

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

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:

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

37 ***Materials and methods***

38 We report a retrospective descriptive study over a period of 4 years, from January
39 2020 to August 2024, including patients with fistulizing crohn's disease followed in
40 our department. Patients with isolated ano-perineal involvement were excluded.

41 ***Résultats:***

42 During the study period, 70 cases of fistulizing Crohn's disease were analyzed. The mean
43 age was 36.18 years (range: 16-65 years), with a male-to-female ratio of 1.4. Pathological
44 history was reported in 50% of patients, primarily appendectomy (14.3%), ileo-cecal resection
45 (7.14%), and a family history of CD (4.28%). The average disease duration was 7.27 years.
46 Ileocolic involvement was observed in 84.28% of cases (Figure 1). A stenosing phenotype
47 was present in 58.6% of patients, while 50% had associated perianal involvement.

48 The most common type of fistula was entero-enteric (68.6%), followed by entero-colic
49 (27.1%), entero-cutaneous (21.4%) (Figure 2), and recto-vaginal or entero-vesical (8.6%)
50 (Figure 3). Abdominal pain (44.3%) was the most frequent reason for consultation, followed
51 by Koenig syndrome (24.3%). Biological assessments revealed elevated CRP in 64.3% and
52 leukocytosis in 58.6% of cases. Radiologically, abdominal CT was performed in 41.4% of
53 patients, enteroscanner in 35.7%, pelvic MRI in 10%, enterography MRI in 8.6%, and
54 abdominal ultrasound in 4.3%. Fistulas were complicated by intra-abdominal abscesses in
55 44.3% of patients, with an average size of 41.8mm, most commonly localized to the right iliac
56 fossa (38.7%). Six cases of perforation (8.6%) were reported.

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

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

63 *Discussion:*

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

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

76 Excluding perianal fistulas, entero-enteric fistulas are the most common type of internal
77 fistulas associated with Crohn's disease, as reported in the literature. An American study
78 involving 639 patients who underwent surgery for Crohn's disease, 34% of whom had
79 fistulas, found that 47% of cases involved entero-enteric fistulas, while 16% were entero-
80 cutaneous fistulas [6]. Similarly, a Moroccan study conducted in Marrakech on 78 patients
81 with the fistulizing form of Crohn's disease confirmed the predominance of entero-enteric
82 fistulas (30%), followed by entero-cutaneous (23%) and entero-vesical fistulas (9%) [7]. In
83 our study, entero-enteric fistulas were the most prevalent, accounting for 68.6% of cases,
84 followed by entero-colic fistulas (27%) and entero-cutaneous fistulas (21.4%). Additionally,
85 50% of patients had associated anoperineal fistulas. It has been shown that the risk of
86 developing an intestinal fistula is significantly higher in cases of ileal involvement compared
87 to isolated colonic involvement [6]. Our findings align with this observation, as the majority
88 of patients (84%) presented with ileocolic disease.

89 The clinical presentation of fistulas varies depending on their type. Entero-enteric fistulas
90 are generally asymptomatic or present with nonspecific abdominal pain [8]. Entero-cutaneous
91 fistulas, on the other hand, lead to the discharge of fecal matter or pus through the fistulous
92 opening, which may be single or multiple, with a variable output depending on the complexity
93 of the tract, the affected intestinal segment, and the possible presence of a downstream
94 stricture [9,10]. The diagnosis of entero-vesical fistulas is primarily clinical. They manifest as
95 recurrent urinary tract infections, the presence of fecal matter in the urine (fecaluria), the
96 passage of gas through the urethra (pneumaturia), or urinary symptoms such as dysuria
97 [11,12]. Rectovaginal fistulas are less common, and their incidence appears to be proportional
98 to the severity of inflammatory colitis and the presence of associated anoperineal lesions [13].
99 The clinical presentation typically includes the passage of gas or fecal matter through the
100 vagina, dyspareunia, vaginal irritation, and recurrent genitourinary infections [14,15].

101 Imaging is essential for the diagnosis and management of intestinal fistulas. Several
102 radiological examinations can contribute to the diagnosis of fistulas in Crohn's disease.
103 Entero-MRI is the gold standard, offering excellent sensitivity and specificity [16]. Fistulas
104 appear as hyperintense tracts on T2-weighted sequences with enhancement after gadolinium
105 injection. Computed tomography (CT) is often indicated in emergency situations or when
106 MRI is contraindicated, although it exposes patients to higher radiation levels [17]. Contrast-
107 enhanced ultrasound is emerging as a promising alternative, particularly for patient follow-up
108 [18]. In our study, abdominal CT scan was the most frequently prescribed imaging modality
109 for diagnosis, performed in 41.4% of patients, followed by CT enterography scan in 36%,
110 while entero-MRI was performed in only 8.6% of cases due to limited availability.

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

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

121 For the medical treatment of fistulas in Crohn's disease, corticosteroids have no
122 role. Some studies have shown that the use of prednisolone in patients with
123 fistulizing Crohn's disease was associated with poor outcomes, with a higher rate of
124 surgical intervention compared to patients who did not receive corticosteroids [20].
125 Regarding thiopurines (azathioprine and 6-mercaptopurine), a meta-analysis
126 including 70 patients with fistulas showed complete closure or a reduction in fistula
127 output in 54% of patients treated with thiopurines, compared to 21% in the placebo
128 group [21]. Another study conducted on 34 patients with fistulas reported complete
129 closure in 39% of cases and significant symptom improvement in 26%, with
130 particularly favorable results for entero-cutaneous fistulas [22]. Infliximab has been
131 widely studied for its efficacy in treating fistulas associated with Crohn's disease,
132 with response rates ranging from 46% to 69% [23,24]. The ACCENT II trial, which
133 included 289 patients (246 with anoperineal fistulas and 39 with entero-cutaneous
134 fistulas), showed that 69% of patients responded to infliximab treatment [25]. An
135 analysis of this cohort also demonstrated a beneficial effect on rectovaginal fistulas,
136 with a closure rate of 60.7% at 10 weeks and 44.8% at 14 weeks [26]. A study by
137 GETAID on 51 patients with entero-cutaneous fistulas reported complete closure in
138 38% of cases, with sustained efficacy at 36 months in 50% of patients. The best
139 outcomes were observed in patients with spontaneous, simple, low-output fistulas
140 without associated intestinal strictures [27].

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

154 intestinal involvement (less than 50 cm), or in the presence of large collections [29-
155 30]. The MICA study by GETAID, conducted on 117 biologic-naïve patients with
156 Crohn's disease complicated by an intra-abdominal abscess, evaluated the
157 effectiveness of adalimumab initiated after abscess resolution. Results showed that
158 72% of patients treated with adalimumab did not require surgery [31]. In a
159 retrospective cohort of 156 patients with fistulizing Crohn's disease treated with
160 anti-TNF agents, 68 patients (43.6%) underwent surgery during follow-up. Factors
161 associated with higher rates of medical treatment failure included C-reactive protein
162 (CRP) >18 mg/L, albumin concentration <36 g/L, the presence of an abscess at the
163 time of fistula diagnosis, and associated intestinal strictures [32]. In our study,
164 immunosuppressive therapy was indicated in 30% of cases, combination therapy in
165 22.9%, and biologic therapy in 14.3%. The low rate of biologic use was primarily
166 due to limited access for most Moroccan patients, mainly because of financial
167 constraints.

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

187 closure rate of 84%, with a mean follow-up of 48 months. The recurrence rate was
188 16% [9]. Similarly, a Moroccan study involving 78 patients with fistulizing Crohn's
189 disease found that 87% required surgical intervention, with a 96% fistula closure
190 rate and a 4% recurrence rate [20]. In our study, 20% of patients underwent
191 immediate surgical management, while 13% required surgery after failure of
192 medical treatment.

193

194 ***Conclusion:***

195 Fistulizing Crohn's disease represents a major therapeutic challenge for
196 gastroenterologists due to its diagnostic complexity, high recurrence rate, and
197 frequent need for surgery. In our study, Crohn's fistulas were predominantly (84%)
198 associated with ileocolic involvement, complicated by intra-abdominal abscesses in
199 44% of cases. Access to biotherapy remains limited among Moroccan patients due to
200 financial constraints. A multidisciplinary approach, integrating personalized
201 management with medical treatment and appropriate surgical intervention, is
202 essential to improve patient prognosis and reduce complications.

203

204 ***Conflicts of interest:***

205 The authors declare no conflicts of interest.

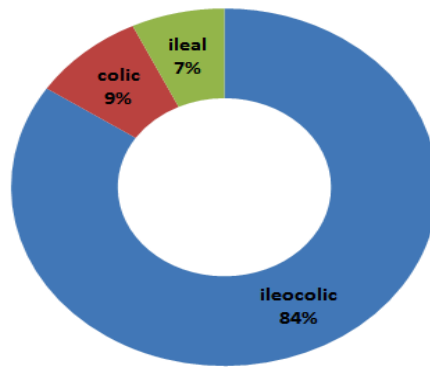


Figure 1: Crohn's disease localization

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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

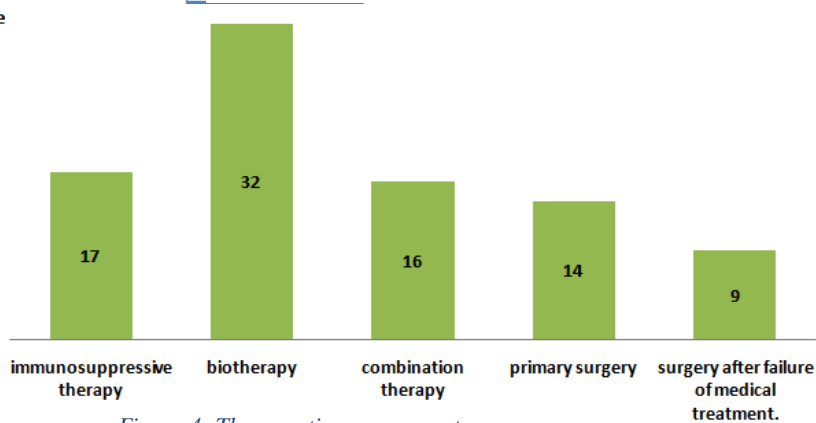


Figure 4: Therapeutic management

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