

Intestinal Fistulas in Crohn's Disease: A Complex Challenge – A Moroccan Experience

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Abstract:

Fistulizing Crohn's disease represents a major therapeutic challenge for gastroenterologists due to its diagnostic complexity, high recurrence rate, and frequent need for surgery. This study aims to assess the epidemiological, radiological, evolutionary, and therapeutic profile of fistulizing Crohn's disease, excluding ano-perineal lesions. Our study is a retrospective descriptive study involving 70 patients diagnosed with fistulizing Crohn's disease in our department. Patients with isolated ano-perineal involvement were excluded from the study. Our results show an average age of 36 years and a male-to-female ratio of 1.4. The average disease duration was 7.27 years, with ileocolic involvement in 84.28% of cases. While a stenosing phenotype was observed in 58.6% of patients, The most frequently observed fistula types were entero-enteric (68.6%), followed by entero-colic (27.1%) and entero-cutaneous (21.4%). Radiological diagnosis was primarily made using abdominal CT (41.4%) and CT enterography (35.7%). Intra-abdominal abscesses were detected in 44.3% of patients. Regarding therapeutic management, immunosuppressive therapy was initiated in 30% of cases, combination therapy in 22.9%, primary surgery in 20%, biologic therapy in 14.3%, and surgery following medical treatment failure in 12.9%. Access to biotherapy remains limited among Moroccan patients due to financial constraints. Clinical remission was achieved in 81.4% of patients, while 15.7% experienced disease recurrence.

Keywords:

Fistulizing Crohn's disease, fistulas, Intra-abdominal abscess, Biologic therapies, surgery.

Introduction:

³³ Fistula formation is a well-known complication of ¹⁹ Crohn's disease (CD), resulting from sustained transmural inflammation of the bowel wall. This condition affects approximately 40% of patients and is a significant source of morbidity. Internal fistulas are less common than perianal fistulas but are more challenging to diagnose and manage. Despite therapeutic advancements, one in three patients experiences fistula recurrence [1,2]. This study aims to evaluate the epidemiological, clinical, radiological, evolutionary, and therapeutic profile of fistulizing Crohn's disease, excluding ano-perineal lesions.

²⁵ **Materials and methods**

We report a retrospective descriptive study over a period of 4 years, from January 2020 to August 2024, including patients with fistulizing Crohn's disease followed in our department. Patients with isolated ano-perineal involvement were excluded.

Résultats:

¹ During the study period, 70 cases of fistulizing Crohn's disease were analyzed. ¹¹ The mean age was 36.18 years (range: 16-65 years), with a male-to-female ratio of 1.4. Pathological history was reported in 50% of patients, primarily appendectomy (14.3%), ileo-cecal resection (7.14%), and a family history of CD (4.28%). The average disease duration was 7.27 years. Ileocolic involvement was observed in 84.28% of cases (Figure 1). A stenosing phenotype was present in 58.6% of patients, while 50% had associated perianal involvement.

¹⁷ The most common type of fistula was entero-enteric (68.6%), followed by entero-colic (27.1%), entero-cutaneous (21.4%) (Figure 2), and recto-vaginal or entero-vesical (8.6%) (Figure 3). Abdominal pain (44.3%) was the most frequent reason for consultation, followed by Koenig syndrome (24.3%). Biological assessments revealed elevated CRP in 64.3% and leukocytosis in 58.6% of cases. Radiologically, abdominal CT was performed in 41.4% of patients, enteroscanner in 35.7%, pelvic MRI in 10%, enterography MRI in 8.6%, and abdominal ultrasound in 4.3%. Fistulas were complicated by intra-abdominal abscesses in 44.3% of patients, with an average size of 41.8mm, most commonly localized to the right iliac fossa (38.7%). Six cases of perforation (8.6%) were reported.

In terms of therapy, immunosuppressive treatment was indicated in 30% of cases, combination therapy in 22.9%, primary surgery in 20%, biologics in 14.3%, and surgery after

medical treatment failure in 12.9%. For maintenance therapy, combination therapy was prescribed in 48.6%, followed by biologics in 25.7%, and immunosuppressants in 22.8% of patients. (Figure 4). Clinical remission was observed in 81.4% of patients, disease recurrence in 15.7%, and two were recorded.

Discussion:

Intestinal fistulas represent a major and frequent complication of Crohn's disease, forming abnormal connections between different bowel segments (Enteric and Colorectal Fistula) or adjacent organs (bladder, vagina, or the peritoneal cavity). Their management remains a challenge, requiring a thorough understanding of their epidemiological profile, radiological characteristics, and clinical progression, with a multidisciplinary approach.

Intestinal fistulas occur in approximately 20 to 40 % of the patients with Crohn's disease during the course of the illness [3]. Risk factors include a prolonged duration of the disease, a history of intestinal surgery, and penetrating behavior according to the Montreal classification [4]. A recent cohort study highlighted the role of environmental factors, such as active smoking, in the development of complex fistulas [5].

Excluding perianal fistulas, entero-enteric fistulas are the most common type of internal fistulas associated with Crohn's disease, as reported in the literature. An American study involving 639 patients who underwent surgery for Crohn's disease, 34% of whom had fistulas, found that 47% of cases involved entero-enteric fistulas, while 16% were entero-cutaneous fistulas [6]. Similarly, a Moroccan study conducted in Marrakech on 78 patients with the fistulizing form of Crohn's disease confirmed the predominance of entero-enteric fistulas (30%), followed by entero-cutaneous (23%) and entero-vesical fistulas (9%) [7]. In our study, entero-enteric fistulas were the most prevalent, accounting for 68.6% of cases, followed by entero-colic fistulas (27%) and entero-cutaneous fistulas (21.4%). Additionally, 50% of patients had associated anoperineal fistulas. It has been shown that the risk of developing an intestinal fistula is significantly higher in cases of ileal involvement compared to isolated colonic involvement [6]. Our findings align with this observation, as the majority of patients (84%) presented with ileocolic disease.

The clinical presentation of fistulas varies depending on their type. Entero-enteric fistulas are generally asymptomatic or present with nonspecific abdominal pain [8]. Entero-cutaneous fistulas, on the other hand, lead to the discharge of fecal matter or pus through the fistulous opening, which may be single or multiple, with a variable output depending on the complexity of the tract, the affected intestinal segment, and the possible presence of a downstream stricture [9,10]. The diagnosis of entero-vesical fistulas is primarily clinical. They manifest as recurrent urinary tract infections, the presence of fecal matter in the urine (fecaluria), the passage of gas through the urethra (pneumaturia), or urinary symptoms such as dysuria [11,12]. Rectovaginal fistulas are less common, and their incidence appears to be proportional to the severity of inflammatory colitis and the presence of associated anoperineal lesions [13]. The clinical presentation typically includes the passage of gas or fecal matter through the vagina, dyspareunia, vaginal irritation, and recurrent genitourinary infections [14,15].

Imaging is essential for the diagnosis and management of intestinal fistulas. Several radiological examinations can contribute to the diagnosis of fistulas in Crohn's disease. Entero-MRI is the gold standard, offering excellent sensitivity and specificity [16]. Fistulas appear as hyperintense tracts on T2-weighted sequences with enhancement after gadolinium injection. Computed tomography (CT) is often indicated in emergency situations or when MRI is contraindicated, although it exposes patients to higher radiation levels [17]. Contrast-enhanced ultrasound is emerging as a promising alternative, particularly for patient follow-up [18]. In our study, abdominal CT scan was the most frequently prescribed imaging modality for diagnosis, performed in 41.4% of patients, followed by CT enterography scan in 36%, while entero-MRI was performed in only 8.6% of cases due to limited availability.

The progression of intestinal fistulas in Crohn's disease is often unpredictable. Some fistulas may remain asymptomatic, while others can lead to severe complications such as abscesses, strictures, or perforations [19]. In our study, fistulas were complicated by intra-abdominal abscesses in 44.3% of patients.

Regarding the therapeutic management of Crohn's-related fistulas, the ECCO 2023 guidelines recommend a personalized treatment approach based on disease severity and the presence of complications. Treatment relies on a multidisciplinary strategy, including immunosuppressive medications (thiopurines, anti-TNF agents) and newer biologics, such as integrin inhibitors and interleukin-12/23 antagonists [19]. Surgery remains an option for refractory or complicated cases.

⁴ For the medical treatment of fistulas in Crohn's disease, corticosteroids have no role. Some studies have shown that the use of prednisolone in patients with fistulizing Crohn's disease was associated with poor outcomes, with a higher rate of surgical intervention ⁶ compared to patients who did not receive corticosteroids [20]. Regarding thiopurines (azathioprine and 6-mercaptopurine), a meta-analysis including 70 patients with fistulas showed complete closure or a reduction in fistula output in 54% of patients treated with thiopurines, compared to 21% in the placebo group [21]. Another study conducted on 34 patients with fistulas reported complete closure in 39% of cases and significant symptom improvement in 26%, with particularly favorable results for entero-cutaneous fistulas [22]. Infliximab has been widely studied for its efficacy in treating fistulas associated with Crohn's disease, with response rates ranging from 46% to 69% [23,24]. ⁴ The ACCENT II trial, which included 289 patients (246 with anoperineal fistulas and 39 with entero-cutaneous fistulas), showed that 69% of patients responded to infliximab treatment [25]. An analysis of this cohort also demonstrated a beneficial effect on rectovaginal fistulas, with a closure rate of 60.7% at 10 weeks and 44.8% at 14 weeks [26]. A study by GETAID on 51 patients with entero-cutaneous fistulas reported complete closure in 38% of cases, with sustained efficacy at 36 months in 50% of patients. The best outcomes were observed in patients with spontaneous, simple, low-output fistulas without associated intestinal strictures [27].

¹⁰ According to the French guidelines for the management of Crohn's disease, the decision between medical or surgical treatment for fistulizing disease should take into account several factors, including the presence of an abscess, the extent of intestinal involvement, prior therapeutic exposure, and local expertise. For patients with extensive ileal involvement without an abscess, treatment with anti-TNF therapy in combination with an immunosuppressant is recommended for biologic-naïve patients. In cases of previous exposure to anti-TNF agents, a second-line therapy should be considered [28]. ²³ In the presence of an intra-abdominal abscess, broad-spectrum antibiotic therapy is recommended, along with percutaneous drainage if the abscess exceeds 3 cm in diameter. Initial segmental resection surgery should be avoided [28]. Surgical drainage is advised when radiological drainage is not feasible, when clinical evolution is unfavorable and persistent abscesses despite optimal initial management or in patients already on biologic therapy with limited

intestinal involvement (less than 50 cm), or in the presence of large collections [29-30]. The MICA study by GETAID, conducted on 117 ¹⁴ biologic-naïve patients with Crohn's disease complicated by an intra-abdominal abscess, evaluated the effectiveness of adalimumab initiated after abscess resolution. Results ² showed that 72% of patients ³ treated with adalimumab did not require surgery [31]. In a retrospective cohort of 156 patients with fistulizing Crohn's disease treated with anti-TNF agents, 68 patients (43.6%) ⁷ underwent surgery during follow-up. Factors ⁸ associated with higher rates of medical treatment failure included C-reactive protein (CRP) >18 mg/L, albumin concentration <36 g/L, the presence of an abscess at the time of fistula diagnosis, and associated intestinal strictures [32]. In our study, immunosuppressive therapy was indicated in 30% of cases, combination therapy in 22.9%, and biologic therapy in 14.3%. The low rate of biologic use was primarily due to limited access for most Moroccan patients, mainly because of financial constraints.

Although ² the use of anti-TNF therapy appears to reduce ⁹ the need for surgery in Crohn's disease [33,34], between 60% and 80% of patients will eventually ⁷ require surgical intervention during their lifetime [35,36]. The fistulizing phenotype is considered a major risk factor for first-time surgery, along with other risk factors such as active smoking, a stricturing phenotype, terminal ileal or jejunal involvement, young age at diagnosis, and early corticosteroid use [28]. In fistulizing Crohn's disease, the most ²⁶ common surgical procedure is ileo-cecal resection. However, this intervention is not curative and carries a 50% risk of postoperative recurrence within five years if no appropriate medical treatment is provided [28]. According to the American study by Michelassi et al., surgery for entero-enteric fistulas was primarily indicated in cases of medical treatment failure (35%), followed by the occurrence of Koenig's syndrome (29%), and, to a lesser extent, by direct intervention for the fistula itself (18%) [37]. Surgical management was also recommended in the following situations; Entero-cutaneous fistulas with high-output drainage and/or associated intestinal stricture [37]. Entero-vesical fistulas, due to infection risks, potential renal complications, and frequent failure of medical treatment alone [12,37]. Rectovaginal fistulas, where surgery remains the preferred treatment option [38]. Another study on 51 patients who underwent surgical treatment for entero-cutaneous fistulas related to Crohn's disease reported a surgical

closure rate of 84%, with a mean follow-up of 48 months. The recurrence rate was 16% [9]. Similarly, a Moroccan study involving 78 patients with fistulizing Crohn's disease found that 87% required surgical intervention, with a 96% fistula closure rate and a 4% recurrence rate [20]. In our study, 20% of patients underwent immediate surgical management, while 13% required surgery after failure of medical treatment.

Conclusion:

Fistulizing Crohn's disease represents a major therapeutic challenge for gastroenterologists due to its diagnostic complexity, high recurrence rate, and frequent need for surgery. In our study, Crohn's fistulas were predominantly (84%) associated with ileocolic involvement, complicated by intra-abdominal abscesses in 44% of cases. Access to biotherapy remains limited among Moroccan patients due to financial constraints. A multidisciplinary approach, integrating personalized management with medical treatment and appropriate surgical intervention, is essential to improve patient prognosis and reduce complications.

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Conflicts of interest:

The authors declare no conflicts of interest.

Figures:

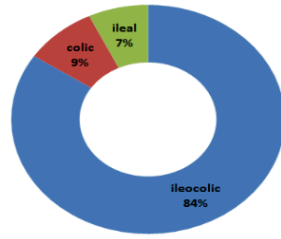


Figure 1: Crohn's disease localization

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Figure 2: Active entero-cutaneous fistula in a patient followed in our department for fistulizing Crohn's disease.

Figure 3: Type of internal fistula

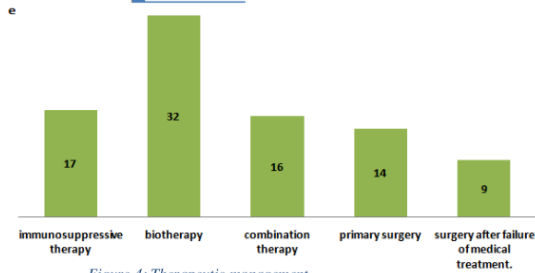


Figure 4: Therapeutic management

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