Emergency surgery for Crohn's disease

Les urgences chirurgicales dans la maladie de Crohn

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RÉSUMÉ

Prérequis: La chirurgie occupe une place privilégiée dans la prise en charge de la maladie de Crohn. Pratiquée en urgence elle peut révéler des complications jusque là inconnues dont le traitement conditionne le pronostic.

Objectifs : Déterminer l'incidence des indications chirurgicales d'urgence dans la maladie de Crohn, préciser le type d'interventions pratiquées dans ces cas et évaluer les résultats de la chirurgie en urgence de la maladies de Crohn en post-opératoire, à court moyen et long terme.

Méthode : Nous avons mené une étude rétrospective transversale portant sur les dossiers de 38 patients porteurs de la maladie de Crohn qui ont subi une résection chirurgicale durant une période de 19 ans, s'étalant du 1er Janvier 1992 au 31 Décembre 2011 au département de chirurgie à l'hôpital Mongi Slim. En plus des caractéristiques socio-démographiques et les
présentations cliniques de notre population d'étude, nous avons évalué les indications, le type d'intervention, la durée d'évolution en préopératoire et les complications postopératoires ainsi que le pronostic global de la maladie.

Résultats : Parmi les 38 patients atteints de la maladie de Crohn nécessitant une intervention chirurgicale, 17/38 patients ont subi une chirurgie d'urgence. La maladie de Crohn a été inaugurée par les complications nécessitant une intervention chirurgicale d'urgence chez 11 patients. La durée moyenne des symptômes avant la chirurgie était de 1,5 an. L'indication la plus fréquente pour une chirurgie d'urgence a été l'occlusion intestinale aiguë (n=6) suivie de la perforation intestinale et la péritonite (n=5). Un faux diagnostic d'appendicite aigue a été retrouvé chez 4 patients et une colite aiguë sévère compliquée pour une maladie de Crohn inaugurale a été trouvée dans 2 cas. La laparotomie a été réalisée pour 15 patients. La résection-iléocolique était l'intervention la plus utilisée. Il y'avait une mortalité périopératoire et 5 morbidités postopératoires. Aucune mortalité postopératoire n'a été identifiée. La durée moyenne d'hospitalisation postopératoire a été de 14 jours (extrêmes 4 et 60 jours).
Six patients ont eu besoin d'une deuxième opération au cours de la période de suivi.

Conclusion : L'incidence de la chirurgie d'urgence pour la maladie de Crohn dans notre expérience était élevée (17/38 patients), et qui n'était pas aussi rare comme les estimations publiées ont montré. L'indication chirurgicale urgente pourrait être souvent la première présentation de la maladie de Crohn. L'occlusion intestinale aiguë et La perforation-péritonite étaient les indications les plus fréquentes de la chirurgie en urgence de la maladie de Crohn.

Mots-clés
Crohn; chirurgie; urgence; complications

SUMMARY

Background: Surgery has played an essential role in the treatment of Crohn's disease.
Emergency can reveal previously unknown complications whose treatment affects prognosis.

Purpose: Indicate the incidence of indications in emergent surgery for Crohn's disease. Specify the types of procedures performed in these cases and assess the results of emergency surgery for Crohn's disease postoperatively, in short , medium and long term.

Methods: Retrospective analysis of collected data of 38 patients, who underwent surgical resection for Crohn's disease during a period of 19 years from 1992 to 2011 at the department of surgery in MONGI SLIM Hospital, and among them 17 patients underwent emergency surgery for Crohn's disease. In addition to socio-demographic characteristics and clinical presentations of our study population, we evaluated the indications, the type of intervention, duration of evolution preoperative and postoperative complications and overall prognosis of the disease.

Results: Of the 38 patients with Crohn's disease requiring surgical intervention, 17/38 patients underwent emergency surgery. Crohn's disease was inaugurated by the complications requiring emergency surgery in 11 patients. The mean duration of symptoms prior to surgery was 1.5 year. The most common indication for emergency surgery was acute intestinal obstruction (n=6) followed by perforation and peritonitis (n=5). A misdiagnosis of appendicitis was found in 4 patients and a complicated severe acute colitis for undiagnosed Crohn's disease was found in 2 cases. The open conventional surgery was performed for 15 patients. Ileocolic resection was the most used intervention. There was one perioperative mortality and 5 postoperative morbidities. The mean of postoperative hospital stay was 14 days (range 4-60 days). Six patients required a second operation during the follow-up period.

Conclusion : The incidence of emergency surgery for Crohn's disease in our experience was high (17/38 patients), and is not as rare as the published estimates. Emergency surgical indication could be frequently the first presentation of Crohn's disease. Acute intestinal obstruction and perforation-peritonitis were the most common indications for emergent surgery in Crohn's disease in our study.

Key-words
Crohn; surgery; emergency; complications

Acute surgical emergencies in patients with Crohn's disease are not often required but may be dangerous for life. Advances in medical therapy especially biological therapies, have reduced the need for emergency surgery due to acute complications. The absolute indications encompass the presence of free perforation of the bowel with fistula or abscess formation, uncontrollable and massive hemorrhage, complete bowel obstruction unresponsive to intensive medical treatment [1] and severe acute colitis complicated with severe bleeding or toxic colitis. Acute surgical emergencies in patients with Crohn's disease can have a high morbidity, and with a multidisciplinary approach, morbidity can be reduced and patients can have a rapid return and improved quality of life. Any operation for Crohn's disease carries with it a significant chance of disease recurrence and the need for further operations.

METHODS

The present study is a retrospective analysis of collected data of 38 patients, and the Crohn's diagnosis was based on clinical, endoscopical, radiological, and histological findings on the basis of endoscopy biopsy or surgical specieman or on both. Intestinal resections were performed to the limit of macroscopic disease, without concern for the presence of microscopic disease. After the emergency surgical treatment of Crohn's disease, follow-up was organized in the gastroenterological department of MONGI SLIM Hospital. At each visit, clinical laboratory tests included complete blood counts-reactive protein, serum creatinine, serum albumin and liver enzyme tests. The patients were asked about their symptoms and any adverse events of medical treatment. An ileocolonoscopy was performed in our department for patients with low risk for recurrence [2] 6 months after the surgery, and the classifications of lesions were described according Rutgeerts and colleagues [3]. Other patients should be placed under preventive treatment of postoperative recurrence after surgery systematically, based on 5-aminosalisylic or aszthioprine, according to the clinical context.

RESULTS

Seventeen patients (10 men and 7 women) required emergency surgical intervention for Crohn's disease i.e. 17/38 operated patients. Their mean age was 31.1years (the youngest patient was aged 16 years, and the oldest was 60 years) at the moment of the surgery. Eleven/ Seventeen patients had an undiagnosed Crohn's disease at the moment of surgery, and the diagnosis was made during operation and confirmed histologically. Only 4 patients had received medical treatment preoperatively based on steroid or on 5-aminosalisylic. Two patients had extraintestinal manifestation. Chronic symptoms were mentioned in 9/17 patients, and the mean duration of symptoms prior to surgery was 1.5 year. Thirteen/ Seventeen patients had clinical signs of acute abdomen, and ten/seventeen patients had peritoneal syndrome on physical examination. Four/ Seventeen patients had pseudo-appendicitis signs on examination i.e. sensitivity of the right iliac fossa associated with fever. The indication for the emergency operation is shown in the figure 1 (Fig. 1). As indicated in the graph, acute intestinal obstruction (6/17 patients) followed by perforation and peritonitis (5/17 patients) were the main reasons for emergency surgery. Indications for emergency operation according different locations are resumed in table 1 (Table 1). Most lesions were ileocolic seat (9/17 patients) with cecal lesions seat in 5 patients. Five / Seventeen patients had ileum lesions, which 4 were in the terminal ileum, and colic lesions were found in 5 cases.

Figure 1 : Indication for emergency surgery for Crohn's disease

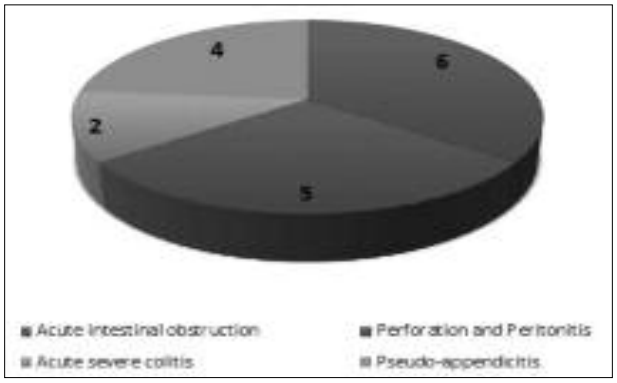

Table 1: Indications for emergency operation according different locations

	Ileocecal	Terminal ileum	Ileum	Colic	Colic+Ileocecal
Acute intestinal obstruction	2	3		1	
Perforation	1		1	2	1
Severe acute colitis				2	
Pseudo-appendicitis	2	1			1

The type of operative procedure applied is shown in figure 2 (Fig. 2). Laparotomy was the first main incision in our study (in 15/17 cases), and a laparoscopy converted to open surgery was made to 2 patients due to septic looped masses, thickened mesentery and technical difficulties. As indicated in the figure 2, the most frequently performed operative procedure was ileocolic resection (9/17 cases), combined with strictureplasty in one case, and followed by side-to-side or end-to-end anastomosis in 7 cases . One segmental small-bowel resection, 5 hemicolectomies (3 right colon and 2 left colon) and 2 subtotal colectomies

with ileostomy and closure of the rectum or distal colostomy were performed. Nine patients had a temporary diversion with an abdominal stoma. It was performed after clearance of the sepsis during the intervention due to peritonitis or to perforation with septic looped masses presented on the examination of pseudo-appendicitis signs, or after subtotal colectomies indicated for complicated acute severe colitis by toxic megacolon or bleeding.

Figure 2 : Different types of operative procedures in our study

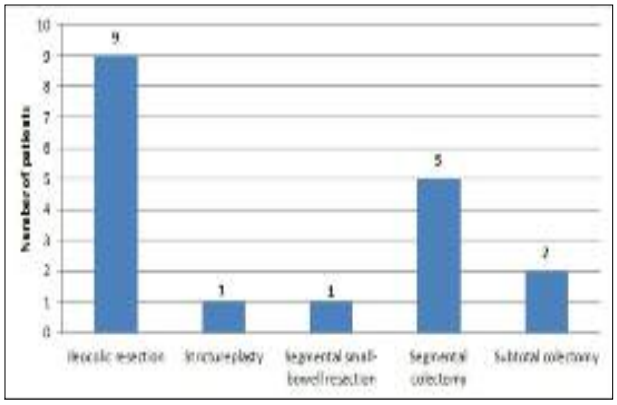

Table 2 : Postoperative complications according to the type of intervention

	Specific complication 1anastomotic	Non specific complication
Right hemicolectomy	leak+wound dehiscence	
Segmental small-bowel resection+ileostomy		1hyponatremia
Right hemicolectomy+ileostomy	1 anastomotic leak	1dehydration+ pneumonia
Subtotal colectomy+ileostomy		1hemorrhagic shock

There were 5 postoperative morbidities and one perioperative mortality for unknown reason after ileocecal resection for perforation. Table 2 summarizes different postoperative complications according to the type of intervention. Two patients developed signs of generalized peritonitis between the 4th and 7th postoperative days. On exploration, partial disruption of the anastomosis with anastomotic leak was detected in 2 patients, whom were subsequently treated surgically. The mean of postoperative hospital stay was 14 days (range; 4-60 days). All patients were followed for 3-480 months (mean of period is 10 years). During follow-up, a recurrence of Crohn's disease was demonstrated in eleven patients (64.7%). Recurrence was detected on endoscopy and clinical examination or by only clinical examination in 5 patients. Six patients required a second operation during the follow-up period, among them, 2 patients required a third operation. Four recurrent operations were due to anastomosis stricture, and one patient underwent total colectomy with ileorectal anastomosis due to colic stricture and low-grade dysplasia lesions, which were found on histology. The last patient underwent mucosal proctectomy with iléal pouch-anal canal anastomosis due to severe Crohn's disease involvement of the rectum. For the latter, because of severe pochitis, significant perianal involvent and anorectal incontinence, he ends with permanent ileostomy five years after the first surgery**.**

DISCUSSION

The incidence of emergency surgery for Crohn's disease in our experience was high (17/38 patients), and is not as rare as the published estimates. Emergency surgical indication could be frequently the first presentation of Crohn's disease. Acute intestinal obstruction and perforation-peritonitis were the most common indications for emergent surgery in Crohn's disease in our study.

Presentation

An acute clinical episode typically presents with abdominal pain, diarrhea and fever, can occur in a patient who previously been entirely well [4]. In fact, emergency surgical indication could be the first presentation of Crohn's disease. In our study, Crohn's disease was inaugurated by the complications requiring emergency surgery in 11/17 patients. This rate was not found in other series, and could be explained by the fact that the majority of our study population lived in rural areas.

In our patient series, acute abdominal pain and symptoms of intestinal obstruction were the most common indications for surgical treatment, causing these patients to undergone emergency operations. This finding is concordant with other studies [5]. The mean duration of symptoms prior to surgery was 18 months, which is a short time compared to the observed delays 57 months in other surgical series [6]. On the other side, it was concordant with that of Tunisian monograph, which were 20 more or less than 2 months [7].

Operative emergencies indications and surgical options

Operative emergencies indications for Crohn's disease include bowel obstruction, perforation with peritonitis or abscess formation, hemorrhage and severe acute colitis. The reasons for failed medical therapy can vary from medication noncompliance to lack of treatment response. Acute intestinal obstruction is the most frequent indication for surgery when Crohn's disease is located in the ileoceacal area, and this may occur in the jejunoileal area with one or multiple stenosis. The surgical treatment may require a resection or strictureplasty deponding on length

and localization. Strictureplasty is recommended especially for patients with multiple strictures and for patients with recurrent disease. Emergency laparoscopic exploration for acute obstruction has been validated by recent guidelines [8]. CT is the gold standard for the preoperative workup of a clinically relevant obstruction so as to spot the probable site and cause and to rule out intestinal ischemia [8]. Limited ileocecal resection is the treatment of choice because it resolves the obstruction and guarantees a specimen for pathological examination. As we demonstrated, the most common surgical procedure in our study was ileocolic resection. No consensus is available regarding the technique for intestinal anastomosis in Crohn's disease, and, to date, and no evidence supports the benefit of one particular type of anastomosis over another [9]. In our series, we opted for side-to-side or end-to-end anastomosis.

Perforation is another surgical emergency in patients with Crohn's disease. It was one of the most important indications for emergency surgery preceded by acute intestinal obstruction in our study. These findings are concordant with an Indian study [10]. Perforation may occur in the small intestine or in the colon associated toxic colitis. When peritonitis is confirmed, exploratory laparotomy with peritoneal lavage and construction of stroma is most commonly required. In the case of intestinal perforation associated with an abscessed small bowel, resection with fecal diversion is the gold standard surgical strategy [11]. In our series, three hemicolectomies and two ileocolic resections were performed for perforation in the terminal ileum and in the colon respectively.

Hemorrhage can be a life-threating complication of Crohn's disease. Bleeding is treated according to typical algorithms with attempts to localize the bleeding site and it rarely indicates an emergency surgery [12]. Recurrent bleeding in an area of small bowel disease is a common phenomenon, for that reason, resection and primary anastomosis should be undertaken. [13-15]. The case of bleeding in our study was due to complicated acute severe colitis. Acute severe colitis is potentially life-threatening complication of Crohn's disease. It can reveal the disease, for this reason it is important to distinguish between Crohn's disease and ulcerative colitis. The usual indications for emergent surgery include: peritonitis, free perforation, increasing colonic dilation, hemorrhage, and septic shock. European Crohn's and Colitis Organisation(ECCO 2008) consensus does not recommend performing a total colonoscopy in the case of acute severe colitis considering the high risk of perforation [15]. The procedure of choice is open colectomy with ileostomy and distal colostomy or closure of the rectum, which was performed for 2 of our patient studies due to bleeding and toxic megacolon.

An acute appendicitis is a differential diagnosis frequent in Crohn's disease. If the patient with known Crohn's disease presents with an acute flare-up, or during first presentation the diagnosis of Crohn disease is established before surgery .It has been demonstrated that the ileocecal resection appears to be the most appropriate solution [16]. In the presence of a localized inflammatory mass or stricture, resection and primary anastomosis may be appreciated. If it turns out to be a localized peritonitis secondary to perforation, resection is necessary without immediate restoration of continuity. If surgery has been carried out for suspected appendicitis and a normal appendix with ileocaecal Crohn's disease is discovered, the appendix should be removed to rule out appendicitis in the case of attacks of pain in the future [4]. Nowadays, the use of computered tomography in the differential diagnosis between Crohn's disease and acute appendicitis results in a diminished number of emergency operations on Crohn's disease patients [17-18] .In our study, we found in the operative room a stricture terminal ileum in one patient and a localized peritonitis secondary to perforation for 3 patients. Ileocolic resection was performed for all these patients and was combined with right segmental resection in one case.

Surgery should to address only to macroscopic lesions, because microscopic disease at the margins will not be associated with recurrence [19], to preserve as much as possible small bowel capital because the patients may need another resection in the future.

Minimally invasive approaches to surgery

Many of the surgical procedures described above can be performed using a minimally invasive technique. The advantages of a minimally invasive approach for Crohn's disease surgery include less pain after the operation, less chance of wound infections, and earlier return of bowel function leading to shorter hospital stay [20-21]. During emergency surgery for life-threatening complications, it is not always possible to perform surgery with minimally invasive techniques. Laparoscopic approach was tried in our series only in 2 patients, and conversion from laparoscopy to laparotomy was needed due to large mesenteric inflammatory masses. That can be explained by the presence of peritoneal syndrome on physical examination in 58.8% of all the patients and the insufficient use of CT scan for our patients before the surgery (it was used only for 2 patients).

Complications: Morbidity And Recurrence

Acute surgical emergencies in patients with Crohn's disease may carry a substantial morbidity, but fortunately today, a low mortality. It has been reported that postoperative morbidity on patients with Crohn's disease operated-on because of an emergency situation is significantly higher compared to elective procedure [22]. Morbidity is frequently due to septic complications, mostly anastomotic leaks [23-24]. Nowadays the mortality is almost never after intestinal resection of Crohn's disease [23]. However, we had one mortality in our population study 10 hours after ilecolicolic resection for perforation.

Perforative Crohn's is accompanied by more postoperative complications, as far as weight loss and prolonged refractory symptoms. In our series, it seems that the complications were probably related to penetrating behavior, because all of the patients had perforation in histology (even toxic megacolon). The patient who had 2 postoperative complications didn't undergo fecal diversion in the intervention.

A bowel resection may offer patients many years of symptoms relief. However, about 50% of patients will have a recurrence of symptomatic Crohn's disease within five years after having a resection. The disease usually recurs at the site of the anastomosis. Recurrent Crohn's disease often can be successfully treated with medications, such as immunomodulators or biologics. However, about one-half of people with recurrent symptoms will need a second surgery.

The postoperative management involves knowing the high risk patients of recurrence requiring treatment maintains (can be aggressive) in the immediate postoperative.

Tobacco and is the only highly predictive factor of surgical recurrence clearly demonstrated to date [25]. It has been shown that penetrating behavior B3 of The Montreal classification of Crohn's disease was regarded as a predictor of postoperative recurrence [19-26]. We must emphasize the importance of treatment of postoperative care in these patients with one or more of these factors and in which the absence of treatment is a high risk factor for recurrence.

During follow-up, a recurrence of Crohn's disease was demonstrated in eleven/seventeen patients. Although, these patient were on preventive therapy based on azathioprine or 5-aminosalicylates. Recurrence was detected on endoscopy and clinical examination or by only clinical examination in 5 patients, and was requiring reoperation for 6/17 patients in a mean period of 7.4 years (range; 1-19years). These findings show that recurrence has a high postoperative rate in our study as in other studies [27]. The worst outcome, which was noticed in our study, was about one patient who ended with a permanent stoma on his third intervention for recurrence. This outcome, which impairs the quality of life, was a result for disabling symptoms and severe pochitis. However, ileal pouch-anal anastomosis was not indicated by the most surgeons, it could be proposed for some carefully selected patients [28].

CONCLUSION

One of the main outcomes of Crohn's disease is the need for surgery during the course of the disease. From the results of the present study, emergency surgery for Crohn's disease is not as rare as the published estimates. Clinicians must bear in mind that emergency operative indication, could be the first manifestation of patients with Crohn's disease. Appendicitis is an usual differential diagnosis of Crohn's disease which can be ruled out by computered tomography. Acute intestinal obstruction and perforation-peritonitis were the most common indications for emergent surgery in Crohn's disease. By avoiding the risk factors and with a multidisciplinary approach we can reduce the morbidity and the morbidity, however recurrence is the main and the inevitable complication.

References

1. Fishera A, Michalessi F. Indications for surgery: a surgeon's opinion. In; Sartor RB, Sandborn WJ, eds, Kirsner's inflammatory Bowel Diseases. Philadelphia: WB Saunders, 2004: 596-601.
2. Karoui S, Serghini M, Trad D and al. Impact de la recherche de la récidive endoscopique précoce après une première résection iléo-colique droite pour maladie de Crohn: résultats d'une étude prospective ouverte. Tunis Med 2008; 17: 24-8.
3. Rutgeerts P, Geobes K ,Vantrappen G, Beyls J, Kerremans R, Hiele M. Predictability of the postoperative course of Crohn's disease. Gastroenterol 1990; 99: 956-63.
4. Paterson-Brown S. Core Topics in General and Emergency Surgery: Companion to Specialist Surgical Practice. 5th ed. Massachusetts: Saunders Elsevier, 2013.
5. Aarnio MT, Mecklin JP, Voutilainen M. The role of surgery in Crohn's Disease: a retrospective analysis from a single Hospital. Scand J Surg 2010; 99: 208-212.
6. Alves A, Panis Y, Bouhnik Y, Pocard M, Vicaut 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. Dis Colon Rectum 2007; 50: 331–6.
7. Nouira R, Moussi A, Khalfallah M, Ghrib S. Présentations générale de la série des formes chirurgicales de la maladie de Crohn. Les formes chirurgicales de la maladie de Crohn. ATC 2010; 7-22.
8. Vettoretto N, Gzzola L, Giovanetti M. Emergency Laparoscopic Ileocecal Resection for Crohn's Acute Obstruction. JSLS 2013; 17: 499-502.
9. McLeod RS, Wolff BG, Ross S, Parkes R, McKenzie M. Recurrence of Crohn's disease after ileocolic resection is not affected by anastomotic type: results of a multicenter, randomized, controlled trial. Dis Colon Rectum 2009; 52: 919-27.
10. Parkash K, Varma D, Mahadevan P, Narayanan RG, Philip M. Surgical treatment for small bowel Crohn's disease: an experience of 28 cases. Indian J Gastroenterol 2008; 27: 12-5.
11. Vallicelli and al. Small bowel emergency surgery: literature's review. World J Emergency Surg 2011; 6:1.
12. Robert JR, Sachar DB, Greenstein AJ. Severe gastrointestinal hemorrhage in Crohn's disease. Ann Surg 1991; 213: 207-11.
13. Sparberg M, Kirsner JB. Recurrent hemorrhage in regional enteritis: Report of 3 cases. Am J Dig Dis 1966; 11: 652-657.
14. Belaiche J, Louis E, D'Haens G, et al. Acute lower gastrointestinal bleeding in Crohn's disease: Characteristics of a unique series of 34 patients. Belgian IBD Research Group. Am J Gastroenterol 1999; 94: 2177-2181.
15. Travis S, Stange E, Lémann M and al. European evidence-based Consensus on the management of ulcerative colitis: Current management. J Crohns Colitis 2008; 2: 24-62.
16. Weston LA, Roberts PL, Schoetz DJ Jr, Coller JA, Murray JJ,

Rusin LC. Ileocolic resection for acute presentation of Crohn's disease of the ileum. Dis Colon Rectum 1996; 39: 841-6.
17. Lee SL HH: Ultrasonography and computed tomography in suspected acute appendicitis. Semin Ultrasound CT MR 2003; 24: 69-73.
18. Whitley S, McLean A, Power N. The appendix on CT. Clin Radiol 2009; 64: 190-199.
19. 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.
20. Duepree HJ, Senagore AJ, Delaney CP, Brady KM, Fazio VW. Advantages of laparoscopic resection for ileocecal Crohn•s disease. Dis Colon Rectum 2002; 45: 605-10.
21. Tilney HS, Constantinides VA, Heriot AG et al. Comparison of laparoscopic and open ileocecal resection for Crohn•s disease: a meta-analysis. Surg Endosc 2006; 20:1036-44.
22. Coerper S, Makowiek F, Starlinger M, Becker HD. Surgery of Crohn's disease in the course of time: a retrospective analysis of 1,044 operations. Langenbecks Arch Chir Suppl Congressbd 1977; 114: 1128-1131.
23. Alves A, Panis Y, Bouhnik Y, Pocard M, Vicaut 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. Dis Colon Rectum 2007; 50: 331-6.
24. 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.
25. Sutherland LR, Ramcharan S, Bryant H, Fick G. Effect of cigarette smoking on recurrence of Crohn's disease. Gastroenterol 1990; 98: 1123-8.
26. Parente F, Sampietro GM, Molteni M et al. Behavior 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.
27. Simillis C, Reese GE, Umegae S, et al. A meta-analysis comparing incidence of recurrence and indication for reoperation after surgery for perforating versus nonperforating Crohn's disease. Am J Gastroenterol 2008; 103: 196-205.
28. Tiret 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.