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Literature Review

# Perianal Disease in Idiopathic Inflammatory Bowel Disease. Updated Approaches to its Management

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## Abstract

Perianal crohn disease is defined as an inflammation at or near the anus, including tags, stenosis, fistulae and abscesses. Perianal disease is a major source of morbidity and a common complication in these patients and in patients with Inflammatory bowel disease in general. Perianal fistulas and abscesses are common manifestations of crohn's disease. Perianal crohn's affects similar numbers of men and women, but women are at greater risk for further complications in the vaginal wall. Diagnosis requires a detailed history, physical and clinical examination, and assessment of luminal disease. It can lead to difficult treatment procedures, a high rate of surgeries, and a low quality of life. The optimum management of perianal disease requires the interdisciplinary collaboration of medical specialties with imaging and systematic clinical and endoscopic evaluation, combined with medical and surgical management and continuous monitoring of these patients.

***Keywords:*** *Perianal Crohn Disease; Fistula; Abscesses; Crohn's Disease; Inflammatory Bowel Disease*

## Abbreviations

IBD: Inflammatory Bowel Disease; CD: Crohn's Disease; UC: Ulcerative Colitis; anti-TNF: anti-tumour necrosis factor; KID: Kids' Inpatient Database; MRI: Magnetic Resonance Imaging; CT: Computerized Tomography; EUS: Endoanal Ultrasound

## Introduction

Idiopathic Inflammatory Bowel Disease (IBD) has emerged as a growing problem in industrialized nations [1]. It is a chronic incurable disease with low mortality [2]. It represents a group of chronic recurrent inflammatory conditions of the gastrointestinal system and includes Crohn's Disease (CD) and Ulcerative Colitis (UC) [3]. UC is a chronic, recurrent disease of the colon and rectum [4]. It causes debilitating symptoms such as rectal bleeding, increased frequency of defecation, abdominal pain, etc. [5]. UC is mainly treated through a variety of anti-inflammatory and immunosuppressive drugs such as aminosalicylates, corticosteroids, anti-tumour necrosis factor/anti-TNF, etc. 6].

The CD is a multi-factorial inflammatory bowel disease with a heterogeneous clinical course [7]. It is typically characterized by trans mural inflammation of the intestine and can affect any part of the gastrointestinal tract from the mouth to the perianal region [8]. Based on epidemiological, genetic, and immunological data, it is considered a heterogeneous disorder with multifactorial etiology in which genetic factors and environment interact in the manifestation of the disease [8].

There is an expanding knowledge about the etiology, morphology, and clinical presentation of IBD, which led to detailed phenotypic sub classification and defined many atypical variants. As a result, their diagnosis became a complex interdisciplinary process [3]. However, the exact cause of IBD is unknown and until more is understood, prevention or complete cure is not possible [8]. Although IBD can be diagnosed at any age (from infancy to the eighth decade of life), the majority of new diagnoses are made in adolescence and early adulthood [2].

CD and UC occur globally with differences in epidemiology, etiology, and phenotype between regions [9]. Since the mid-twentieth century, the incidence of ulcerative colitis and CD has steadily increased in the Western world, which includes North America, Europe, Australia, and New Zealand [1]. IBD was relatively rare in developing countries. However, in recent decades the emergence of IBD in the newly industrialized countries of Asia, South America, and the Middle East has been documented [10].

## Operational treatment of IBD

The development of medical treatment of IBD has significantly postponed the need for surgery and reduced the number of acute surgeries [11,12]. However, if medication combined with dietary changes is not sufficient to manage the disease, then surgery should be considered. It should be noted, however, that the decision between elective surgery and ongoing medical treatment also depends on patient preferences [13]. In recent decades, in addition to medical care, surgical management, surgical methods, preoperative and postoperative care have undergone many changes. Due to the predisposition to relapses and the necessity of sequential surgical treatment, experts recommend that extensive surgical resections in IBD be avoided [11].

Studies comparing ongoing medical treatment with elective surgery show contradictory results in a quality of life despite using the same questionnaire. This variability of outcomes concerning the quality of life highlights that decisions about treatment management of the disease must be based on patient preferences [14]. Approximately 20%-30% of patients with ulcerative colitis will undergo surgery during the course of the disease [15]. Patients may undergo emergency surgery. However, the vast majority of patients undergo elective surgery due to chronic refractory disease [16. In general, various risks have been reported for elective surgery [17]. Similarly, the majority of patients with CD still need one or more surgeries during their disease [12].

## Perianal disease in inflammatory bowel disease

Perianal disease is a major source of morbidity and a common complication in these patients and in patients with IBD in general. It can lead to difficult treatment procedures, a high rate of surgeries, and a low quality of life [18,19].

Perianal lesions are recorded in a significant proportion of patients (up to 47%) and may constitute the first manifestation of the disease [20,21]. They include a wide range of lesions and different conditions from more serious ones, such as abscesses and fistulas, to more benign ones such as hemorrhoids, skin lesions, and fissures. Most research has focused on sepsis and fistulas of the anus, as they carry most of the burden of the disease and often alter its natural course. Hemorrhoids and fissures in patients with idiopathic inflammatory bowel diseases have been overlooked, although they can also be a difficult problem [22].

Perianal Crohn's disease affects a significant number of patients with CD and is associated with poor quality of life. The nature of the disease, combined with the existence of varying levels of severity, has made it difficult to treat. The field continues to evolve using historical and contemporary solutions to address the challenges associated with it [23].

The incidence of perianal CD ranges from 17% to 43% of patients with this disease [24]. There is some evidence that the prevalence of perianal CD is higher in Asia than in Western countries and Asian patient outcomes may differ from those of Western patients [23]. Also, the incidence is similar in men and women. However, women have greater complications associated with the adjacent vaginal wall and risks associated with childbirth. Some may report fecal incontinence [24,25].

Perianal disease is associated with more extensive CD, is an indicator of more severe disease, and is associated with multiple surgeries and frequent relapses [23,26]. However, in 5% of individuals, CD manifests itself only as a perianal disease without coexisting lumen disease [24,27]. Individuals most often develop perianal disease before diagnosis [24]. The etiology of perianal CD is still unclear. Theories suggest that it results from deep ulcers or abscesses of the gland. It is most likely a combination of genetic, microbiological, and immunological factors [28].

The disease can manifest naturally as perianal fistula, fissure, narrowing of the canal, rectovaginal fistula, or abscess [25]. In particular, the incidence of CD is increasing worldwide [29] and perianal disease occurs in up to 90% of patients with CD [30]. Many of these patients have only mild symptoms or are asymptomatic and therefore no intervention is required [29,30]. On the other hand, perianal complications of CD are also common in the adult and pediatric population [31]. These complications have a negative impact on the quality of life of patients with CD and are a predictor of poor long-term outcomes [32].

The clinical features of the disease vary and include hypertrophic skin markings, ulceration, perianal abscess and fistulas, ulcers, stretch marks, hardening, and stenosis [33]. Perianal abscesses and fistulas are often found in patients with CD, often as the first manifestation of the disease or even as a manifestation of the disease during periods of mild intestinal tract involvement [30-33]. Such perianal abscess and fistulas occur in 10% of patients at diagnosis [34]. In a study involving 185 patients with newly diagnosed CD, perianal lesions were recorded in 23% of patients [20,21].

Perianal localizations of Crohn's disease often begin as erythro-violet edematous skin lesions, which along the way can ulcerate and form persistent ulcers with clear, undug lips, a "clean", not dirty bottom and a histopathological picture of sarcoid-granulomatous inflammation characteristic of Crohn's disease [22,26]. Many patients with perianal CD will eventually develop an abscess [29,34]. Perianal abscesses are associated with inflammatory bowel disease, and people who develop them are at increased risk of subsequent diagnosis of CD and UC [35]. However, the incidence of inflammatory bowel disease after diagnosis of perianal abscess and the possible prognostic factors of a future diagnosis of IBD is unknown [24,35].

Perianal abscesses and fistula often occur simultaneously and are usually symptomatic. Symptoms range from pain, discharge, and bleeding to heavy fecal incontinence with restriction of lifestyle and sexual activity [33]. This is due, in part, to variability in both frequency and severity of cases and spontaneous remissions and exacerbations of perianal disease. The wall thickness is increased in patients with perianal CD and may reflect disease activity [29,36].

## Updated literature

The Thomas., *et al*. (2019) found that the risk for CD was higher in the perianal abscess group than in the control group. Correspondingly, the risk of ulcerative colitis was also higher in patients with perianal abscesses compared to the control group [35]. Anemia in men and the use of antidiarrheal drugs were associated with an increased risk of CD after perianal abscess. Also, anemia in men, diarrhea, and use of antidiarrheal drugs was associated with an increased risk of ulcerative colitis after perianal abscess. On the other hand, perianal disease is also an important prognostic factor in the clinical course of inflammatory bowel diseases. Thus, along with other variables such as young age, colon resection, repeated resection of the small intestine, stenotic phenotype, significant weight loss, specific endoscopic lesions, and the immediate need for corticosteroids predict the poor course of the disease [37].

Also, the presence of perianal disease in CD is one of the factors of postoperative relapse, and patients with perianal lesions have a higher risk of reoperation. In the research of Han., *et al*. (2016) the 132 patients included in the study were divided into 2 groups, those with perianal disease (45 patients) and those without perianal disease (87 patients) [38]. Patients with perianal disease were younger (33.8 years vs. 39.8 years; p = 0.015) and diagnosed with CD at an earlier age (21.9 years vs. 28.6 years; p = 0.005) than patients without perianal disease. Patients with perianal disease had greater extraintestinal manifestations than patients without perianal disease (8 versus 3, p = 0.008). Reoperation was required in 46 (44.8%) patients during the follow-up period. The presence of perianal disease independently increased the risk of repeat surgery (hazard ratio = 3,112; 95% CI = 1,707 - 5,675). In addition, patients with perianal disease had an increased risk for repeat abdominal surgery (hazard ratio = 1,978; 95%CI = 1,034 - 3,784) [38].

Zwintscher., *et al*. (2009), studied 12,465 cases of inpatients ≤ 20 years of age with inflammatory bowel disease using the Kids' Inpatient Database (KID). Patients were stratified based on the primary diagnosis: UC or CD. Of the 511 (4.1%) patients with perianal disease, 480 had Crohn's disease (94%, p < 0.001) and girls were less likely to have perianal disease (OR = 0.63, CI 0.52 - 0.76, p < 0.001). Those with perianal disease were more likely to suffer from complex fistulas (OR = 3.5, CI 1.98 - 6.20, p < 0.001) but less likely to suffer from enterintestinal fistulas (OR = 0,30, CI 0,15 - 0,63, p = 0,001) in relation to people without perianal disease. Perianal disease doubled the likelihood of an operation of any type at admission (p < 0.001). In addition, patients with perianal disease spent an average of 1.29 more days in the hospital (7.45 versus 6.16 days, p < 0.001) and had an additional $5838 in hospital charges (p = 0,005) [39].

Of interest are also the cases of patients whose disease is manifested by fever, pain (right iliac fossa or periumbilical), diarrhea, nausea, and vomiting, in which case the diagnosis of acute appendicitis is initially made and the patient is taken to the operating room, where the lesion of the final ileum is revealed [20,21].

Makowiec., *et al*. (1997) evaluated in a prospective follow-up study the factors influencing the occurrence and recurrence of perianal abscesses. Of the 126 patients with perianal CD who were treated on an outpatient basis, 61 had at least one perianal abscess (mean follow-up, 32 +/- 17 months). In total, 110 cases of abscess with 145 anatomically distinct abscesses were documented. The appearance of the first abscesses depended on the type of fistula (ischiorectal, 73%, transsphincteric, 50%, superficial, 25%, p < 0.02). Surgical treatment consisted of seton drainage (34%), mushroom catheter drainage (49%), or incision and drainage (29%) and resulted in abscess inactivation in all patients. The overall relapse rates over two years after the first and second abscess were 54% and 62%, respectively [34]. Abscess recurrence was less common in patients with a stomy (13% versus 60% in patients without a stomy after two years) and in patients with superficial fistulas (0% versus 55%/56% in patients with trans sphincter/ischiorectal fistulas). Only two abscesses recurred within a year after removal of the seton's drainage, while 13 abscesses reappeared while the seton was still in place. The intestinal activity of CD did not significantly affect the occurrence of an abscess. During the study period, only two patients developed partial fecal incontinence [34].

## Diagnosis of perianal disease in IBD

The first step in diagnosing perianal CD is taking a detailed history and physical examination. The history should include information on possible pain, purulent discharge, persistent drainage, rectal bleeding, recurrent urinary tract infection, or fecal incontinence. Regarding perianal abscesses and fistulas, diagnostic methods for perianal CD are changing due to the limitations of conventional fistulography, computed tomography, and clinical evaluation. Magnetic Resonance Imaging (MRI) evaluation was introduced more recently; however, it requires endorectal spiral endorectal coil to achieve good anatomical imaging and has limited availability [33].

Intrarectal ultrasound has been shown to detect more abscesses and fistulas in patients with CD than clinical examination, proctosigmoidoscopy and Computerized Tomography (CT) scan. It also contributes to better fistula demarcation from fistulography and has the ability to change the clinical management applied by doctors [33,36]. Most fistulas are not surgically investigated and therefore fistula documentation in symptomatic CD is limited [32,33].

Examination under anesthesia remains the standard test for the diagnosis and classification of perianal fistula with up to 90% accuracy [24]. It should be performed by a qualified surgeon with good knowledge of the disease. During the examination under anesthesia, abscesses are drained, and fistula pathways are delineated and placed on the floor if indicated. During the examination, great attention is paid to the vaginal wall and scrotum to assess the presence of complex fistula pathways. Examination under anesthesia with drainage of the abscess and placement of a seton is considered the first step before the intervention of anti-TNF and leads to higher resolution and lower recurrence [40].

In combination with examination under anesthesia, endoscopy can also facilitate the recognition of inflammation of the lumen and the presence of internal lesions, while also excluding strictures and cancer [40]. To the above diagnostic strategies can be added the addition of Endoanal Ultrasound (EUS) and MRI. Transrectal Ultrasound is also effective for diagnosing and monitoring patients with rectal abscesses and fistulas in CD [41].

## The therapeutic approach to perianal disease

Despite advances in medical and surgical interventions for perianal CD, treating it remains a challenge. Treatment is critical in perianal CD and should be initiated as soon as the active disease is diagnosed [23,38].

H Perianal CD is particularly difficult to manage because of its complexity. The main goals of treatment are to achieve and maintain disease remission [25,38]. In general, however, there is little agreement among clinicians in the investigation and management of perianal CD [42] and treatment can have large differences between professionals [43]. The care of patients with perianal CD, therefore, requires a multidisciplinary approach with imaging and systematic clinical and endoscopic evaluation, combined with medical and surgical management [29,32].

Conservative treatment includes antibiotic administration, immunosuppression, and TNF antagonists, which are effective in achieving lasting remission 23]. Surgery is still necessary for a large proportion of patients and should not be delayed when the criteria for medication failure are met [32]. Surgical procedures for perianal CD vary depending on the extent and severity of the disease and can be combined with the simultaneous use of medical drug therapy. Although efforts are made to make surgeries conservative, the primary goal is to manage perianal sepsis, drain any abscesses, and place seton in delimited fistulas [43].

The development of perianal abscesses in CD depends on the flow of feces and the anatomical type of fistula. Seton and catheter drainage are safe and highly effective in treatment. However, long-term use of setons to prevent recurrent abscesses is not supported [34]. In the case of perianal abscesses and fistulas, assessing disease severity and response to treatment is difficult to measure objectively in a quantitative way. In these cases, the purpose of treatment is to improve the quality of life and not to treat perianal disease. Concerning fistulas in particular, although current solutions for their management show varying degrees of success, additional research is needed to further manage this difficult disease [23.

Full evaluation of fistula characteristics is the basis for optimal management and should include clinical evaluation of fistula openings, endoscopic evaluation of the presence of proctitis, and MRI to determine the anatomy of fistula pathways and the presence of abscesses [32].

Topical injection of mesenchymal stem cells may induce remission in patients who do not respond to medication or avoid exposure to systemic immunosuppression in patients who have not received biologics due to the absence of active lumen disease [32]. Regarding hemorrhoids and stretch marks, their management in patients with Idiopathic IBD can be difficult and differ significantly compared to the unaffected population. Historically, surgery was not the treatment of choice, and hemorrhoidectomy or sphincterotomy in patients with Idiopathic IBD was considered harmful, although literature data are minimal and based on a small number of patients. Several authors

reported a higher incidence of postoperative complications in Idiopathic IBD than in general populations, with potentially serious events 22].

Considering that spontaneous healing of hemorrhoids and stretch marks in patients with Idiopathic IBD is possible, the first line of treatment should be a medical treatment. In patients who do not respond to conservative measures, a prudent choice of surgical options is possible on a highly selective basis. This can lead to acceptable results, but the risk of possible complications must be taken into account [22].

## Conclusion

Perianal disease is a particularly difficult complication of IBD, which can create difficulties in the diagnostic and therapeutic approach but also contributes to the reduction of the patient's quality of life with all the consequences. The optimum management of perianal disease requires the interdisciplinary collaboration of medical specialties with imaging and systematic clinical and endoscopic evaluation, combined with medical and surgical management and continuous monitoring of these patients.

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