

Surgical treatment of Crohn's disease: Indications, results and predictive factors of recurrence and morbidity

Traitement chirurgical de la maladie de Crohn: Indications, résultats et facteurs prédictifs de récurrence et de morbidité post opératoire

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R É S U M É

Prérequis : La prise en charge de la maladie de Crohn constitue un problème majeur en chirurgie et en gastro-entérologie étant donné qu'elle affecte les sujets jeunes et qu'elle a un impact majeur sur leur vie personnelle et professionnelle. Les buts de notre étude étaient de décrire les indications, les résultats et les complications de la chirurgie au cours de la maladie de Crohn, et d'identifier d'éventuels facteurs prédictifs de récurrence et de morbidité postopératoire.

Méthodes : Nous avons réalisé une étude descriptive rétrospective incluant 38 patients ayant une maladie de Crohn traitée chirurgicalement dans le service de chirurgie générale de l'hôpital Mongi Slim, entre Janvier 1992 et Décembre 2011.

Résultats : La survenue d'une sténose symptomatique était l'indication la plus fréquente de la chirurgie au cours de la maladie de Crohn dans notre série, et la résection iléo-colique était l'intervention la plus fréquemment pratiquée. 26 patients (soit 58%) avaient reçu un traitement d'entretien après la chirurgie. Parmi les 33 patients ayant un suivi à long terme, 22 patients avaient rechuté et 13 avaient nécessité une reprise chirurgicale pour leur récurrence. En analyse univariée, les facteurs prédictifs de morbidité post-opératoire étaient l'hyperleucocytose, le phénotype pénétrant et la présence d'un foyer infectieux intra-abdominal. Par ailleurs, la localisation iléo-colique était le seul facteur prédictif de récurrence post opératoire objectivé dans notre série. En analyse multivariée, seul le phénotype pénétrant était prédictif de morbidité post opératoire.

Conclusion : Malgré le développement du traitement médical, le traitement chirurgical garde une place de choix dans la prise en charge des complications de la maladie de Crohn. Cette chirurgie doit être une alternative aux immunosuppresseurs. Actuellement la prévention des récurrences postopératoires est bien codifiée, permettant de réduire le risque de complications.

Mots-clés

Maladie de Crohn, chirurgie, récurrence

S U M M A R Y

Background: Crohn's disease management represents a major problem in gastroenterology and general surgery because it affects young subjects and has a major impact on their quality of life. The aims of our study were to identify the indications for surgery in Crohn's disease, the results and the complications of surgery in our series, and to identify possible predictive factors of recurrence and postoperative morbidity.

Methods: A retrospective descriptive study including 38 cases of patients with Crohn's disease who underwent surgical treatment in the department of surgery in Mongi Slim Hospital, during the period between January 1992 and December 2011 was performed.

Results: The occurrence of stenosis was the most common indication for surgical treatment in Crohn's disease in our series, and ileocecal resection was the most performed surgery. Twenty six patients (58%) received maintenance therapy after surgery. Twenty two patients relapsed and 13 had surgical management for recurrence. In univariate analysis, predictive factors of post operative morbidity in our study were leukocytosis, penetrating phenotype and intra-abdominal sepsis. Ileocecal location was the only factor that significantly improved the incidence of recurrence. In multivariate analysis, only penetrating phenotype was a predictive factor of post operative morbidity.

Conclusion: Despite the development of medical treatment, surgical treatment keeps large indications for the management of complications of Crohn's disease. The surgery should be an alternative to immunosuppressive therapy. Currently, prevention postoperative recurrence is well codified, reducing the risk of complications.

Key - words

Crohn's disease, Surgery, Recurrence

Crohn's disease management represents a major problem in gastroenterology and general surgery because it affects young subjects and has a major impact on their quality of life due to the frequency of relapses and complications often requiring surgery. Surgical treatment is needed in the majority of patients with Crohn's disease despite a large number of available medical therapies including corticosteroids, immunosuppressive and anti-TNF which are nowadays more efficient. But surgery remains indicated in several situations: in acute complications (obstruction, perforation, severe acute colitis, intra-abdominal or pelvic abscesses) and in chronic Crohn's disease (stenosis, internal or external fistula, abdominal mass), and resistant forms to medical treatment [1]. The modalities of surgical treatment are primarily based on the intestinal resection, and rarely stricturoplasty [1]. Whatever the type of procedure performed, it will not cure the patient, but just treat the symptoms and the patient will be exposed to long-term recurrence of the remaining intestine [2]. The problem lies in the surgical treatment early outcomes such as post operative morbidity and late outcomes especially recurrence. The aims of our study were to identify the indications for surgery in Crohn's disease, the results and the complications of surgery in our series, and to identify possible predictive factors of recurrence and postoperative morbidity.

METHODS

Type of study: A retrospective descriptive study including 38 cases of patients with Crohn's disease who underwent surgical treatment in the department of visceral surgery of Mongi Slim Hospital, during the period between January 1992 and December 2011 was performed.

Inclusion criteria: Only patients who had histological confirmation of Crohn's disease obtained by surgical specimen or endoscopic biopsy were included in the study.

Exclusion criteria: We excluded from the study patients who had complicated Crohn's disease but who did not need surgery. Were also excluded patients where surgical treatment involved only for perianal lesions of Crohn's disease.

Statistical analysis: Statistical analysis was performed by SPSS @ 16.0 software. Variables were compared by using the khi 2 test for qualitative variables and Student test for quantitative variables. Univariate than multivariate analyses were performed to determine the predictive factors of relapse and post operative morbidity. p value was considered significant if lower than 0.05.

RESULTS

Characteristics of the population: Thirty-eight patients were included in the study. The average age at the time of surgery was 33 years [Range: 14 – 60 years]. Thirty-four patients (84%) were aged less than 40 years. There were 21 men and 17 women with a sex ratio of 1.23. Twenty-one patients (55%) had previous surgery: 7 patients (18%) underwent surgery for perianal Crohn's disease, 9 patients (24%) had appendectomy. Five patients were smokers. Patients were classified according to the American Society of Anesthesiologists as ASA I in 28 cases (74%) and ASA II in 10 cases (26%). The location of Crohn's disease was unifocal in 71% and 29% in bifocal cases. The terminal ileum and ileo-cecal involvement was predominant (Table 1).

Table 1: Topography of Crohn's disease

Number of localisations	Localisations	Number	(%)
One localisation (71.1%)	Ileo-caecal	10	26%
	Ileal	10	26%
	Colonic	3	8%
	Small intestine	2	5%
	Colorectal	2	5%
Two localisations (13.1%)	Colonic and ileal	3	8%
	Ileo-caecal and small intestine	1	3%
	Ileo-caecal and colonic	1	3%

Surgical treatment:

Indications of surgery: Twenty-one patients (55%) underwent programmed surgery. In emergency cases (45%), the indication for surgery was dominated by occlusion in 16% of cases (n = 6) and peritonitis in 13% of cases (n = 5). Crohn's disease was inaugurated by a complications requiring emergency surgery in eleven patients. A digestive stenosis was the main indication for programmed surgery and in some cases, it was associated with other lesions (external or internal fistula, abdominal mass, or intra-peritoneal abscess). Table 2 shows the various surgical indications in our patients.

Table 2 : Indications of surgery

Indications	Number	(%)
Emergency Occlusion	5	13%
Occlusion and abscess	1	3%
Peritonitis	5	13%
Diagnosis mistake	4	11%
Acute severe colitis	2	5%
Retarded	9	24%
Stenosis	1	3%
Stenosis and abdominal mass	1	3%
Stenosis and internal fistula	1	3%
Stenosis and abscess and enterovesical fistula	1	3%
Stenosis and external fistula	2	5%
External fistula	2	5%
Internal fistula	1	3%
External and internal fistulas and abscess	1	3%
Internal fistula and abscess	1	3%
Internal fistula and abscess and abdominal mass	1	3%
Failure of medical treatment	1	3%

Incision: The incision was median in 76% while 24% cases had laparoscopy. A laparoconversion was necessary in 5% of cases, because of the presence of adhesences.

The immediate postoperative complications: Two patients died (5%) in the immediate postoperative due to pulmonary embolism in one case and intravascular coagulation in the other. The postoperative morbidity in our series was 24%: Five patients (13%) developed specific and/or nonspecific complications within the 30 days after surgery. Four

patients (11%) developed between 2 and 4 complications in the immediate postoperative course. Three patients had new surgery at day 3 and day 5 after the first intervention because of dropping anastomosis in 2 cases and evisceration in one case. Patients with abscess of the wall received a flat pattern. An abscess in the liver was evacuated under computed tomography in one case. A digestive fistula occurred in two cases. It dried up in one case after infliximab treatment. In the second case, the flow rate was low and fistula dried up after a month. A patient presented acute respiratory distress and hemorrhagic shock with a favorable outcome in intensive care unit. The outcome was good in all complication cases. The mean duration of post operative hospitalization was 12 days [range 3 – 60 days].

The late post-operative complications: Except two lost of view patients, all patients had a one month consultation in surgical department and were referred after that to a 6 month consultation in gastroenterology department. The post-operative follow was evaluated in our series on the number of stools/24 hours, weight gain, the quality of the scar and anorectal function. A favorable postoperative evolution was noted in 79% of patients (n = 30). Only 10 patients had lower endoscopy control within 6 months after surgery, 3 patients were explored by other imaging techniques. Control colonoscopy was normal in three of 10 patients (30%). Regarding the remaining seven patients endoscopic lesions are summarized as below: ulceration of the anastomosis, aphthous ulcerations, congestive-proctitis and stenosis in respectively 2, 3, 1 and 1 patients.

Recurrence: Twenty-two patients (58%) had a confirmed clinical, radiological or endoscopic recurrence, within 6 months to twenty years after the first surgery. Thirteen of them needed second surgical intervention [14 men, mean age 36 years], including 4 smokers. The localization of the disease was ileo-cecal in 6 cases, colic in 4 cases, ileal in 3 cases, grelic 3 cases, ileo-colic in 2 cases, and more than one location was observed in 4 patients. Initial operative procedures were: Twelve ileo-caecal resections (with stricturoplasty in one case), four ileo-colic resections, two small bowel resections (with stricturoplasty in one case), two left hemi-colectomy, one total colectomy and one subtotal colectomy.

After the initial response, nine patients (24%) relapsed between 6 months and 8 years. Three patients were under maintenance treatment (5 ASA or azathioprin). The evolution was favorable with conservative treatment consisting of gastric aspiration. Thirteen patients had at least one relapse requiring surgery. The average time to recurrence in these patients was 9.8 years, [range 2 - 20 years]. Eight patients had stenosis of the anastomosis responsible for occlusive symptoms.

Predictive factors of recurrence and post-operative morbidity: Predictive factors of recurrence and post-operative morbidity found in univariate analysis are respectively resumed in tables 3 and 4. In our study, the ileo-cecal localization of lesions was the only factor associated with a higher risk of recurrence, while postoperative morbidity was increased in case of leukocytosis, intra-abdominal sepsis or penetrating disease phenotype. Penetrating phenotype was confirmed as a risk factor of relapse in multivariate analysis.

Table 3 : Predictive factors of recurrence

	Group 1 : Recurrence n=22	Group 2 : No recurrence n= 16	p value
Sex-ratio	7/9	14/8	>0,05
Age/surgery	31.06	32.05	>0,05
Tobacco consumption	1	4	>0,05
Appendectomy	5	4	>0,05
Ano-perineal lesions	2	8	>0,05
Extra-digestive lesions	1	6	>0,05
Pre-operative medical treatment	5	11	>0,05
Penetrant phenotype (abcess or fistula)	10	11	>0,05
Resection of more than 20cm of small intestine	11	9	>0,05
Ileo-caecal resection	13	13	>0,05
Colic resection	2	3	>0,05
Colic and ileal resection	2	3	>0,05
Sick margin of resection	0	4	>0,05
Granuloma	4	9	>0,05
Grelic localisation	0	2	>0,05
Ileal localisation	6	7	>0,05
Ileo-caecal localisation	4	7	>0,05
Colic localisation	1	5	>0,05
Ileo-colic localisation	5	1	0.02

Table 4: Predictive factors of post-operative morbidity

	Group 1 : Post operative morbidity	Group 2 : no post operative morbidity	p value
Sex-ratio	16/13	5/4	>0,05
Pre-operative corticotherapy	9	2	>0,05
Loss of weigh	14	6	>0,05
Hyperleucocytosis	12	7	0,05
Penetrant phenotype (abcess or fistula)	12	9	0,02
Intra-abdominal sepsis	6	8	0,001
Median laparotomy	22	7	>0,05
Cœlioscropy	5	2	>0,05

DISCUSSION

In our study, stenosis was the most common complication indicated for surgical treatment in Crohn's disease, and ileocecal resection was the most performed surgery. The major risk factor of post operative morbidity was penetrating phenotype.

Surgery in Crohn's disease is frequently indicated. Crohn's disease is discovered during emergency surgery in 20-30% of cases [3]. It is necessary in this case, to avoid too large bowel resection [3]. Near 25% of patients underwent surgery for intestinal occlusion [4]. The indication for emergency surgery for intestinal obstruction was brought in 16% of patients (n = 6) in our series. Occlusion was attached in five cases with stenosis of the ileocecal region or the last ileum, and in one case a stenosis of the rectosigmoid associated with a pelvic abscess. Acute peritonitis is rare with a prevalence of 1% to 4% [5]. It is often associated with stenosis [6,7]. In our study, 13% of patients had

emergency surgery for acute peritonitis, was associated with perforation of the terminal ileum in two cases and colonic perforation in three cases.

Intra-abdominal abscesses should be treated with antibiotics, parenteral nutrition and scanno-guided drainage if possible. Surgery should be reserved for failure of the first-line treatment.

If this initial management is consensual, secondary treatment in cases of failure of first line treatment remains controversial and surgical resection is proposed only "if necessary" in the last consensus ECCO guidelines [8]. After the resolution of the abscess, surgical resection of stenosed bowel segment 6 weeks after the initial episode is recommended by experts, especially in the presence of obstructive symptoms [9]. A recent study of 32 Tunisian patients with Crohn's disease complicated by intra-peritoneal abscess found that the therapeutic approach based on first percutaneous drainage followed by a surgical resection in the presence of stenosis or persistent fistula was associated with a low risk of recurrence [10]. The surgical resection was ideally laparoscopic in this study [10]. In our study, only one patient underwent surgery for intra-abdominal abscess after failure of the first line treatment. Four patients presented intra-peritoneal abscess with internal fistulas and/or external in 8% of cases and associated with stenosis in 3% of cases.

Severe acute colitis is nowadays the main indication for surgery in Crohn's disease. Subtotal colectomy with ileo-sigmoidostomy is the gold standard procedure after failure of first line and second line medical treatment. In our series, only 5% of patients were operated on for severe acute colitis complicated by toxic megacolon and massive bleeding.

Stenosis is the most common complication in Crohn's disease [11]. It can result from inflammatory lesions, fibrosis or neoplasia (for long developing disease). These three types of lesions may be associated in the same patient. ECCO guidelines offer surgical treatment in two cases [9]

- Ileal inflammatory stenosis responsible for occlusive syndrome (Koenig syndrom) resisting to medical treatment.
- Stenosis of the small intestine, symptomatic, with no signs of endoscopic, biological or radiological inflammation.

Colonic strictures of Crohn's disease must always lead to search degenerescence which is present in 7% of cases [12]. In our work, the stenosis was noted in 40% of cases and localisation was ileal in 27% of cases. Surgery was indicated in 27% of cases.

Dysplasia in Crohn's disease can occur both in the small intestine than the colon. It is estimated respectively at 0.6% and 1.4% of cases. A study published in 2007 focused on the potential risk of increased gastrointestinal cancer in these patients. This risk must indeed be taken seriously in Crohn's disease because it affects young people. Therefore, explorations may be repeated during follow-up [13,14]. A case of low-grade dysplasia was noted after colonic resection in our series.

Surgery has little influence on the evolution of the disease and its role is limited to avoid complications [15]. Only symptomatic lesions should be treated [15].

Whatever the type of procedure performed, it will not cure the patient, who will be exposed to long-term recurrence of the remaining intestine [2]. For this reason, surgery should be avoided or delayed up in situations where it would be more harmful than beneficial. Surgery

may expose the patient to nutritional (short bowel syndrome), psychological (definitive stoma after abdominoperineal amputation) or functional (diarrhea, incontinence) consequences.

Regarding postoperative morbidity, Yamamoto et al reported a postoperative intra-abdominal sepsis rate (anastomotic leakage, intra-abdominal abscess surgery or post enterocutaneous fistula) in the order of 13% [16]. The main factors contributing to this complication were: treatment with corticosteroids and presence of an abscess. However, the risk does not increase with the number of anastomosis, the emergency nature of the intervention, the importance of preoperative malnutrition, the extent of resection and the iterative nature of the surgery. The postoperative complications appear to be higher in case of surgical treatment for recurrence with rates of around 38% [17]. In our study, only one case of postoperative mortality was noted in the first hours after ileocecal resection and the cause of death was unknown. The post operative morbidity concerned however four patients. All these patients had intra-abdominal septic complications (abscesses and/or digestive fistulas).

Recurrence concerned 14 patients (37%). The postoperative management involves identification of predictive factors of recurrence. Indeed, it is important because it would allow the selection of patients at high risk of recurrence requiring maintenance postoperative treatment. Tobacco is the only highly predictive of surgical recurrence clearly demonstrated to date. In a study conducted on 174 patients who underwent surgery, recurrence rate was 70% among smokers against 41% in non-smokers. This difference was more pronounced among women [18]. It has been shown that the penetrating phenotype was predictive of recurrence in several studies [19,20]. This factor was found in our series. Finally, two other factors are currently identified as a risk factor for postoperative recurrence: a history of anterior resection (appendectomy included) and extensive resection of the small intestine (between 20 and 50 cm or more) [21,22].

The consensus of ECCO 2010 recommended [9]

- To stop smoking
- To introduce preventive thiopurine therapy after small bowel resection in patients at high risk of recurrence and mesalazine or no treatment in patients at low risk in the two weeks following surgery and with a minimum of two years treatment.
- To perform a systematic endoscopy 6 months to a year after surgery and to classify lesions according to Rutgeerts classification [2].

Simillis et al concluded in there metanalysis, that End to-end anastomosis after resection for Crohn's disease may be associated with increased anastomotic leak rates. Side-to side anastomosis may lead to fewer anastomotic leaks and overall postoperative complications, a shorter hospital stay, and a perianastomotic recurrence rate comparable to end to-end anastomosis [23].

CONCLUSION

The occurrence of stenosis was the most common complication indicated for surgical treatment in Crohn's disease in our series, and ileocecal resection was the most performed surgery. These results are consistent with those in the literature. The analysis of the various factors that influence the post operative morbidity retain leukocytosis, penetrating phenotype and intra-abdominal sepsis as statistically

significant risk factors in postoperative morbidity. In our series, 26 patients (58%) had received maintenance therapy after surgery. Among the 33 patients followed long-term, 22 patients had relapsed and 13 had surgical management of recurrence. In our series, the

ileocecal location was the only factor that significantly altered the incidence of recurrence, and this factor was not objectified in other series.

Références

1. Turet E, Karoui M. Traitement chirurgical de la maladie de Crohn: principes de tactique et de technique opératoires. *EMC Techniques chirurgicales appareil digestif* 2006;40:667.
2. Rutgeerts P, Geobes K, Vantrappen G, Kerramans R, Coenegrachts JL, Coremans G. Natural history of recurrent Crohn's disease at the ileocolonic anastomosis after curative surgery. *Gut* 1984;25:665-72.
3. Itzkowitz SH, Present DH. Consensus conference: Colorectal cancer screening and surveillance in inflammatory bowel disease. *Inflamm Bowel Dis* 2005;11:314-21.
4. Michelassi F, Balestracci T, Chappell R, Block GE. Primary and recurrent Crohn's disease. Experience with 1379 patients. *Ann Surg* 1991;214:230-8.
5. Greenstein AJ, Mann D, Sachar DB, Aufses AH Jr. Free perforation in Crohn's disease: I. A survey of 99 cases. *Am J Gastroenterol* 1985;80:682-9.
6. Panis Y. Traitement chirurgical de la maladie de crohn. *Ann Chir* 2002;127:9-18.
7. Faik M. Principes et indications du traitement chirurgical de la maladie de Crohn. *Espérance médicale*. Tome 6, n° 50, p : 252-54. Mai 1999.
8. Dignass A, Van Assche G, Lindsay JO, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Current management. *J Crohns Colitis* 2010;4:28-62.
9. Van Assche G, Dignass A, Reinisch W, et al. The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Special situations. *J Crohns Colitis* 2010;4:63-101.
10. Bedioui H, Baraket O, Daghfous A et al. Maladie de Crohn compliquée d'abcès intra-abdominaux : stratégie diagnostique et thérapeutique. *Journal Africain d'Hépatologie-Gastroentérologie* 2012;6:96-102.
11. Travis SP, Stange EF, Lémann M, et al. European evidence based consensus on the diagnosis and management of Crohn's disease: current management. *Gut* 2006;55:i16-35.
12. Yamazaki Y, Ribeiro MB, Sachar DB, Aufses AH Jr, Greenstein AJ. Malignant colorectal strictures in Crohn's disease. *Am J Gastroenterol* 1991;86:882-5.
13. Brenner DJ, Hall EJ. Computed tomography-an increasing source of radiation exposure. *N Engl J Med* 2007;357:2277-84.
14. Desmond AN, O'Regan K, Curran C, et al. Crohn's disease: factors associated with exposure to high levels of diagnostic radiation. *Gut* 2008;57:1524-9.
15. Detry R. Place de la chirurgie dans le traitement de la maladie de crohn. *Louvain Med* 2002;121:195-8.
16. Yamamoto T, Allan RN, Keighley MR. Risk factors for intra-abdominal sepsis after surgery in Crohn's disease. *Dis Colon Rectum* 2000;43:1141-5.
17. Brouquet A, Blanc B, Bretagnol F, Valleur P, Bouhnik Y, Panis Y. Surgery for intestinal Crohn's disease recurrence. *Surgery* 2010;148:934-46.
18. Sutherland LR, Ramcharan S, Bryant H, Fick G. Effect of cigarette smoking on recurrence of Crohn's disease. *Gastroenterology* 1990;98:1123-8.
19. Sachar DB, Lemmer E, Ibrahim C, et al. Recurrence patterns after first resection for stricturing or penetrating Crohn's disease. *Inflamm Bowel Dis* 2009;15:1071-5.
20. Parente F, Sampietro GM, Molteni M, et al. Behaviour of the bowel wall during the first year after surgery is a strong of symptomatic recurrence of Crohn's disease: a prospective study. *Aliment Pharmacol Ther* 2004;20:959-68.
21. Buisson A, Chevaux JB, Allen PB, Bommelaer G, Peyrin-Biroulet L. Review article: the natural history of postoperative Crohn's disease recurrence. *Aliment Pharmacol Ther* 2012;35:625-33.
22. Rutgeerts P, Van Assche G, Vermeire S, et al. Ornidazole for prophylaxis of postoperative Crohn's disease recurrence: a randomized, double-blind, placebo-controlled trial. *Gastroenterology* 2005;128:856-61.
23. Simillis C, Purkayastha S, Yamamoto T, Strong SA, Darzi AW, Tekkis PP. A Meta-Analysis Comparing conventional end-to-end anastomosis vs. Other anastomotic configurations after resection in crohn's disease. *Dis Colon Rectum* 2007;50:1674-87.