

## Research Article

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# Risk factors and therapeutic options for postoperative intra-abdominal septic complication in Crohn's disease

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## Background

Crohn's Disease (CD) is a nonspecific chronic inflammation of the intestine. Approximately 70% of CD patients must undergo operations during their lives [24], even after active pharmacological treatment. According to several studies, a patient's lifetime risk of surgical treatment is estimated at around 90% during the first 15 years after diagnosis [23]. Patients affected by CD require surgical intervention when complications such as bowel occlusion, fistulas, and abscesses occur. The postoperative course is complex, with higher complication rates as compared

## Abstract

**Background:** Approximately 70% of patients suffering from Crohn's disease require surgery in their lifetime. The postoperative course is complex, with higher complication rates compared to major colorectal surgery and with a high incidence of Intra-Abdominal Septic Complications (IASC). We aimed to assess risk factors for IASC in CD patients and evaluate whether patients' prognosis is affected by different treatment strategies through a literature review.

**Materials and methods:** We conducted a systematic literature research with PubMed as the primary database. Relevant papers were evaluated and included in the review.

**Results:** A total of 69 studies were included. The main prognostic factors examined were: nutritional status, surgical aspects, disease activity, and medical therapy. The therapeutic options examined were medical therapy, US or CT-guided drainage, and surgery.

**Conclusion:** An impaired nutritional status, valued through the need for pre-operative parenteral nutrition, low albumin level, and low BMI is a risk factor for IASC; operating technique does not appear to affect the outcomes, while a previous surgery increases the risk for IASC; a penetrating disease, as well as the presence of intra-abdominal abscess or fistula at the time of surgery increase the risk for IASC. Surgery is the most frequent choice in managing post-operative IASC and appears to have better outcomes. Prospective studies and randomized control trials are required to clarify risk factors and therapeutic options along with recommendations published to date.

to patients undergoing major colorectal surgery: complications are classified into two groups, septic and non-septic [68]. The most fearsome septic complications are the IASC (Intra-Abdominal Septic Complications) and include abscesses, anastomotic fistulas, and dehiscence [20,24,59]. The purpose of the present study is to assess risk factors for IASC in CD patients and evaluate whether patients' prognosis is affected by different treatment strategies.

Systematic literature research was conducted: we used PubMed as the primary database, searching for papers pub-

lished between 01/01/1980 and 01/12/2022. Three different pieces of research were conducted with the following keywords:

- (“crohn’s disease”) AND (“postoperative” or “post-operative” or “after surgery”) AND (“leak” or “leakage” or “abscess” or “peritonitis” or “fistula”)
- ((crohn’s disease) AND (iasc) AND (surgery OR postoperative OR “after surgery”))
- (“crohn’s disease” AND (“postoperative morbidity” OR “surgery morbidity” OR “after surgery morbidity”) AND (“strategy” OR “management”)).

The first part of the search was limited to titles and abstracts: for those who fitted our topics, we read the entire article. Finally, we selected a total of 69 articles, including research articles, observational studies, and reviews.

### Prognostic factors

Several studies aim to assess risk and protective factors for postoperative complications in relation to the high complication rate of CD patients undergoing surgery. Controversial data result from such literature, likely because of scarce cohorts of patients. The main examined factors are outlined below.

#### Nutritional status

An impaired nutritional status can be determined by 3 criteria: low Albumin, BMI <15, and the need for preoperative nutrition (enteral or parenteral). A nutritional target of at least 30 Kcal/kg/die should be achieved in all patients affected by complicated CD undergoing surgery [24].

#### Albumin and other lab tests

While a few observational studies did not consider serum albumin levels to be significant [24], a meta-analysis investigating larger groups of patients and newer studies found that albumin level <30 g/L is related to increased risk of postoperative IASC [5,59]. Some studies also assessed that low levels of hemoglobin and hematocrit are related to unfavorable outcomes [14,23,46,58], that is why supplementary iron therapy should be considered [58].

#### BMI

Preoperative BMI is a clinical predictive value in determining the occurrence of IASC. Papers that investigated nutritional aspects of CD patients suggested BMI=16.2 being the cut-off value with an 85% sensitivity and 68,4% specificity [24].

#### Preoperative nutritional supplementation

A correlation between postoperative complications and preoperative parenteral nutrition has been proved, with an OR of 2.85 (IC95% 1,20-6,74). This association is probably due to the impaired nutritional status of the patient and not to the parenteral nutrition itself [14].

No IASC was detected in a group of patients who had nutritional enteral supplementation from 3 to 6 weeks before surgery, as described in a Swedish study [38,46]. In patients with CD, preoperative optimization with enteral nutrition reduced the overall rate of postoperative complications and significantly decreased postoperative septic complications in a paper pub-

lished in 2020 [7].

At any rate, the indication for parenteral nutrition should be reserved for cases where enteral nutrition is contraindicated, such as an occlusive syndrome [46].

### Surgical aspects

We considered several technical features to assess the predisposing conditions and procedures for the occurrence of IASC.

Method of anastomosis (manual or mechanical, side-to-side or end-to-end, interrupted or continuous suture technique) [2,18,31,44,46,58], operating technique (laparoscopic or laparotomic) [46,48], one-stage anastomosis vs ileostomy creation [46], have not reached clinical significance in determining postoperative IASCs. A single study described a lower septic complication rate in patients operated with a laparoscopic technique [22], and a second one with mechanical anastomosis [35]. Another paper analyzed the relationship between ileostomy creation and increased risk of IASC [17], highlighting how stoma creation could be an independent protective factor for IASC.

Previous surgical history contributes to the development of IASCs [8,9,18,20,46,59]. This phenomenon is probably due to the pre-existent adherence syndrome at the time of surgery.

Urgent surgery and intraoperative adverse events were described as risk factors for IASCs [14] with an OR of 2 (IC95% 1,13-3,55) and 2,31 (IC95% 1,20-4,45) respectively, in the multivariate analysis.

Among the studies taken into consideration, there is no evidence for a better outcome if anastomosis involves disease-free margins. One single study claims that anastomosis on affected margins is related to post-operative IASCs [23], while other papers did not reach any statistical significance [20,58].

Several studies have identified prolonged operating time as a risk factor for IASC [3, 12].

### Disease activity

Disease activity is crucial in determining the risk for postoperative septic complications.

Conditions like the presence of an intra-abdominal abscess or fistula before surgery, stricturing or penetrating disease, and pre-operative CRP value, are used to assess the disease status.

#### Pre-operative abscess, fistula or bowel occlusion

The presence of an abscess is related to an increased risk of IASC with an OR of 7.5 (CI 95% 1,5-37,69) [47] if the abscess is not drained before surgery [23,59]. In the case of pre-operative drainage, the risk of complications was found to be similar to the one in patients without preoperative abscess in one study [18], while in a more recent paper patients with CD who require preoperative radiological guided drainage of intra-abdominal abscesses are at increased risk of postoperative morbidity and septic complications following ileocecal or re-do ileocolic resection [1]. A French paper [47], in particular, emphasizes the advantages of pre-operative CT/US-guided drainage: a CT scan before surgery is therefore advisable, to evaluate the disease and assess the risk of the patient [5].

As in the case of abscesses, the presence of a fistula at the time of the intervention is a risk factor to develop IASC [18,23,25,59], according to the majority of studies we analyzed. Finally, it is well established that a patient affected by bowel occlusion at the time of surgery has a higher risk of postoperative complications [47].

### Disease behaviour

The Montreal Classification categorizes disease behavior as non-stricturing and non-penetrating (B1), stricturing (B2), and penetrating (B3). In the literature, several studies did not find a clear relation between the disease phenotype and post-operative IASC [25,65]. On the other hand, four studies observed that penetrating disease is related to an increased risk of postoperative IASC [5,12,23,35], since penetrating disease frequently determines intra-abdominal fistulas and abscesses formation

### CRP levels

The utility of CRP levels as a prognostic index of IASC is unclear. One of the examined studies [25] obtained statically significant results using 10 mg/L as the cut-off value and proved that the CRP trend during the two weeks before surgery is related to the outcome: a decreasing CRP value determines a lower risk, while its increase is related to developing septic complications. Another study [14] shows that the CRP value, measured during post-operative recovery, and IASC are positively related; the high negative predictive value (NPV) of CRP was described by a recent study [4] with a threshold of 20.3 mg/dL on POD 3, 19.5 mg/dL on POD 4 and 16.7 mg/dL on POD 5: these values had high NPVs and can be used to rule out anastomotic leaks in patients with Crohn's disease.

### Medical therapy

We evaluated the impact of different medications, such as steroids, immunomodulators, and biologics, on the occurrence of post-operative IASC.

### Steroids

It is well established that steroids may lead to side effects that worsen the patient's condition, making him liable to septic complications. Severe disease requiring steroid therapy is related to IASC as well.

It is not clear if steroid use causes anastomosis dehiscence or IASC in general. A meta-analysis (2014) assesses that pre-operative steroid use is associated with a greater risk of IASC with an OR of 1,99 (CI 95% 1,54-2,57) [59]. Other studies did not reach any statistical significance [23,46,55].

These conflicting results are probably due to different timing in steroid use.

### Immunomodulators

The use of Azathioprine, 6-mercaptopurine, and methotrexate is not related to an increased risk of IASC [18,20,46]. A single study defined immunomodulators as protective against complications [55], likely because of their effectiveness in inducing disease remission.

### Biologics

The relationship between biologic drugs and the development of IASC is controversial. Anti-TNF antibodies are proven to increase the risk of infectious complications, not specifically IASC [14,20,26]. Two studies demonstrated that anti-TNF antibodies use represents a specific risk factor for post-operative IASC [16,23,42].

Recently published studies found that preoperative biological therapy is predictive of a lower rate of complications [3]. A meta-analysis published in 2020 examined 2064 patients with CD and indeterminate colitis treated with biological therapy in the preceding 12 weeks compared to patients who had intra-abdominal surgery without biological therapy within the defined time frame: there were no increased complications associated with anti-TNF exposure, while Vedolizumab increased surgical site infection and small bowel obstruction, but not IASC [6]. Similar results were seen in a 2020 Greek study [9].

### Others risk factors

Smoking and co-morbidities have also been considered as possible risk factors for developing IASC after surgery.

Particularly, as concerns smoking, we examined a paper [23] that claims that upto 16% of smokers undergo postoperative septic complications as compared to 2% of non-smokers. Conversely, another paper [14] considering smoking as a risk factor did not reach any statistical significance (OR 1,29; CI 95% 0,78-2,11). Other studies demonstrate how smoking increases the risk of postoperative complications in general, not specifically IASC [18,55].

Patients who have comorbidities [14] at the time of surgery have a greater risk of IASC with an OR of 3.67 (CI 95% 1.2-11.1) and 2.67 (CI 95% 0,81-8,83) from univariate and multivariate analysis, respectively.

ASA score is frequently revealed as an independent risk factor for postoperative complications, including IASC [2, 8].

### Postoperative outcomes

The post-operative outcome has a key role in the patient's quality of life and hospitalization period [35].

We examined several complications, especially IASC, occurring after surgery in patients affected by Crohn's Disease. In literature a well-defined time interval to evaluate patients' outcomes is not described; however, we consider such an interval to be up to 30 days after surgery [35].

Physical and clinical examination (i.e. fecal or enteric output from the drainage, signs of peritonitis, evidence of enterocutaneous fistula), as well as the instrumental investigations (US or CT-guided percutaneous abscess drainage), are crucial to achieving an early diagnosis [35,41].

The final assessment of the type of complication occurs at the time of re-laparotomy (i.e. peri-anastomotic fluid collection, fibrinous peritonitis) [23].

What emerged from our research is that postoperative IASCs have an incidence ranging from 2,7% to 31,3% of patients affected by CD; most of the studies reported an incidence of around 10% [5,9,12,23,24,42,46,47,59,68].

**Table 1:** Review of literature.

Source	Wound infection	Septic complication	IASCS	Abscess	Anastomotic leak	Enterocutaneous fistula
Wang K. et al. 2021 [5]			7.5%	5.2%	2.6%	
Yamamoto T. et al. 2020 [7]	6.3%	14.6%		8.3%	8.3%	2.1%
Duan Y. et al. 2020 [8]	17.1%	22.5%		5.4%	12.4%	
Gklavas A. et al. 2020 [9]	2.0%		12.4%	0.7%	11.8%	
Gutiérrez A. et al. 2019 [10]	9.1%			7.7%	7.4%	
Galata C. et al. 2018 [11]		4.3%			1.8%	
Xie T. et al. 2018 [12]	25.4%		31.3%	13.4%	7.4%	7.4%
2015 European Society of Coloproctology collaborating group 2017 [14]	11.2%				8.8%	
Waterland P. et al. 2016 [16]	9.1%	22.4%	5.2%		4.6%	
Moghadamyeghaneh Z. et al. 2015 [22]	2.6%			6.1%		14.8%
Morar P.S. et al. 2015 [23]			9.7%			
Zhang M. et al. 2015 [24]			11.0%			
Zuo L. et al. 2015 [25]			11.3%	5.5%	4.7%	1.2%
Ahmed A. et al. 2014 [26]	7.5%	13.6%		4.7%	3.4%	
Zurbuchen U. et al. 2013 [31]	10.4%				3.0%	
Kanazawa A. et al. 2012 [35]			2.7%	0.6%	2.1%	1.7%
Samimi R. et al. 2010 [42]	3.0%		24.0%	18.0%	6.0%	
Yoon Y.S. et al. 2010 [44]						
lesalnieks I. et al. 2008 [46]	5.0%		14.0%	7.0%	8.5%	5.0%
Alves A. et al. 2007 [47]	6.8%		9.3%	1.9%	8.0%	1.9%
Penner R. et al. 2005 [50]	6.3%			4.0%	2.0%	
Smedh K. et al. 2002 [56]	4.6%					
Sampietro G.M. et al. 2000 [58]		5.8%		2.9%		
Yamamoto T. et al. 2000 [59]	6.0%		13.0%	10.0%	6.0%	5.0%
Heimann T.M. et al. 1985 [68]	2.3%	20.8%	12.3%	10.8%	1.5%	

The most frequent complications between IASCS are intra-abdominal abscesses (0,6%-18%) [35,37], with an average incidence of around 5% [25,26,46,50], followed and often determined by the anastomotic leak (1,5%-12,4%) [68,3], and fistulas, with a reported incidence between 1,2% and 14,8% [7,12,22,25,35,46,47,59].

Septic complications in general (including pneumonia and urinary tract infection) resulted in an incidence between 13% and 22% [16,26], while wound infections between 2,0%-25,4% [9,12]. A single study reports that 19 (41%) out of 46 patients with IASC had a simultaneous wound infection [46].

In the same study, we observed that re-intervention at 2 and 5 years after bowel resection or strictureplasty was significantly more frequent in patients with IASC, with an incidence of 29% and 50% respectively, against 7% and 19% in patients without IASC.

Finally, we observed that disease recurrence is significantly more frequent in patients with IASC, as compared to those without IASC.

### Therapeutic options

Acting on risk factors and protective factors appears to be related to a better outcome, in fact, several studies in the literature focus on those issues. On the other hand, there is very little

data about the treatment of post-operative IASC. The purpose of this review is to search for a better strategy to improve short and long-term outcomes from the moment when IASCS occur.

The most widely used therapeutic options are pharmacological therapy, percutaneous US-CT guided drainage, and surgical therapy.

- Medical therapy: mainly including antibiotics and nutritional support, with careful clinical observation. In the studies we reviewed conservative treatment for IASC varies from 13% to 41% [23,39,47,53].
- US or CT-guided percutaneous drainage: this option was chosen from 20% to 35% [23,39,40,47] of cases with intra-abdominal septic complications.
- Surgical therapy: currently representing the most frequent choice, it involves from 23% to 78% of patients [23,39,40,46,47,53,66]. Surgical strategies are various and include exploratory laparotomy with peritoneal washing and drainage of the abscess, repair of bowel injury, resection of the intestinal tract involved in the fistula, resection of the previous anastomosis and re-creation, creation of a lateral or terminal ileostomy. It is interesting to note that in the studies we analyzed no data were reported about laparoscopic surgery in treating IASCS.

Moreover, no indication was given about the choice of antibiotic and its related outcome nor for percutaneous drainage.

In our opinion, the most comprehensive and complete study about treatment options is the work by Iesalnieks et al. [39]. This study divided the patients with CD that underwent surgery into two groups: Group 1 including patients treated with reintervention, resection of the previous anastomosis, and creation of terminal ileostomy; Group 2 including patients treated conservatively (antibiotics and radio-guided drainage), patients treated with the repair of bowel injury and those who underwent anastomotic take down and creation of a new one (in some cases with lateral enterostomy). Patients included in Group 1 undergoing ileocolonic resection for complicated Crohn's disease, had a re-operation rate at 1, 2, and 5 years of 0%; patients in group 2 had a reoperation rate at 1,2, and 5 years of 50, 57, and 65% respectively. No statistically significant difference was found between the two groups as concerns patients affected by Crohn's colitis, also because of the scarcity of data. Another significant difference between the two groups consists of mortality due to short and long-term CD complications, with no mortality in group 1 (p-value 0.046). Re-operation between POD 1 and 3 has had a better outcome in terms of hospitalization (p-value 0.0018). It is important to underline that the restoration of intestinal continuity is not to be considered as reintervention.

### Conclusion

In conclusion, the most favorable therapeutic attitude remains the less conservative and more radical one. However, in our opinion, this issue deserves greater attention and further discussion.

### References

1. Celentano V, Giglio MC, Pellino G, Rottoli M, Sampietro G, et al. High complication rate in Crohn's disease surgery following percutaneous drainage of intra-abdominal abscess: a multicentre study. *International Journal of Colorectal Disease*. 2022; 37: 1421–1428.
2. Mittelstädt A, von Loeffelholz T, Weber K, Denz A, Krautz C, et al. Influence of interrupted versus continuous suture technique on intestinal anastomotic leakage rate in patients with Crohn's disease—a propensity score matched analysis. *International Journal of Colorectal Disease*. 2022; 37: 2245–2253.
3. Emile SH, Freund MR, Horesh N, Garoufalia Z, Gefen R, et al. Risk factors and predictors of 30-day complications and conversion to open surgery after repeat ileocolic resection of Crohn's disease. *Surgical Endoscopy*. 2022.
4. Slavin M, Goldstein A, Ragan B, Rudnicki Y, Avital S, et al. Post-operative CRP Levels Can Rule out Anastomotic Leaks in Crohn's Disease Patients. *Journal of Personalized Medicine*. 2022; 12.
5. Wang K, Huang L, Huang W, Liu R, Chen X, et al. Predictive Value of CT Enterography Index for Postoperative Intra-abdominal Septic Complications in Patients with Crohn's Disease: Implications for Surgical Decision-Making. *Diseases of the Colon and Rectum*. 2021; 964-976.
6. Byrne LW, McKay D. Does perioperative biological therapy increase 30-day post-operative complication rates in inflammatory bowel disease patients undergoing intra-abdominal surgery? A systematic review. *In Surgeon*, 2021; 5: 153-e167.
7. Yamamoto T, Nakahigashi M, Shimoyama T, Umegae S. Does preoperative enteral nutrition reduce the incidence of surgical complications in patients with Crohn's disease? A case-matched study. *Colorectal Disease*. 2020; 22: 554-561.
8. Duan Y, Liu Y, Li Y. Previous Intestinal Resection Is Associated with Postoperative Complications in Crohn's Disease: A Cohort Study. *Gastroenterology Research and Practice*. 2020.
9. Gklavas A, Poulaki A, Dellaportas D, Papaconstantinou I. Risk factors for postoperative complications after elective ileocolic resection for crohn's disease: A retrospective study. *Annals of Gastroenterology*. 2020; 33: 645-655.
10. Gutiérrez A, Rivero M, Martín-Arranz MD, Garcíá Sánchez V, Castro M, et al. Perioperative management and early complications after intestinal resection with ileocolonic anastomosis in Crohn's disease: Analysis from the PRACTICROHN study. *Gastroenterology Report*. 2019; 7: 168-175.
11. Galata C, Weiss C, Hardt J, Seyfried S, Post S, et al. Risk factors for early postoperative complications and length of hospital stay in ileocecal resection and right hemicolectomy for Crohn's disease: a single-center experience. *International Journal of Colorectal Disease*. 2018; 33: 937-945.
12. Xie T, Zhao C, Ding C, Zhang L, Cheng M, et al. Postoperative Interleukin-6 Predicts Intra-abdominal Septic Complications at an Early Stage After Elective Intestinal Operation for Crohn's Disease Patients. *Inflamm Bowel Dis*. 2018.
13. 2015 European Society of Coloproctology collaborating group. The relationship between method of anastomosis and anastomotic failure after right hemicolectomy and ileo-caecal resection: an international snapshot audit. *Colorectal Disease: The Official Journal of the Association of Coloproctology of Great Britain and Ireland*. 2017; 140: 874-888.
14. 2015 European Society of Coloproctology collaborating group. Risk factors for unfavourable postoperative outcome in patients with Crohn's disease undergoing right hemicolectomy or ileo-caecal resection An international audit by ESCP and S-ECCO. *Colorectal Disease: The Official Journal of the Association of Coloproctology of Great Britain and Ireland*. 2017; 20: 219-227.
15. Patil SA, Cross RK. Medical versus surgical management of penetrating Crohn's disease: the current situation and future perspectives. *Expert Review of Gastroenterology & Hepatology*. 2017; 11: 843-848.
16. Waterland P, Athanasiou T, Patel H. Post-operative abdominal complications in Crohn's disease in the biological era: Systematic review and meta-analysis. *World Journal of Gastrointestinal Surgery*. 2016; 8: 274-283.
17. Cayci M, Bostanci EB, Turhan N, Karaman K, Dalgic T, et al. The analysis of clinico-pathologic characteristics in patients who underwent surgery due to stricturing and non-perineal fistulizing forms of Crohn's disease: a retrospective cohort study. *International Journal of Surgery (London, England)*. 2015; 15: 49-54.
18. Crowell KT, Messaris E. Risk factors and implications of anastomotic complications after surgery for Crohn's disease. *World Journal of Gastrointestinal Surgery*. 2015; 7: 237-242.
19. Hefaidh R, Sabbeh M, Miloudi N, Ennaifer R, Romdhane H, et al. Surgical treatment of Crohn's disease: indications, results and predictive factors of recurrence and morbidity. *La Tunisie Médicale*. 2015; 93: 356-360.
20. Huang W, Tang Y, Nong L, Sun Y. Risk factors for postoperative intra-abdominal septic complications after surgery in Crohn's disease: A meta-analysis of observational studies. *Journal of Crohn's & Colitis*. 2015; 9: 293-301.
21. Michetti P. Postsurgical Prophylaxis in Crohn's Disease: Which Patients, Which Agents? *Digestive Diseases (Basel, Switzerland)*. 2015; 1: 78-81.
22. Moghadamyeghaneh Z, Carmichael JC, Mills SD, Pigazzi A, Sta-

- mos MJ. Outcomes of Bowel Resection in Patients with Crohn's Disease. *The American Surgeon*. 2015; 81: 1021-1027.
23. Morar PS, Hodgkinson JD, Thalayasingam S, Koysombat K, Purcell M, et al. Determining Predictors for Intra-abdominal Septic Complications Following Ileocolonic Resection for Crohn's Disease—Considerations in Pre-operative and Peri-operative Optimisation Techniques to Improve Outcome. *Journal of Crohn's & Colitis*. 2015; 9: 483-491.
  24. Zhang M, Gao X, Chen Y, Zhi M, Chen H, et al. Body Mass Index Is a Marker of Nutrition Preparation Sufficiency Before Surgery for Crohn's Disease From the Perspective of Intra-Abdominal Septic Complications: A Retrospective Cohort Study. *Medicine*. 2015; 94: e1455.
  25. Zuo L, Li Y, Wang H, Zhu W, Zhang W, et al. A Practical Predictive Index for Intra-abdominal Septic Complications After Primary Anastomosis for Crohn's Disease: Change in C-Reactive Protein Level Before Surgery. *Diseases of the Colon and Rectum*. 2015; 58: 775-781.
  26. Ahmed Ali U, Martin ST, Rao AD, Kiran RP. Impact of preoperative immunosuppressive agents on postoperative outcomes in Crohn's disease. *Diseases of the Colon and Rectum*. 2014; 57: 663-674.
  27. Buda A, Okolo PI. Endoscopic treatment of Crohn's complications. *Expert Review of Gastroenterology & Hepatology*. 2014; 8: 887-895.
  28. de Groof EJ, Carbonnel F, Buskens CJ, Bemelman WA. Abdominal abscess in Crohn's disease: multidisciplinary management. *Digestive Diseases (Basel, Switzerland)*. 2014; 32: 103-109.
  29. Mallick IH, Hull TL, Remzi FH, Kiran RP. Management and outcome of pouch-vaginal fistulas after IPAA surgery. *Diseases of the Colon and Rectum*. 2014; 57: 490-496.
  30. Nguyen GC, Steinhart AH. The impact of surgeon volume on postoperative outcomes after surgery for Crohn's disease. *Inflammatory Bowel Diseases*. 2014; 20: 301-306.
  31. Zurbuchen U, Kroesen AJ, Knebel P, Betzler M-H, Becker H, et al. Complications after end-to-end vs. side-to-side anastomosis in ileocecal Crohn's disease—early postoperative results from a randomized controlled multi-center trial (ISRCTN-45665492). *Langenbeck's Archives of Surgery*. 2013; 398: 467-474.
  32. de Buck van Overstraeten A, Wolthuis A, D'Hoore A. Surgery for Crohn's disease in the era of biologicals: a reduced need or delayed verdict? *World Journal of Gastroenterology*. 2012; 18: 3828-3832.
  33. Hoentjen F, Colwell JC, Hanauer SB. Complications of peristomal recurrence of Crohn's disease: a case report and a review of literature. *Journal of Wound, Ostomy, and Continence Nursing: Official Publication of The Wound, Ostomy and Continence Nurses Society*. 2012; 39: 297-301.
  34. Iesalnieks I, Dederichs F, Kilger A, Schlitt HJ, Agha A. Postoperative morbidity after bowel resections in patients with Crohn's disease: risk, management strategies, prevention]. *Zeitschrift Fur Gastroenterologie*. 2012; 50: 595-600.
  35. Kanazawa A, Yamana T, Okamoto K, Sahara R. Risk factors for postoperative intra-abdominal septic complications after bowel resection in patients with Crohn's disease. *Diseases of the Colon and Rectum*. 2012; 55: 957-962.
  36. Lee KY, Yu CS, Lee KY, Cho YB, Park KJ, et al. Risk factors for repeat abdominal surgery in Korean patients with Crohn's disease: a multi-center study of a Korean inflammatory bowel disease study group. *Journal of the Korean Society of Coloproctology*. 2012; 28: 188-194.
  37. Nguyen GC, Saibil F, Steinhart AH, Li Q, Tinmouth JM. Postoperative health-care utilization in Crohn's disease: the impact of specialist care. *The American Journal of Gastroenterology*. 2012; 107: 1522-1529.
  38. Sagar PM, Pemberton JH. Intraoperative, postoperative and re-operative problems with ileoanal pouches. *The British Journal of Surgery*. 2012; 99: 454-468.
  39. Iesalnieks I, Kilger A, Kalisch B, Obermeier F, Schlitt HJ, et al. Treatment of the anastomotic complications in patients with Crohn's disease. *International Journal of Colorectal Disease*. 2011; 26: 239-244.
  40. Müller-Wille R, Iesalnieks I, Dornia C, Ott C, Jung EM, et al. Influence of percutaneous abscess drainage on severe postoperative septic complications in patients with Crohn's disease. *International Journal of Colorectal Disease*. 2011; 26: 769-774.
  41. Schwartz M, Regueiro M. Prevention and treatment of postoperative Crohn's disease recurrence: an update for a new decade. *Current Gastroenterology Reports*. 2011; 13: 95-100.
  42. Samimi R, Flasar MH, Kavic S, Tracy K, Cross RK. Outcome of medical treatment of stricturing and penetrating Crohn's disease: a retrospective study. *Inflammatory Bowel Diseases*. 2010; 16: 1187-1194.
  43. Shen B. Diagnosis and management of postoperative ileal pouch disorders. *Clinics in Colon and Rectal Surgery*. 2010; 23: 259-268.
  44. Yoon YS, Yu CS, Yang SK, Yoon SN, Lim SB, et al. Intra-abdominal fistulas in surgically treated Crohn's disease patients. *World Journal of Surgery*. 2010; 34: 1924-1929.
  45. Doherty G, Bennett G, Patil S, Cheifetz A, Moss AC. Interventions for prevention of post-operative recurrence of Crohn's disease. *The Cochrane Database of Systematic Reviews*. 2009; CD006873.
  46. Iesalnieks I, Kilger A, Glass H, Müller-Wille R, Klebl F, et al. Intra-abdominal septic complications following bowel resection for Crohn's disease: detrimental influence on long-term outcome. *International Journal of Colorectal Disease*. 2008; 23: 1167-1174.
  47. Alves A, Panis Y, Bouhnik Y, Pocard M, Vicaud E, Valleur P. Risk factors for intra-abdominal septic complications after a first ileocecal resection for Crohn's disease: a multivariate analysis in 161 consecutive patients. *Diseases of the Colon and Rectum*. 2007; 50: 331-336.
  48. Welsch T, Hinz U, Löffler T, Muth G, Herfarth C, et al. Early re-laparotomy for post-operative complications is a significant risk factor for recurrence after ileocaecal resection for Crohn's disease. *International Journal of Colorectal Disease*. 2007; 22: 1043-1049.
  49. Yamamoto T, Fazio VW, Tekkis PP. Safety and efficacy of stricture-plasty for Crohn's disease: a systematic review and meta-analysis. *Diseases of the Colon and Rectum*. 2007; 50: 1968-1986.
  50. Penner RM, Madsen KL, Fedorak RN. Postoperative Crohn's disease. *Inflammatory Bowel Diseases*. 2005; 11: 765-777.
  51. Chambers WM, Mortensen NJMM. Postoperative leakage and abscess formation after colorectal surgery. *Best Practice & Research. Clinical Gastroenterology*. 2004; 18: 865-880.
  52. Yamaguchi A, Matsui T, Sakurai T, Ueki T, Nakabayashi S, et al. The clinical characteristics and outcome of intraabdominal abscess in Crohn's disease. *Journal of Gastroenterology*. 2004; 39: 441-448.

53. Elton C, Makin G, Hitos K, Cohen CRG. Mortality, morbidity and functional outcome after ileorectal anastomosis. *The British Journal of Surgery*. 2003; 90: 59-65.
54. Nakagoe T, Sawai T, Tsuji T, Nanashima A, Shibasaki S, et al. Successful resection of a duodenal fistula complicated with recurrent Crohn's disease at the site of previous ileocolonic anastomosis: report of a case. *Surgery Today*. 2003; 33: 537-541.
55. Tay GS, Binion DG, Eastwood D, Otterson MF. Multivariate analysis suggests improved perioperative outcome in Crohn's disease patients receiving immunomodulator therapy after segmental resection and/or strictureplasty. *Surgery*. 2003; 134: 565-72-3.
56. Smedh K, Andersson M, Johansson H, Hagberg T. Preoperative management is more important than choice of sutured or stapled anastomosis in Crohn's disease. *The European Journal of Surgery = Acta Chirurgica*. 2002; 168: 154-157.
57. Bernell O, Lapidus A, Hellers G. Risk factors for surgery and recurrence in 907 patients with primary ileocaecal Crohn's disease. *The British Journal of Surgery*. 2000; 87: 1697-1701.
58. Sampietro GM, Cristaldi M, Porretta T, Montecamozzo G, Danelli P, et al. Early perioperative results and surgical recurrence after strictureplasty and miniresection for complicated Crohn's disease. *Digestive Surgery*. 2000; 17: 261-267.
59. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Diseases of the Colon and Rectum*. 2000; 43: 1141-1145.
60. Yamamoto T, Keighley MR. Factors affecting the incidence of postoperative septic complications and recurrence after strictureplasty for jejunoileal crohn's disease. *The American Journal of Surgery*. 1999; 178: 240-245.
61. Yamamoto T, Keighley MR. Enterovesical fistulas complicating Crohn's disease: clinicopathological features and management. *International Journal of Colorectal Disease*. 2000; 15: 211-5-7.
62. Jawhari A, Kamm MA, Ong C, Forbes A, Bartram CI, et al. Intra-abdominal and pelvic abscess in Crohn's disease: results of non-invasive and surgical management. *The British Journal of Surgery*. 1998; 85: 367-371.
63. Longo WE, Milsom JW, Lavery IC, Church JC, Oakley JR, et al. Pelvic abscess after colon and rectal surgery--what is optimal management? *Diseases of the Colon and Rectum*. 1993; 36: 936-941.
64. Olaison G, Smedh K, Sjö Dahl R. Natural course of Crohn's disease after ileocolic resection: endoscopically visualised ileal ulcers preceding symptoms. *Gut*. 2003; 33: 331-335.
65. Sachar DB. The problem of postoperative recurrence of Crohn's disease. *The Medical Clinics of North America*. 1990; 74: 183-188.
66. Greenstein AJ, Lachman P, Sachar DB, Springhorn J, Heimann T, et al. Perforating and non-perforating indications for repeated operations in Crohn's disease: evidence for two clinical forms. *Gut*. 1988; 29: 588-592.
67. Bundred NJ, Dixon JM, Lumsden AB, Gilmour HM, Davies GC. Free perforation in Crohn's colitis. A ten-year review. *Diseases of the Colon and Rectum*. 1985; 28: 35-37.
68. Heimann TM, Greenstein AJ, Mechanic L, Aufses AH. Early complications following surgical treatment for Crohn's disease. *Annals of Surgery*. 1985; 201: 494-498.
69. Hollender LF, Meyer C, Avet D, Zeyer B. Postoperative fistulas of the small intestine: therapeutic principles. *World Journal of Surgery*. 1983; 7: 474-480.