36/113 (31.9)	0.585
Overall postoperative morbidity	8/23 (34.8)	42/113 (37.2)	0.829
Length of stay mean±SD, median (IQR)	7.8±3.4; 7(4-8.5)	9.54±7.4; 7(6-10)	0.297

*One center of this group was excluded from this analysis because no IICR was performed (n=3 patients, among which 3 PICR and 0 IICR)

% are in parentheses

Table 5. Univariate and multivariate analyses of risk factors of overall postoperative morbidity in 136 patients undergoing IICR.

	Univariate analysis	Multivariate analysis		
	p	p	OR	IC95%
Age > 65 years	0.770	0.848	0.926	0.229-3.747
Male gender	0.154	0.490	0.759	0.331-1.744
BMI <18	0.673	0.104	3.885	0.755-19.995
BMI > 30	0.955	-		
Denutrition	0.298	0.225	0.429	0.107-1.722
Current smoker	0.768	0.627	1.249	0.481-3.245
ASA status > 2	0.279	0.230	0.401	0.090-1.783
Duration of CD > 2 years	0.122	-		
Acute episode < 3 months	0.644	-		
Previous acute episode > 3	0.103	-		
Disease behavior				
Stricturing CD	0.347	-		
Inflammatory CD	0.770	-		
Perforating CD	0.680	0.547	0.718	0.257-2.009
Preoperative CD length > 50 cm	0.753	-		
Multifocal intestinal CD	0.653	-		
Associated colorectal CD	0.529	-		
Associated perianal CD	0.325	-		
Associated extra-digestive CD	0.209	-		
Prior isolated small bowel resection	0.320	-		
Prior colorectal resection	0.926	-		
Number of previous ICR				
Second ICR vs. 3rd or more	0.513	0.470	1.254	0.493-3.191
Preoperative biologic parameters				
Hemoglobin level < 10 g/dL	0.247	-		
Albumin serum level < 30 g/L	0.168	-		
C reactive protein serum level > 10 mg/L	0.468	-		
Preoperative nutritional support	0.724	-		
Medical treatment < 3 months before surgery				
Steroids	0.127	0.999	-	-
Any anti-TNF	0.911	0.460	1.434	0.533-3.854
Intraoperative findings				
Internal fistula	0.347	-		
Abscess	0.752	-		
Intraoperative CD length > 50 cm	0.242	-		
Emergency surgery	0.296	-		
Surgical approach				
Laparoscopy vs Laparotomy	0.667	-		
Conversion	0.734	-		
Associated procedures				
Strictureplasty	0.901	-		
Additional intestinal resection	0.349	-		
Length of resected bowel > 50 cm	0.966	-		
Primary anastomosis	0.395	-		
Stapled vs handsewn anastomosis	0.678	-		

Operative time > 180 min	0.525	-