

# Evolution and Prognosis of Digestif Fistulas in Crohn's Disease (CD) Other Than Ano-Perineal Manifestations (APM)

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## Abstract

**Background and Objectives:** Crohn's disease (CD) is a chronic inflammatory disease of the intestine. It can evaluate by the occurrence of intestinal complications in particular fistulas whose management can be medical or surgical. The objective of our work is to specify the evolutionary modalities, as well as the predictive factors of bad prognosis. **Patients and Methods:** this is a monocentric, descriptive and analytical retrospective study conducted in a hepato gastroenterology department including patients with fistulizing Crohn's disease, outside ano perineal fistulas from 1990 to 2023. Statistical analysis was performed using SPSS22.0 software. **Results:** Of a total of 960 patients, 38 had fistulizing CD. 65% of our patients were classified as A3 according to the Montreal classification, and 34% as A2. They were 24 women with a sex ratio of 1.71 F/H. The type of fistula was Greco-Greatic in 4 patients (10.5%), Greco-Colic in 5 patients (13%), Entero-Cutaneous in 12 patients (31.5%), Gastro-Colic in 3 patients (7.9%), Interdigestive and Entero-Cutaneous in 10 patients (26%), Interdigestive and Greco-Vesical in 2 patients. All our patients had benefited from a bi-antibiotic therapy, 33 had benefited from surgical resection. Postoperative treatments were based on therapeutic abstention in 5 patients (13.1%), immunosuppressive treatment in 18 patients (47%), anti TNF treatment in 7 patients (18%). The endoscopic recurrence rate 6 months after treatment was 32.5%. In univariate analysis, the factors influencing the evolution of fistulizing crohn's disease were the number of fistulas and age with p values lower than 0.05 (respectively 0.022 and 0.009). **Conclusion:** Digestive fistulas represent a complication during CD, which pose a problem of medical-surgical management and have an impact on the quality of life of the patients. Our study showed that age (p=0.022) and the number of fistulas (p=0.009) represent the factors influencing the natural history of fistulizing CD.

**Keywords:** Crohn disease- digestif fistulas – prognosis and evolution.

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## INTRODUCTION

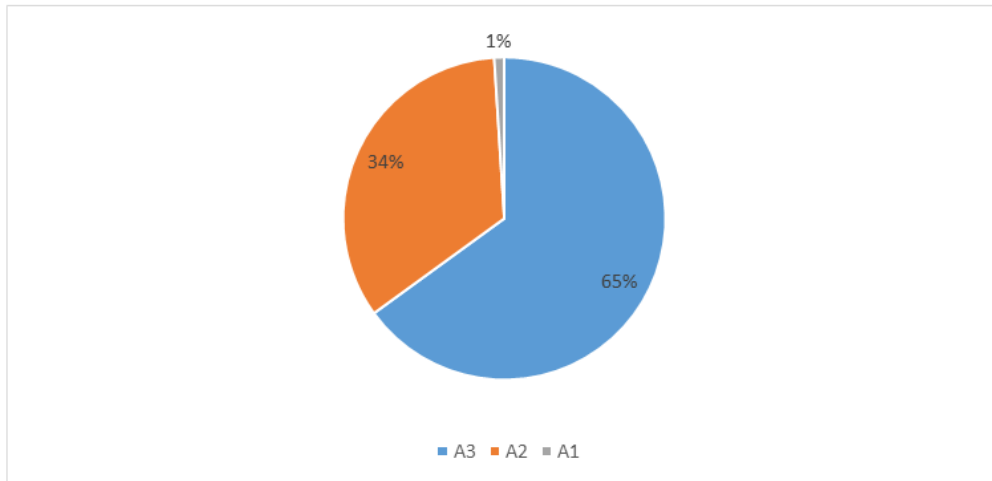
Crohn's disease (CD) is a chronic inflammatory disease of the intestine responsible for a chronic inflammation of the intestinal wall which leads progressively to a loss of the physiological functioning of the intestine and whose evolution can be marked by the occurrence of intestinal complications in particular fistulas whose management can be medical or surgical. The objective of our work is to specify the evolutionary modalities, as well as the predictive factors of bad prognosis.

## MATERIALS AND METHODS

This is a monocentric, descriptive and analytical retrospective study conducted in a hepato gastroenterology department including patients with fistulizing Crohn's disease, outside PAD from 1990 to 2023. Statistical analysis was performed using SPSS22.0 software.

## RESULTS

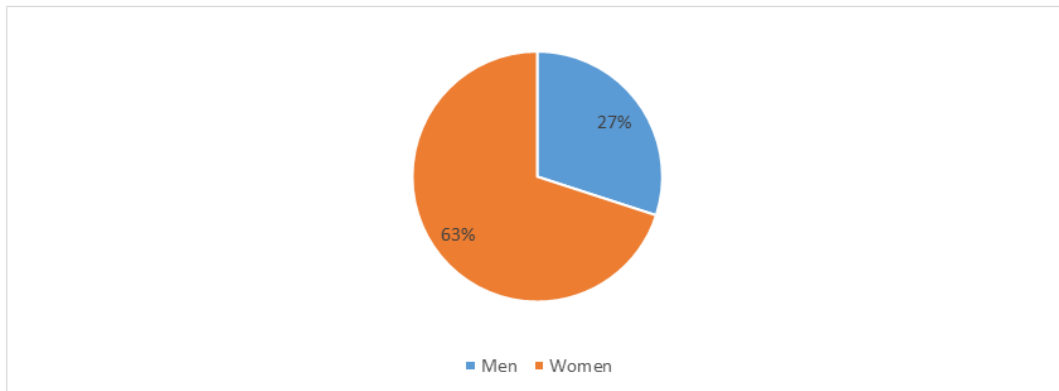
Of a total of 960 patients, 38 had fistulizing CD. 65% of our patients were classified as A3 according to the Montreal classification, and 34% as A2.



**Graphic 1: Montreal classification of our patients**

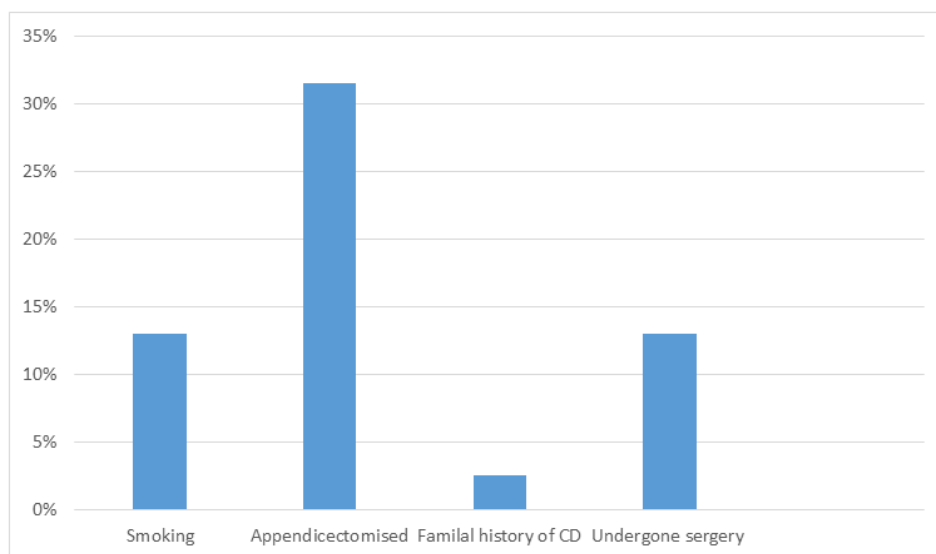
They were 24 women with a sex ratio of 1.71 F/H. 12 (31.5%) were appendectomized, 5 were smokers (13%), only one (2.6%) had a family history of Crohn's

disease. 5 patients (13%) had undergone surgery before the appearance of a fistula, of which 4 were ileocaecal resections, and one was a segmental colectomy.



**Graphic 2: Gender distribution of our patients**

The figure below show the risk factors of our patients:



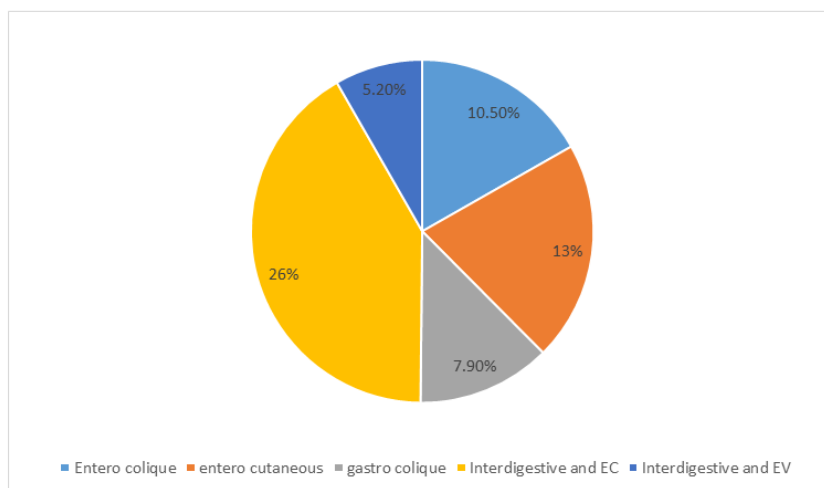
**Figure 1: Risk factors of our patients**

The location of the disease was L1 (according to the Montreal classification) in 3 patients (7.9%), L2 in only 1 patient (2.6%), L3 in 33 patients (87%), and extensive in only one patient (2.6%).

The type of fistula was entero-enteric in 4 patients (10.5%), entero-colique in 5 patients (13%),

entero-Cutaneous in 12 patients (31.5%), gastro-colique in 3 patients (7.9%), interdigestive and entero-Cutaneous (EC) in 10 patients (26%), interdigestive and entero-vesical (EV) in 2 patients.

The graphic below shows the different type of fistulas in our patients:



**Graphic 3: Different type of fistulas in our patients**

The diagnosis was made by small bowel transit (SBT) in 5 patients (13%), by entero-CT in 27 patients (71%), by entero-MRI in 6 patients (16%).

Biologically, hypoalbuminemia was present in 28 patients (74%), and anemia in 33 patients (87%).

Therapeutically, all patients had benefited from a bi-antibiotic therapy, 33 had benefited from surgical resection. Postoperative treatments were based on therapeutic abstention in 5 patients (13.1%), immunosuppressive treatment in 18 patients (47%), anti TNF treatment in 7 patients (18%). The endoscopic recurrence rate 6 months after treatment was 32.5%.

In univariate analysis, the factors influencing the evolution of fistulizing crohn's disease were the number of fistulas and age with p values lower than 0.05 (respectively 0.022 and 0.009).

## DISCUSSION

Digestive fistula is a frequent and serious complication of Crohn's disease (CD), affecting up to 50% of patients within 20 years of initial diagnosis. It is associated with significant morbidity and impairment of health-related quality of life [1].

Treatment options are limited and often provide only transient benefit, with more than a third of patients experiencing recurrent fistulas despite medical treatment [2].

Fistulae in patients with CD are typically classified according to their anatomical location: anal,

recto-vaginal, enterocutaneous (very common), enterovesical (very rare), enterocolonic or colo-gastric. Compared with isolated fistulae, multiple fistulae are associated with a poorer prognosis and are more likely to require surgical intervention [3].

Ignacio *et al.*, in a U.S. study including 77,000 Crohn's disease patients over a 20-year period, estimated incidence was 8.2/100,000 person-years and prevalence was 1.5% per year in the U.S [4].

## Risk Factors

The pathophysiology of fistula formation in Crohn's disease is still poorly understood, however there are factors that may be associated with fistula development. Male patients, patients whose colon was exclusively affected or whose disease extended to the colon and ileum, as well as patients treated with prednisone, had an increased relative risk of developing fistulas. In patients with ileitis alone and after laparotomy associated with bowel resection, the relative risk was less than 1. In addition, fistulas developed during active disease. In addition, patients were underweight at the time of fistula formation. We conclude that disease localization, a factor that cannot be influenced, as well as active disease and malnutrition, two factors that can be influenced, may be involved in fistula formation in Crohn's disease [5].

Jonas *et al.*, in a retrospective study carried out in Paris in 2002, including 2002 Crohn's disease patients, demonstrated that in the course of the disease, the initial location of lesions was the main determinant of the timing and type of complication in CD. Ileocolic, colonic

or upper gastrointestinal manifestations of CD were associated with fistula formation [6, 7].

### Diagnostic

The majority of the available literature on penetrating Crohn's disease focuses on the perianal phenotype, with only a few trials specifically addressing non-perianal intra-abdominal fistulas. However, identifying patients with a more aggressive phenotype is essential for the initiation of appropriate therapy and the need to adhere to closer follow-up. Failed detection may lead to inappropriate treatment, and may also result in increased morbidity and mortality [10].

### Management

The management of digestive fistulas is always complicated. It relies essentially on antibiotic therapy, anti-TNF drugs and surgery in the majority of cases. Surgical treatment has been the standard in the treatment of internal fistulas, as there was insufficient evidence to help decide whether or not each internal fistula could be treated with medical therapy [11].

Taku *et al.*, in a retrospective study including 93 patients with fistulizing Crohn's disease treated with anti TNF (infliximab and adalimumab) between January 2002 and November 2015, demonstrated that complete closure was confirmed in 29% of patients during the follow-up period, with a cumulative 5-year closure rate of 27.0%. It is also interesting to note that the cumulative 5-year surgery rate was 47.2% [12].

A few case reports subsequently demonstrated successful closure of enterovesical fistulas with IFX. Another report on 108 fistulizing CD patients, including 12 patients with intern fistulas (IF), showed that a complete response was achieved in 40% and 68% of enterovesical and enterovaginal fistulas, respectively; however, the follow-up period was only 4 weeks. A post hoc analysis of the ACCENT II trial evaluated the efficacy of IFX for a total of 27 recto-vaginal fistulas and demonstrated that 44.8% of fistulas were closed at week 14 and better maintained by IFX, although its long-term outcome, particularly maintenance without the need for surgery, remains uncertain. Our data also demonstrated the results of surgery as a second line of treatment after initial anti-TNF agents.

### CONCLUSION

Digestive fistulas represent a complication during CD, which pose a problem of medical-surgical management and have an impact on the quality of life of the patients. Our study showed that age ( $p=0.022$ ) and the number of fistulas ( $p=0.009$ ) represent the factors influencing the natural history of fistulizing CD.

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