Surgical management of primary crohn's disease. descriptive study about 226 patients.

Prise en charge chirurgicale de la maladie de crohn primaire. etude descriptive de 226 patients.

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RÉSUMÉ

Prérequis: Le recours à la chirurgie est nécessaire chez 80% des patients porteurs de maladie de Crohn (MC). Certaines études avaient démontré que cette maladie présente chez le patient Tunisien quelques spécificités génétiques par rapport aux autres groupes éthniques.

But: Le but de cet article est de dresser dans un groupe Tunisien de patients opérés pour MC un profil épidémiologique, topographique, les principes thérapeutiques et de dégager les facteurs de risque de récidive de cette maladie sous nos cieux

Matériel et méthodes: Nous rapportons une étude rétrospective étalée de Janvier 1998 à Septembre 2010 qui a répertorié 226 patients originaire de la Tunisie (Nord Afrique) et opéré pour une MC. Nous avons étudié des variables cliniques, thérapeutiques et évolutifs.

Resultats: L'âge moyen était de 33 ans. La durée moyenne entre le début de la maladie et le recours à un traitement chirurgical était de 31 mois. Le diagnostic de la MC était déjà connu en pré-opératoire chez 213 patients (94%). Le diagnostic était fait en per-opératoire chez 5 patients (2.2%) à l'occasion d'une complication aigue chirurgicale et en post-opératoire chez 8 patients (3.5%). La localisation iléo-caecale était la plus fréquente (n=184 ; 81.4%). La forme mixte sténosante et fistulisante était la plus fréquente (n=123 ; 54.4%). La mortalité opératoire était de 0.04% (n=1). La morbidité spécifique était de 8.4% (n=19). A long terme, le risque de récidive chirurgical était de 7.5% (n=17). En étude multi-variée, les risques indépendants de récidive chirurgicale étaient : Le tabagisme (p = 0.012, ORs = 3.57) et le recours à un traitement médical en post-opératoire (p = 0.05, ORs = 2.6).

Conclusions: L'atteinte mixte sténosante et fistulisante du carrefour iléo-caecal et la plus fréquente des formes chirurgicales de la MC. Cette série est caractérisée par un taux faible de récidive chirurgicale (7.5%).

Mots-clés

Maladie de Crohn, chirurgie, récidive, sténose, fistule.

SUMMARY

Background: The surgery is required in more than 80% of patients with Crohn's disease (CD). Studies before confirm the specific genetic variation of CD in the Tunisian population compared with the others ethnic groups.

Aim: This article aims to study the epidemiological, anatomical and therapeutic principles of surgical forms of CD in a cohort of Tunisian patients.

Methods: We report a retrospective study from January 1998 to September 2010 that studied 226 patients originated only from Tunisia (in North Africa), operated on for MC. We had been interested in epidemiological, anatomical, clinical, therapeutic, topographic progression of the disease, the procedure and the postoperative follow-up.

Results: The median age was 33 years. The average time between the onset of the disease and the surgical procedure was 31 months. The diagnosis of CD was established preoperatively in 213 patients (94%). The diagnosis was made intraoperatively because of an acute complication in 5 cases (2.2%) and postoperatively in 8 cases (3.5%). The most common location was the ileocecal junction in 184 cases (81.4%). Achieving the most common was the mixed form (stricture and fistula) in 123 cases (54.4%). Operative mortality was 0.04% (n = 1). Specific morbidity was 8.4% (n = 19). In long term, a surgical recurrence was noted in 17 patients (7.5%). In multivariate analysis the independent risk factors for surgical recurrence were: smooking (p = 0.012, ORs = 3.57) and post-operative medical treatment (p = 0.05, ORs = 2.6).

Conclusions: Achieving stenosing and fistulizing the ileocecal junction is the most frequent surgical form in Crohn's disease. Our series is unique for a lower rate of the postoperative recurrence (7.5%).

Key-words

Crohn's disease, surgery, recurrence, stricture, fistula.

The surgery is required in more than 80% of patients with Crohn's disease (CD) [1]. The aim of surgery is not to cure the disease, which evolves in most cases to the recurrence of the remaining intestine [2]. Surgical treatment of intestinal lesions caused by the CD is guided by two main criteria: operate only complicated shapes, and refractory to medical treatment, and perform an intestinal resection as limited as possible, removing only lesions responsible for the symptoms observed. Studied before, demonstrated the existence of the genetic variation of CD in different ethnic groups. Indeed, the frequency of the CARD15 variants in the Tunisian population is significantly lower than that observed in the European and American population [3], even more, the three candidate genes of CD: NOD2, HSP70-2 and TLR4, studied in the Tunisian population, were not associated with the disease, contrarily to European and American results [4-8]. These findings confirm the specific genetic variation of CD in the Tunisian population compared with the others ethnic groups. What about the clinical features of surgical forms of CD? There for, this study aims to conduct a descriptive study about demographic, clinical, pathologic, and therapeutic characteristics of patient operated on for Crohn' disease in La Rabta Teaching-Hospital.

METHODS

Study design and patient selection

This is a retrospective descriptive study, with prospective collection of data, conducted from January 1998 to September 2010, which included all patients undergoing surgery for CD. All patients born and living in Tunisia in North Africa. The diagnosis of CD was confirmed in all cases by histological examination of endoscopic biopsies or specimen after bowel resection. We excluded from this study, patients operated during this period for a relapse of Crohn's disease, patients initially operated in another center and isolated anoperineal lesions of CD. Indeed, the perineal CD is problematic as regards to the diagnostic, prognostic and specific management. The management was multidisciplinary and standardized for all patients.

The assessement of Crohn's disease

The exploration was conducted in pre-or postoperatively according to the chronology of the discovery of Crohn's disease. The exploration had included at least: a laboratory tests of inflammation (blood count, C-reactive protein, serum protein electrophoresis), an endoscopy (colonoscopy with catheterization of the distal ileum, upper gastrointestinal endoscopy), barium small bowel and a research of extra-intestinal manifestations. Other tests were requested according to the clinical presentation, namely abdominal CT scan (looking for an intra-abdominal abscess sometimes completely asymptomatic, in patients who have reached the fistulizing ileocecal junction), the abdominal magnetic resonance imaging (to assess the inflammatory component of stenosis or the importance of sclerolipomatosis) and / or a barium enema (in patients who had colorectal stricture impassable by the colonoscope).

Indication for surgery

The indication for surgery was: a complication of chronic disease (symptomatic stenosis, fistula complicated by an intra-abdominal abscess, ileo-vesical fistula, an internal fistula between two digestive segments responsible for a digestive by-pass and a malnutrition), an acute complication (acute peritonitis, a persisted acute intestinal obstruction despite resuscitation, acute severe colitis with failure of first-line and second-line treatment), a false diagnosis of acute appendicitis or a failure of medical treatment to limit the therapeutic escalation.

The postoperative course

Prophylaxis of deep vein thrombosis was based on the requirement of low molecular weight heparin for 21 days. Postoperatively, oral feeding was allowed after recovery of the transit as soon as possible in hospitals. In the case of anastomotic dehiscence, the management was based on the firs-line conservative management, as soon as possible and had included: total parenteral nutrition, antibiotic therapy, the introduction of an irrigation and aspiration system- drains placed intraoperatively and the establishment of additional drains percutaneously under CT scan guidance when necessary. The postoperative complications were classified according to Clavien and Dindo criteria [9].

A protocol was established to ensure regular monitoring during the postoperative period. Patients were followed both by the surgical team than gastroenterology. All results of clinical, biological and endoscopic have been noted and transcribed on patient records. Patients who were unable to sign this protocol surveillance were considered lost.

Data studied

For each patient, we had reported the age, sex, co-morbidity, age of onset and duration of the disease, the presence and characteristics of a possible abdominal mass and the treatment which the patient had already received. We were also interested to complications such as: intra-abdominal abscesses, acute peritonitis, acute intestinal obstruction and degeneration. We have also reported intra-operative data, including the incision, the procedure performed, the causes of a possible conversion of the laparoscopic approach. The characteristics of pathological lesions were noted: location and extension of lesions, the type of lesions (stenosing, fistulizing or mixed), the characteristics of the

fistulizing form (the segment vector and the segment victim). In the case of a multi-focal lesion, we had defined the site of disease as that on which we were based to indicate surgical treatment; other locations were considered to be associated with. Similarly, it was interested in both postoperative early and late, with an update on risk factors for surgical recurrence. We had defined the surgical recurrence, occurrence of recurrence disease after intestinal resection which had indicated a surgical procedure. This recurrence occurred at the operative site or remotely.

Statistical analysis

All data were reported as mean (with standard deviation (SD)) and/or median (with range value). The data were analyzed by means of SPSS 9.00 statistical package for Windows. Mann-Whitney *U* test and Chi-square test (Fisher exact test in the case of small numbers) were used for group comparison and Student's *t* test to analyze normally distributed quantitative data. $P < 0.05$ was considered statistically significant.

The final date for follow-up was December 2015. Follow-up information was obtained regularly from outpatient clinical visits. To identify risk factors of the surgical recurrence of CD, we performed in the first step, univariate analysis: The survival rates and 95% confidence intervals [CI] were calculated using the Kaplan-Meier method. The Kaplan-Meier method was used for the management of patients lost who were considered as such during the follow-up. Differences in survival were compared by the Log Rank test. Next, the multivariate analysis was performed using Cox's proportional-hazards regression model.

RESULTS

Epidemiological and clinical data

The median age at diagnosis was 33.6 years (SD=12.2 years). The median age of onset was 31 years (SD=11.9 years). They were 103 women and 123 men (sex-ratio=1.19). The notion of smoking was present in 59 patients (26.1%). Five patients (2.2%) were classified as ASA II [Diabetes mellitus (n=1), hypertension (n=1), thyroid dysfunction (n = 1), asthma (n=1)]. The others were classified as ASA I. Crohn's disease was known before surgery in 213 patients (94%), for these patients, duration of disease before surgery was 31.3 months (SD=3.1 months). Otherwise, the discovery of CD was made during an emergency laparotomy performed on patients who presented an acute complication of unknown CD in five cases (2.2%) [Peritonitis (n=3), acute bowel obstruction (n=2)] or after histological examination of a specimen in eight cases (3.5%) [Appendectomy (n=7), ileal resection for a migration of mesh in the gastrointestinal tract (n=1)]. Among the 226 patients, 102 (45.1%) were receiving at least one medical treatment for CD. Corticosteroid therapy was prescribed in 86 patients (38.1%), whereas the immunosuppressive treatment was prescribed in 23 patients (10.2%). Physical examination revealed an abdominal mass in 58 patients (25.7%). This mass was located in all cases at the right iliac fossa, the average size of the mass was 6.38 cm (SD = 2.7 cm). Anoperineal lesions were present in 45 patients (19.9%). One or more extra-intestinal manifestations were present in 39 patients (17.2%) [Rheumatologic (n=19), dermatological (n=12), ophthalmic (n=7), hematologic (n=3), hepatobiliary (n=2), nephrological (n=2), neurological (n = 1) and gynecological such as primary infertility (n =1)].

Of the 226 patients, Crohn's disease was complicated by intra-abdominal abscess in 65 patients (28.8%). Treatment consisted of antibiotics alone in 36 cases (15.9%), and associated with a first drainage of the abscess in 29 cases (12.8%) [Surgical drainage (n=10), percutaneous drainage (n=22)].

Pathological, topographic and therapeutic data

Regarding the topography of lesions, the CD was single or multi-focal. The distribution of the surgical lesions was: ileocecal (n=184), colic (n=24), jejuno-ileal (n=10), appendicular (n=7) or duodenal (n=1) [Figure 1]. Table 1 summarizes characteristics of fistulizing form of Crohn's disease.

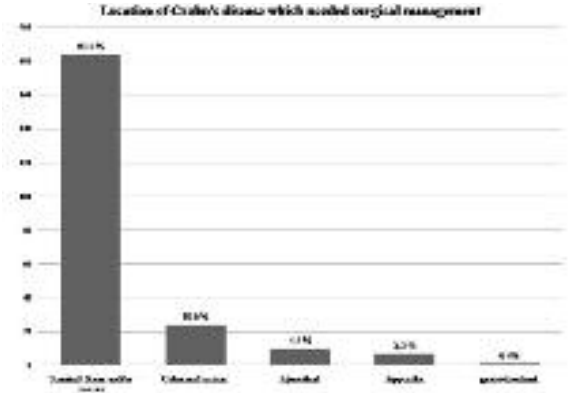

Figure 1: Location of Crohn's disease which needed surgical management.

The ileocecal location (81.4%)

It was the most common location which had imposed a surgical procedure. It was either a stenosing form in 64 cases (34.7%), a fistulizing form in 4 cases (2.1%) or somewhat of a mixed form (stenoting and fistulizing) in 116 cases (63%). Achieving ileocecal was isolated in 90 cases (48.9%). For the remaining 94 patients (51%), ileocecal achievement was associated with at least one other intestinal localization in 10 cases (5.4%) [ileum (n=6), duodenum (n=3) and colon (n=2)]. Anoperineal lesions were present in 36 patients (19.5%).

Table 1: characteristics of fistulizing form of Crohn's disease

Characteristics of fistulizing form	Number of patients (rate %)
Location of fistula	
Abdominal fistula	130 (58)
Internal fistula	119 (53)
Blind fistula	76 (34)
Entero-sigmoid fistula	17 (8)
Entero-enteric fistula	12 (5)
Entero-transverse fistula	8 (4)
Entero- or colo-vesical fistula	7 (3)
Entero- rectal fistula	2 (0,8)
Entero- or colo-gastric fistula	1 (0,4)
Entero-cutaneous fistula	17 (8)
Anoperineal fistula	45 (20)
Number of abdominal fistula	
Blind fistula	76 (34)
Between 2 anatomic areas	54 (24)
One fistula	44 (20)
Two fistula	10 (4)

† some patients had more than one fistula

Of the 120 fistulizing lesions (65.2%), internal fistula was simple in 70 cases (58.3%), internal complex in 34 cases (28.3%), entero-cutaneous in 10 cases (8.33%), mixed internal and external in 6 cases (5%). The complex internal fistulas were one or more paths: ileo-sigmoid fistula (n=16), ileo-ileal fistula (n=9), ileo-transverse fistula (n=8), ileo-vesical fistula (n=6), ileo-jejunal fistula (n=3) and ileorectal fistula (n=1). The procedure performed was ileocecal resection in all cases, by laparotomy in 112 cases (60%) or by laparoscopy in 72 cases (39.1%). The conversion rate was 16% (n=12). The causes of laparoscopic conversion were: a complex internal fistula (n=4), a large inflammatory mass (n=3), intestinal distension (n=2), extensive involvement (n=1), adhesions (n=1) or intraoperative bleeding (n=1). In the batch of patients who had a complex internal fistula (n=40) (isolated or associated with entero-cutaneous fistula), the procedure performed against the victim segment was either: a disconnection-freshening of the banks-suture of the fistula orifice (n=27), resection of bowel segment (n=6) [sigmoidectomy (n=3), ileal resection (n=3)], an extension of the resection from the vector segment to the the victim segment (n=7).

The colonic location (10.6%)

It was frequently a pure stenosing form (n=13; 54.16%), more rarely a pure fistulizing (n=1; 4.1%) or mixed form (n=3; 12.5%). For the remaining 7 cases (29.1%) there was a severe acute colitis with failure of medical treatment. For stenosing forms (n=16), it was multiple stenoses in 6 cases (37.5%) or single in 10 cases [sigmoid colon (n=4), splenic flexure (n=3), rectum (n=3)]. Crohn's disease was complicated by dysplasia associated with lesions of mucosa (DALM) in one case (4.1%) and degeneration in 2 cases (8.2%). The procedure performed was a subtotal colectomy with ileostomy and sigmoidostomy in 9 cases (37.5%), segmental colectomy in 7 cases (29.1) [up (n=3), low (n=4)] , a total colectomy in 5 cases (20.8%), a proctectomy in 2 cases (8.3%) and total proctocolectomy with permanent ileostomy in 1 case (4.1%).

Jejuno-ileal location (4.4%)

It was essentially a stenosing forms (n=9), which were pure in 5 cases (50%) and 4 were associated with fistulizing form. Two patients underwent emergency surgery [acute intestinal obstruction (n=1), acute peritonitis (n=1)]. Two patients had a complex internal fistula [ileo-sigmoid fistula (n=1), ileorectal fistula (n=1)]. In terms of the extended of lesions, one patient had multiple stenoses and one had an associated ileocecal localization. The presence of ano-perineal lesions (n=1) and extra-intestinal manifestations (n=1) were particularly rare.

Primary and isolated appendicular location (3.1%)

Achieving appendicular was isolated in 7 patients. Five had an emergency surgery, because the retained diagnosis was: acute appendicitis (n=3), peritonitis (n=1) or appendiceal abscess (n = 1). Two were operated with the diagnosis of appendicular tumor that required performing an appendectomy with an intra-operative histological examination of the appendix. In all cases, the appendix was macroscopically abnormal, the outcome of the disease have not allowed to reveal the other site of disease or extra-intestinal manifestation.

The duodenal location (0.4%)

This was an isolated stenosing form with neither anoperineal lesions nor extra-intestinal manifestations. However, cholelithiasis was present. Treatment consisted of a bi-truncal vagotomy, a gastro-entero-anastomosis associated with cholecystectomy.

For these locations, surgery was indicated in cold in 90.2% of patients (n=204). For other patients, surgery was indicated for emergency: an acute intestinal obstruction with a failure of resuscitation (n=8; 3.5%), acute peritonitis (n=8; 3,5%) [Perforation in free peritoneum (n = 4), intraabdominal abscess ruptured (n=4)], Crohn's disease complicated by appendicitis (n = 5) and low cataclysmic hemorrhage (n=1, 0, 4%).

Table 2 summarizes indications for operations in 226 patients with Crohn's disease.

Table 2: Indications for surgery in 226 Crohn's disease patients

Indication of surgery	Number of patients (Rate %)
Elective situation	204 (90)
Mixed form	114 (50)
Stenosing form	72 (31,8)
Fistulizing form	6 (3)
Failure of medical traitment	7 (3)
Degeneration of Crohn's disease	3 (1,3)
Suspected tumour	2 (1)
Emergency context	22 (10)
Free perforation	8 (3,5)
Small bowel obstruction	8 (3,5)
Suspected acute appendicitis	5 (2,2)
Acute intestinal bleeding	1 (0,4)

The postoperative results

The early postoperative results

Two hundred four patients (90.2%) had uneventful postoperative course. At least one complication was present postoperatively in 22 patients (9.7%): 8 (3.5%) were grade I, 12 (5.3%) grade II and 1 (0.4%) grade IIIb. Mortality (grade V) was 0.4% (n=1). Specific complications were present in 19 patients (8.4%) [Wound infection (n=9), digestive fistula (n=8), intraabdominal collection (n=3), postoperative hemorrhage (n=3), post-operative peritonitis (n = 1), postoperative bowel obstruction (n = 1)]. The non-specific complications were occurred in 4 patients (2.2%). Postoperative therapy was instituted in 75 patients (33.1%) [Immunosuppressive (n=44), amino-salicylates (n=26)].

The long-term outcomes

The mean follow-up was 110 months (SD = 48 months), the number lost to follow-up was 21 patients (9.2%). Acute adhesive obstruction of the small intestine was occurred in 17 patients (7.5%) including one patient (0.4%) who had required resection of necrotic small bowel of 3 m, and currently he is still alive after falling 36 months of the occlusive episode, with a short bowel syndrome (small bowel remaining length = 0.5 m). Incisional hernia was occurred in 13 patients (5.7%). Surgical recurrence had occurred in 18 patients (8%) (Figure 2). It was an anastomotic recurrence in 76.6% of cases (n=13). The anastomotic recurrence was occurred only in patients who initially had an ileocecal resection. The median time to onset of surgical recurrence was 60 months (Min= 7 months, Max= 156 months).

Risk factors of surgical recurrence

Regarding risk factors of surgical recurrence in univariate analysis, it had been retained: laparotomy approach [Figure 2], smoking [Figure 3] and postoperative medical treatment [Figure 4]. In multivariate analysis the independent risk factors for surgical recurrence were: smooking (p=0.012, ORs=3.57) and post-operative medical treatment (p=0.05, ORs=2.6).

Table 3 shows data studied as risk factors of surgical recurrence in univariate analysis.

Table 4 shows data studied as risk factors of surgical recurrence in multivariate analysis.

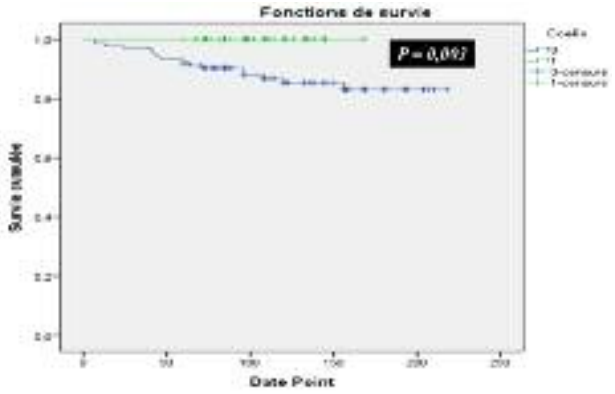

Figure 2: Survival curve without surgical recurrence in relation to the approach (Laparoscopy vs laparotomy)

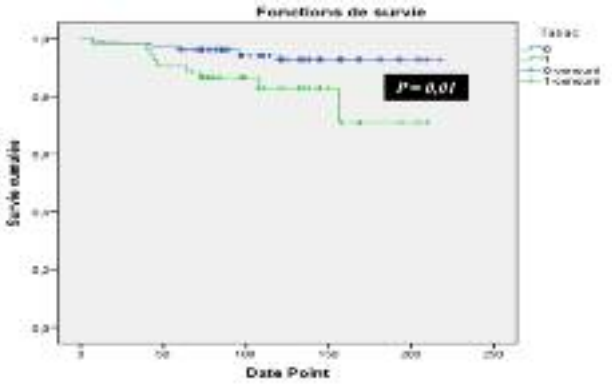

Figure 3: Survival curve without surgical recurrence in relation to smoking (Somoking vs non smoking)

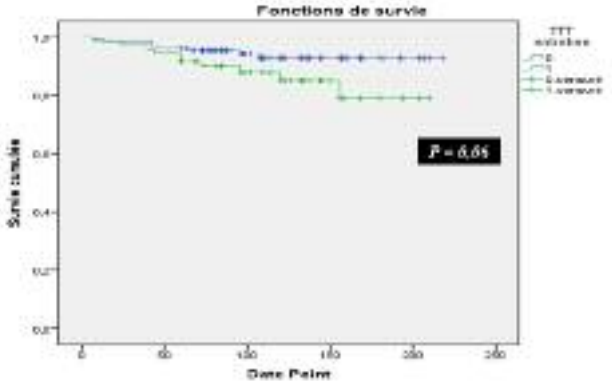

Figure 4: Survival curve without surgical recurrence in relation to post-operative medical treatment (Post-operative treatment vs non post-operative treatment)

Table 3: Risk factors of surgical recurrence in univariate analysis

	No recurrence		Recurrence		P value	Odds ratio (CI‡)
	n = 186	91,2 (%)	n = 18	8,8 (%)		
Smoking	43	23	9	50	***0,01****	3, 33 [1,25 – 9]
Laparoscopy approach	69	37	0	0	***0,003***	1,25 [1,11 – 1,33]
Postoperative medical treatment	62	33	10	55	***0,06***	2,50 [0,94 – 6,66]

* Fisher exact test ‡CI: Confident interval at 95%

Table 4: Risk factors of surgical recurrence in multivariate analysis

	P value	Odds ratio	Confident interval at 95%
Smoking	*0,01*	3,57	1,32 – 9,52
Postoperative medical treatment	*0,05*	2,61	1 – 6,83

DISCUSSION

The present study has collected the largest number of patients operated on for Crohn's disease in Africa.

Indications, locations and surgical procedures

In the present study, 90 % of patients underwent an elective operation. This percentage varies depending on the study, from 62% reported by Aarnio et al [10] to 80% reported by Siassi et al [11]. In this context, the most common indications for operation were the mixed form (50%) (stenosing and fistulizing form) followed by a stenosing form when caused bowel obstruction (31%). Michelassi et al [12] reported among 1379 patients with Crohn's disease, 639 surgical procedures, in which, the most common indications for operation were: failure of medical treatment (33%), presence of fistula (24%) and bowel obstruction (22%).

With respect to indications in emergency, acute peritonitis (3,5%) and acute small bowel obstruction (3,5%) were the most common indications. The incidence of free perforation in the peritoneal cavity, was higher than that reported by Ikeshi et al (2,5%) [13], by Greenstein et al (2%) [14], and by Hurst et al (1,6%) [15].

As regards to location of the disease. Most of our patients requiring surgery had involvement of the distal ileum and or caecum. The most common surgical procedure therefore was ileocolic resection (81,4%), as it has been reported earlier [10,16].

In the present study, colo-rectal location (10,6%) was lesser than that reported by Lapidus (52%) [17].

The isolated appendiceal Crohn's disease was found in 3,1% of our patients. Prieto-Nieto et al [18] reported in 20, the incidence of 0,2% of Crohn's disease confined to the vermiform appendix.

With respect to the surgical procedure performed, the intestinal resections were indicated in almost all patients. In the present study, stricturoplasty was used in only one case associated to an ileo-caecal resection for Crohn's disease with extensive lesions. However, Hurst et al reported among 542 surgical procedures, 97 (17%) stricturoplasty.

The postoperative results

The early postoperative results

The postoperative results were particular by a low mortality rate from 0 to 0.3%, however, a relatively high morbidity of between 9 and 16%. Risk factors for septic complications occurred post-operatively are: presence of abscess discovered during surgery, the severity of disease, perioperative malnutrition and long-term corticosteroid-therapy [12,19-21].

The long-term outcomes

The postoperative recurrence is a major problem especially common in the management of this disease. Results depend of definition of recurrence. Using, the need for a second resection as the definition for recurrent disease, authors found a recurrence rate of about 20% at 5 years and 35% at 10 years [12,19-23]. In the present study the risk of recurrence was lesser than the previous report, it was about 7,5%.

Risk factors of surgical recurrence

Risk factors for recurrence, different from one series to another, but overall we can say that the severity of the disease, fistulizing form (for some enterocutaneous fistulas) [24,25], the multifocal nature of the infringement, the early age of onset, reaching proximal (duodenojejunal), open laparotomy approach [26,27] and smoking are risk factors most implicated. In the present study, the independent risk factors for surgical recurrence were: smooking and post-operative medical.

CONCLUSION

In this study, the most common form and location are

mixed form (perforating and stenosing) and terminal ileum. The rate of the colorectal location (10.6%) is less than pervious described studies. Primary and isolated appendicular location is relatively higher (3.1%). Conservative management based on stricturoplasty is rarely indicated. Early postoperative results are comparable to those already reported. However our series is unique for a lower rate of the postoperative recurrence (7.5%), it could be a particular phenotype of Crohn's disease, which is typical of patients in our series, and they are actually North African patients.

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