

Surgical Treatment of Crohn's Disease while Distinguishing between Perforating and Non-Perforating Types

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Abstract

[Background] Medical treatment for Crohn's disease (CD) has progressed ; however, the condition requires surgical treatment, and therefore surgery cannot be eliminated as a treatment option. The current study summarizes the current state of surgery for CD and examines future surgical strategies.

[Patients and methods] The study population included patients who underwent initial surgery for CD in our department from 1985 to 2017. The reason for surgery, surgical procedure, and preoperative and postoperative course were examined.

[Results] When the reason for surgery was classified as an absolute or a relative indication for surgery, surgery was required in 8% of patients and suggested in 92% of patients. Various surgical procedures were used to treat CD ; the procedures that were applied depended on the patient. Patients who developed CD and who underwent initial surgery after 2000 underwent surgery approximately 3 and a half years later than patients who developed CD and underwent initial surgery before 1999. In addition, the rate of additional surgery significantly decreased in patients who developed CD and underwent initial surgery after 2000. When CD was categorized as perforating disease or non-perforating disease, patients with perforating disease were treated prior to initial surgery for approximately 2 years longer in comparison to patients with non-perforating disease ; however, patients with perforating disease underwent additional surgery 1 year and 3 months sooner than patients with non-perforating disease.

[Conclusion] Patients with CD may undergo multiple surgeries ; thus, the timing of the initial surgery is crucial, given the number of surgeries that they will undergo in their lifetime.

Key words : Crohn's disease, surgery, perforating type, non-perforating type

Introduction

Since 2000, remarkable progress has been made in the medical treatment for CD thanks to the development of biologics and immunomodulators ; however, the condition still requires surgical treatment, and surgery cannot be eliminated as a treatment option. Surgery for CD is not intended to be curative. Surgery eliminates the complications of CD, such as strictures and abscesses. Surgery is thus intended to improve the patient’s general condition and QOL. The current study examined the reasons for surgery, the procedure performed, and the course of treatment in patients undergoing surgery for CD in our Department. This study also discusses the future of surgical treatment for CD.

Patients and methods

The study population included 453 patients (male, n= 314 ; female, n=139) who were clinically or pathologically diagnosed with CD and who underwent initial surgery in this Department from 1985 to 2017 (mean age at initial surgery, 33 years old). The form of CD was small intestine type in 172 patients (38%), small and large intestine type in 243 patients (54%), and large intestine type in 38 patients (8%) (Table 1).

Table 1. Patients characteristics

453cases	
M/F	: 314/139
Age at surgery	: 33 y.o
Period of follow up	: 13 y.o
Type of CD	: Small intestine type 172 (38%)
	Small and large intestine type 243 (54%)
	Large intestine type 38 (8%)

Table 2. The indications of surgery in Crohn’s disease

Absolute indications	Relative indications
Perforation	Refractory stenosis
Massive bleeding	Fistula (internal, external)
Bowel obstruction refractory to medical therapy	Refractoriness to medical treatment
Abscess	Refractory perianal lesions
Cancer	

Matsuoka K *et al* : Evidence-based clinical practice guidelines for inflammatory bowel disease. *J Gastroenterol.* 53:305–353, 2018.

Results

Indications for surgery and the reasons for surgery

CD cannot be cured with surgery ; thus, the indications for surgery are considered to be either absolute or relative¹⁾. In other words, absolute indications are life-threatening and involve emergency surgery (perforation, massive bleeding, bowel obstruction refractory to medical therapy, or abscess) or cancer. Relative indications include refractory stenosis, extraintestinal complications such as internal and external fistulas and failure, failure to respond to medical treatment, and refractory anal lesions (Table 2). When looking solely at the patients in this study, approximately 8% required surgery, while surgery was suggested for the remaining 92%.

Greenstein *et al.* proposed classifying the surgical indications for CD into perforating and non-perforating indications²⁾. This approach classified CD into 2 forms, one where the continuity of the gastrointestinal tract was disrupted (perforating type), and one where the continuity of the gastrointestinal tract was intact (non-perforating type). The clinical course of these forms differs (Table 3 ; Fig. 1). Regarding the proportion of patients with perforating type or non-perforating type before 1999 and after 2000, more patients seen after 2000 had perforating type (Fig. 2). Patients seen after 2000 tend to receive treatment primarily with biologics or immunomodulators (Fig. 3). Biologics were used at our hospital starting from the clinical trial stage. Regarding the proportion of patients with perforating disease or non-perforating type in each year after 2000, the proportion of perforating type increased in around 2002, when biologics were officially approved by the Japanese National Health Insurance Program, and they continued to increase until 2005. This period precludes a distinction between the efficacy of biologics and the timing of surgery. The prevalence of the non-perforating type increased after 2006 and has remained

Table 3. Perforating and non-perforating indications

Perforating indications	Non-perforating indications
Fistula	Obstruction
Abscess	Intractability
Acute free perforation	Hemorrhage
	Toxic dilatation

Greenstein AJ *et al* : Perforating and non-perforating indications in Crohn’s disease : evidence for two clinical forms. *Gut* 29:588, 1988.

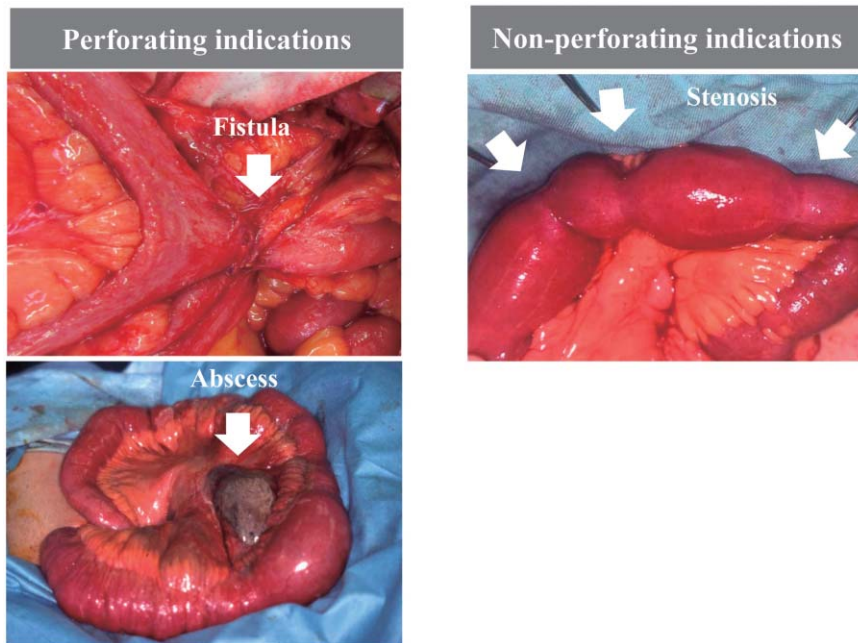


Fig. 1. Surgically treated cases of perforating type and non-perforating type Crohn's disease.

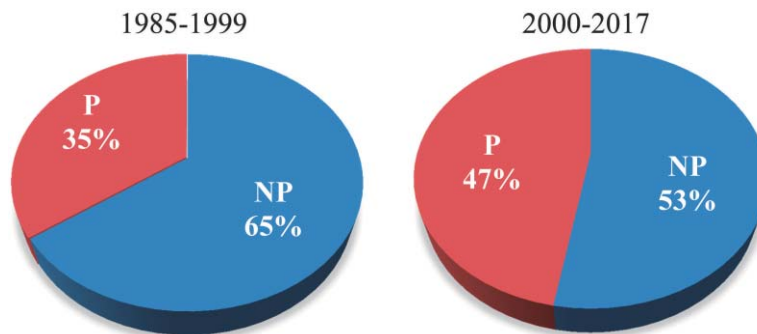


Fig. 2. Change in the ratio of perforating type and non-perforating type Crohn's disease. P, perforating type ; NP, non-perforating type.

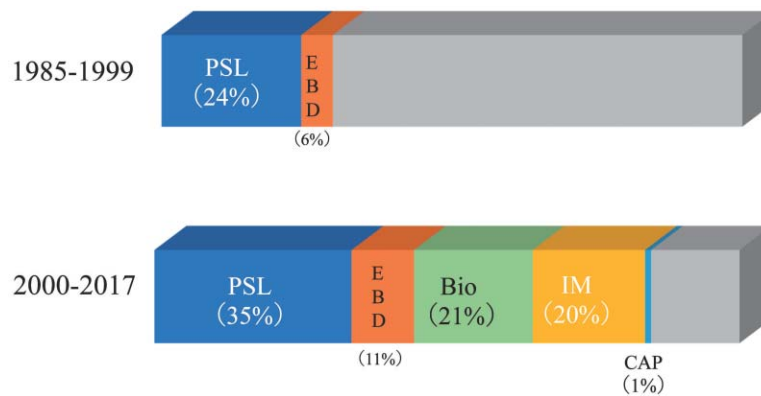


Fig. 3. Comparison of the preoperative medical treatments (excluding nutritional therapy and mesalazine). EBD, Endoscopic balloon dilation ; IM, immunomodulator ; CAP, cytopheresis.

as prevalent as it was before 2000 (Fig. 4). When the rate of additional surgery was compared in patients seen before 1999 and patients seen after 2000, the rate of additional surgery within 5 years significantly decreased from 34% to 16% and the rate within 10 years significantly decreased from 59% to 37%. Presumably, this is largely the result of advances in medical treatment (Fig. 5).

Surgical procedure

Proctocolectomy is the standard surgical procedure

for the treatment of ulcerative colitis, which is an inflammatory bowel disease like CD ; however, there is no standard surgery for CD.

Three types of basic procedures are used to treat CD : strictuoplasty, resection and bypass. Surgery is performed with a combination of these 3 procedures. Bowel segments excluded with a bypass are difficult to assess and the procedure can increase the risk of cancer, so it is seldom performed³.

A problem with resection is that CD often recurs at the site of anastomosis⁴. Anastomosis can be per-

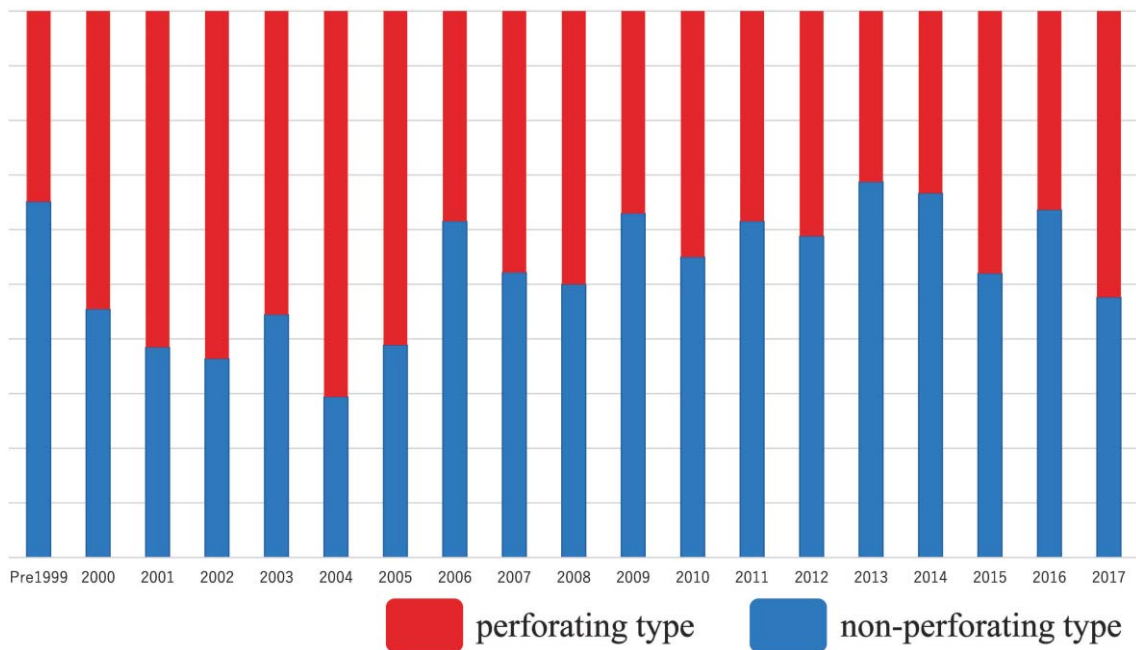


Fig. 4. Comparison of the annual rates of perforating type and non-perforating type Crohn's disease.

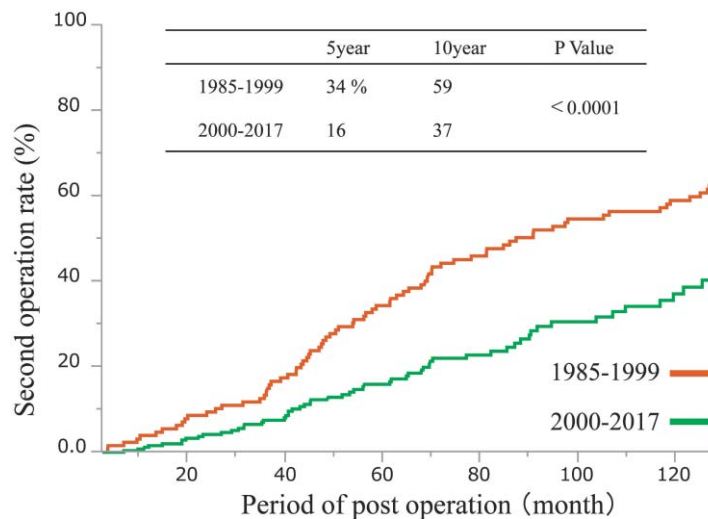


Fig. 5. Change in the second operation rate.

formed either by hand or with a stapler. The merits and demerits of the 2 techniques have been debated ; however, no definitive conclusion has yet been reached⁵⁾⁻⁸⁾. End-to-end anastomosis, side-to-side anastomosis, functional end-to-end anastomosis, or Kono-S anastomosis can be performed at the anastomotic site⁹⁾⁻¹²⁾. Various techniques are used to keep CD from recurring at the site of anastomosis.

Laparoscopic surgery has become a mainstay of gastrointestinal surgery. Its indications for CD are expanding, but there is little evidence of its usefulness¹³⁾¹⁴⁾. Laparoscopic surgery is more aesthetically pleasing than laparotomy ; however, its indications must be carefully determined in cases involving severe inflammation.

Discussion

CD is a condition that involves a great deal of additional surgery¹⁵⁾, and various approaches to postoperative management and drug therapy have been examined¹⁶⁾¹⁷⁾. However, there are no absolute or definitive approaches to postoperative treatment or managements that can forestall additional surgery¹⁸⁾¹⁹⁾. It remains important to reduce the number of surgeries over the course of treatment as much as possible. As mentioned earlier, Greenstein et al. followed 770 patients undergoing initial surgery, and found that perforating disease resulted in higher rate of recurrence and additional surgery in comparison to non-perforating dis-

ease²⁾. Greenstein et al. also found that CD often recurs in the same form (perforating or non-perforating). The classification devised by Greenstein et al. is still used today, even though their study was published 30 years ago, when biologics and immunomodulators were not in use. The current study investigated whether this classification system is applicable to patients seen in our department. A total of 324 patients have undergone initial surgery for CD in this department since 2000, when new medical treatments were introduced. One of those patients underwent initial surgery to treat cancer. The patient was excluded because the classification system of Greenstein et al. does not indicate whether CD and cancer should be classified as perforating disease or non-perforating disease. Thus, the course of treatment of 323 patients was examined according to the methods of Greenstein et al. (Fig. 6). Patients with perforating disease underwent additional surgery 1 year and 4 months earlier than patients with non-perforating disease. Similar to the study by Greenstein et al., the current study also revealed that CD often recurred in the same form (perforating or non-perforating) as was present when initial surgery was performed. In patients with perforating disease, the period from the diagnosis to be the initial surgery was 1 year and 8 months longer than that in patients with non-perforating disease. Medical treatment did not differ substantially between the patients with perforating disease and those with non-perforating disease, both be-

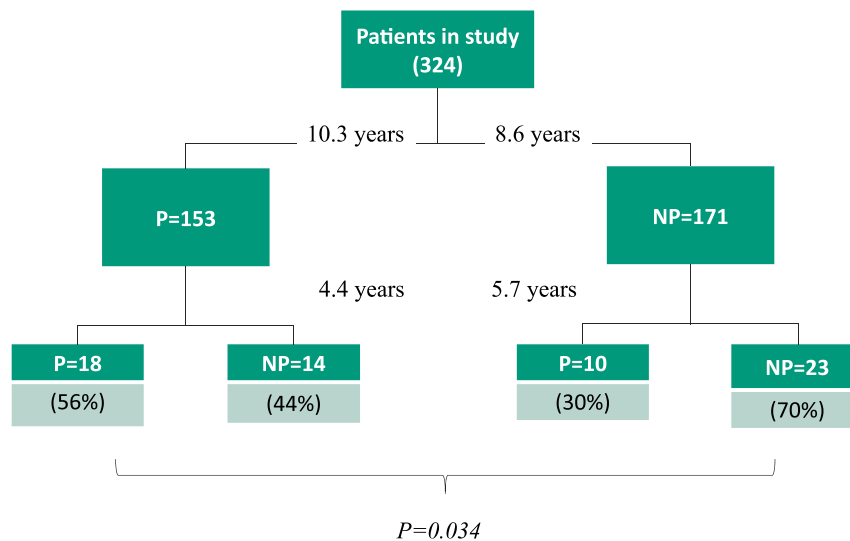


Fig. 6. Postoperative course of perforating and non-perforating type Crohn's disease.

This figure was created with reference to Dr. Greenstein's thesis*, based on the data of our department.
*Greenstein AJ et al : Perforating and non-perforating indications in Crohn's disease : evidence for two clinical forms. Gut 29 : 588, 1988.

fore and after initial surgery (Fig. 7). Treatment was not modified because of the form of CD.

Conclusion

Based on the above results, the sole consideration during the course of treatment for CD should not be delaying the period prior to initial surgery, given the number of surgeries the patient will undergo in their lifetime. Rather, non-perforating disease should be treated surgically before the condition worsens.

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References

- 1) Matsuoka K, Kobayashi T, Ueno F, Matsui T, Hirai F, Inoue N, Kato J, Kobayashi Kenji, Kobayashi Kiyonori, Koganei K, Kunisaki R, Motoya S, Nagahori M, Nakase H, Omata F, Saruta M, Watanabe T, Tanaka T, Kanai T, Noguchi Y, Takahashi K, Watanabe K, Hibi T, Suzuki Y, Watanabe M, Sugano K, Shimosegawa T : Evidence-based clinical practice guidelines for inflammatory bowel disease. *J Gastroenterol.* 53 : 305–353, 2018.
- 2) Greenstein AJ, Lachman P, Sachar DB, Springhorn J, Heimann T, Janowitz HD and Aufses Jr. AH : Perforating and non-perforating indications in Crohn's disease : evidence for two clinical forms. *Gut.* 29 : 588–592, 1988.
- 3) Higashi D, Futami K, Kojima D, Futatsuki R, Ishibashi Y, Maekawa T, Yano Y, Takatsu N, Hirai F, Matsui T, Iwashita A : Cancer of the Small Intestine in Patients with Crohn's Disease. *Anticancer Res* 33 : 2977–2980, 2013.
- 4) Higashi D, Futami K, Egawa Y, Tomiyasu T, Ishibashi Y, Harimura T, Tanaka R, Sato K, Nii K, Kuroki H, Naritomi K, Hiratsuka M, Mikami K, Maekawa T : Postoperative course for intestinal lesion in Crohn's disease. *Med. Bull Fukuoka Univ.* 36(1), 17–22, 2009.
- 5) He X, Chen Z, Huang J, Lian L, Rouniyar S, Wu X, Lan P : Stapled Side-To-Side anastomosis might be better than handsewn end-to-end anastomosis in ileocolic resection for Crohn's disease : A meta-analysis. *Dig Dis Sci.* 59(7), 1544–1551, 2014.
- 6) Simillis C, Purkayastha S, Yamamoto T, Strong SA, Darzi AW, Tekkis P. : A meta-analysis compar-

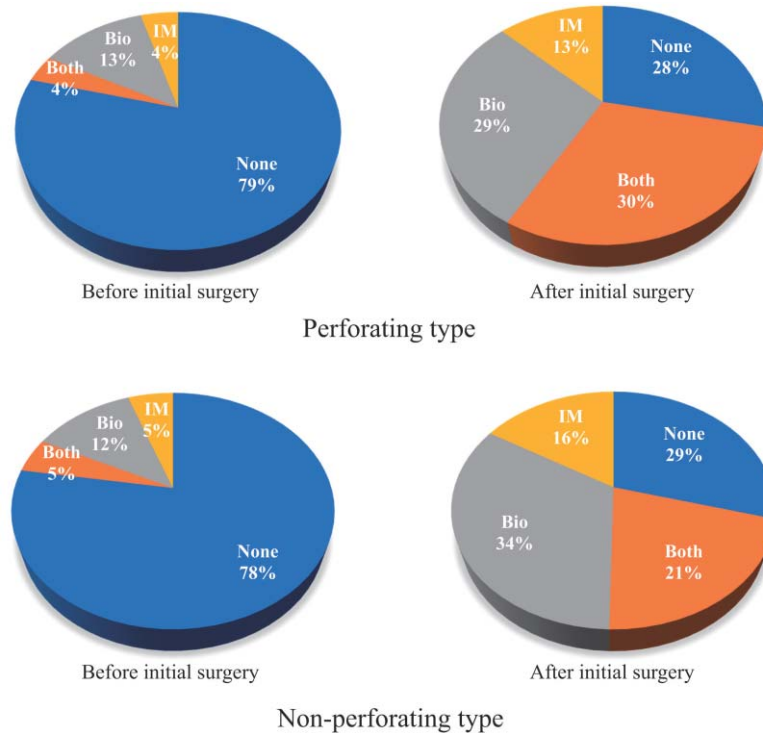


Fig. 7. Medical treatment (excluding nutritional therapy and mesalazine) before and after initial surgery for Crohn's disease.

- ing conventional end-to-end anastomosis vs. other anastomotic configurations after resection in Crohn's disease. *Dis Colon Rectum*. 50(10), 1674–1687, 2007.
- 7) Guo Z, Li Y, Zhu W, Gong J, Li N, Li J. : Comparing outcomes between side-to-side anastomosis and other anastomotic configurations after intestinal resection for patients with Crohn's disease : A meta-analysis. *World J Surg*. 37(4), 893–901, 2013.
 - 8) Gajendran M, Bauer AJ, Buchholz BM, Watson AR, Koutroubakis IE, Hashash JG, Ramos-Rivers C, Shah N, Lee KK, Cruz RJ, Regueiro M, Zuckerman B, Schwartz M, Swoger J, Barrie A, Harrison J, Hartman DJ, Salgado J, Rivers WM, Click B, Anderson AM, Umapathy C, Babichenko D, Dunn MA, Binion DG. : Ileocecal anastomosis type significantly influences long-term functional status, quality of life, and healthcare utilization in postoperative Crohn's disease patients independent of inflammation recurrence. *Am J Gastroenterol*. 113(4), 576–583, 2018.
 - 9) Kono T, Ashida T, Ebisawa Y, Chisato N, Okamoto K, Katsuno H, Maeda K, Fujiya M, Kohgo Y, Furukawa H. : A new antimesenteric functional end-to-end handsewn anastomosis : Surgical prevention of anastomotic recurrence in Crohn's disease. *Dis Colon Rectum*. 54(5), 586–592, 2011.
 - 10) Michelassi F, Hurst RD, Melis M, Rubin M, Cohen R, Gasparitis A, Hanauer SB, Hart J. : Side-to-side isoperistaltic strictureplasty in extensive Crohn's disease : A prospective longitudinal study. *Ann Surg*. 232(3), 401–408, 2000.
 - 11) Michelassi F. : Side-to-side isoperistaltic strictureplasty for multiple Crohn's strictures. *Dis Colon Rectum*. 39(3), 345–349, 1996.
 - 12) Michelassi F, Mege D, Rubin M, Hurst RD. : Long-term results of the side-to-side isoperistaltic strictureplasty in Crohn disease : 25-year follow-up and outcomes. *Ann Surg*. [Online ahead of print], 2019.
 - 13) Patel SV, Patel SVB, Ramagopalan SV, Ott MC. : Laparoscopic surgery for Crohn's disease : A meta-analysis of perioperative complications and long term outcomes compared with open surgery. *BMC Surg*. 13 : 14, 2013.
 - 14) Moorthy K, Shaul T, Foley RJ. : Factors that predict conversion in patients undergoing laparoscopic surgery for Crohn's disease. *Am J Surg*. 187(1), 47–51, 2004.
 - 15) Bernell O, Lapidus A, Hellers G. : Risk factors for surgery and recurrence in 907 patients with primary ileocaecal Crohn's disease. *Br J Surg*. 87(12), 1697–1701, 2000.
 - 16) Cruz PD, Kamm MA, Hamilton AL, Ritchie KJ, Krejany EO, Gorelik A, Liew D, Prideaux L, Lawrance IC, Andrews JM, Bampton PA, Gibson PR, Sparrow M, Leong RW, Florin TH, Geary RB, Radford-Smith G, Macrae FA, Debinski H, Selby W, Kronborg I, Johnston MJ, Woods R, Elliott PR, Bell SJ, Brown SJ, Connell WR, Desmond PV. : Crohn's disease management after intestinal resection : A randomised trial. *Lancet*. 385 (9976), 1406–1417, 2015.
 - 17) Peyrin-Biroulet L, Sandborn W, Sands BE, Reinisch W, Bemelman W, Bryant RV, D'Haens G, Dotan I, Dubinsky M, Feagan B, Fiorino G, Geary R, Krishnareddy S, Lakatos PL, Loftus Jr EV, Marteau P, Munkholm P, Murdoch TB, Ordás I, Panaccione R, Riddell RH, Ruel J, Rubin DT, Samaan M, Siegel CA, Silverberg MS, Stoker J, Schreiber S, Travis S, Assche GV, Danese S, Panes J, Bouguen G, O'Donnell S, Pariente B, Winer S, Hanauer S, Colombel J-F. : Selecting therapeutic targets in inflammatory bowel disease (STRIDE) : Determining therapeutic goals for treat-to-target. *Am J Gastroenterol*. 110(9), 1324–1338. 2015.
 - 18) Cruz PD, Kamm MA, Hamilton AL, Ritchie KJ, Krejany EO, Gorelik A, Liew D, Prideaux L, Lawrance IC, Andrews JM, Bampton PA, Jakobovits S, Florin TH, Gibson PR, Debinski H, Geary RB, Macrae FA, Leong RW, Kronborg I, Radford-Smith G, Selby W, Johnston MJ, Woods R, Elliott PR, Bell SJ, Brown SJ, Connell WR, Desmond PV. : Efficacy of thiopurines and adalimumab in preventing Crohn's disease recurrence in high-risk patients—A POCER study analysis. *Aliment Pharmacol Ther*. 42(7), 867–879, 2015.
 - 19) Shinagawa T, Hata K, Ikeuchi H, Fukushima K, Futami K, Sugita A, Uchino M, Watanabe K, Higashi D, Kimura H, Araki T, Mizushima T, Itabashi M, Ueda T, Koganei K, Oba K, Ishihara S, Suzuki Y. : Rate of reoperation decreased significantly after year 2002 in patients with Crohn's disease. *Clin Gastroenterol Hepatol*. [Online ahead of print], 2019.
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「The authors declare no conflict of interest.」