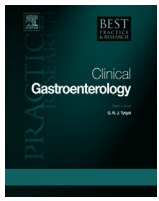
Best Practice & Research Clinical Gastroenterology 28 (2014) 505–518

Contents lists available at ScienceDirect

Best Practice & Research Clinical Gastroenterology



13

Improving the outcome of fistulising Crohn's disease

Ilse Molendijk, MD, PhD Student [a,1], Koen C.M.J. Peeters, MD, PhD, GE-surgeon [b,2], Coen I.M. Baeten, MD, PhD, GE-surgeon [c,3], Roeland A. Veenendaal, MD, PhD, Gastroenterologist, Head of Department [a,4], Andrea E. van der Meulen-de Jong, MD, PhD, Gastroenterologist, Head of IBD Unit [a,*]

[a] *Dept. of Gastroenterology and Hepatology (C4-14), Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands*
[b] *Dept. of Surgery (K6), Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, The Netherlands*
[c] *Dept. of Surgery, Groene Hart Hospital, P.O. Box 1098, 2800 BB Gouda, The Netherlands*

Keywords:
Crohn's disease
Perianal fistulas
Classical treatment
Potential future therapies
Research targets

A B S T R A C T

Fistulas are a frequent manifestation of Crohn's disease (CD) and can result in considerable morbidity. Approximately 35% of all patients with CD will experience one fistula episode during their disease course of which 54% is perianal. The major symptoms of patients with perianal fistulas are constant anal pain, the formation of painful swellings around the anus and continuous discharge of pus and/or blood from the external fistula opening. The exact aetiology of perianal fistulas in CD patients remains unclear, but it is thought that a penetrating ulcer in the rectal mucosa caused by active CD forms an abnormal passage between the epithelial lining of the rectum and the perianal skin. Genetic, microbiological and immunological factors seem to play important roles in this process. Although the incidence of perianal fistulas in patients with CD is quite high, an effective treatment is not yet

* Corresponding author. Tel.: +31 71 526 2915; fax: +31 71 524 8115.
E-mail addresses: i.molendijk@lumc.nl (I. Molendijk), k.c.m.j.peeters@lumc.nl (K.C.M.J. Peeters), coen.baeten@ghz.nl (C.I.M. Baeten), r.a.veenendaal@lumc.nl (R.A. Veenendaal), ae.meulen@lumc.nl (A.E. van der Meulen-de Jong).
[1] Tel.: +31 71 526 5719; fax: +31 71 524 8115.
[2] Tel.: +31 71 526 2309; fax: +31 71 526 6750.
[3] Tel.: +31 182 505420; fax: +31 182 505519.
[4] Tel.: +31 71 526 2915; fax: +31 71 524 8115.

http://dx.doi.org/10.1016/j.bpg.2014.04.011

discovered. In this review all available medical and surgical therapies are discussed and new treatment options and research targets will be highlighted.

Introduction

Fistulas in Crohn's disease (CD) are a major problem which can result in considerable morbidity. Approximately 35% of all CD patients have at least one fistula episode. A quarter of the fistulas is between two parts of intestine, 9% is rectovaginal and 13% is different, including fistulas between the intestine and bladder and around a stoma [1]. In case of an enterovesical fistula there may be recurrent polymicrobial urinary tract infections, pneumaturia and faecaluria. When a rectovaginal fistula develops, dyspareunia, malodorous vaginal discharge and recurring episodes of vaginitis can occur. Perianal fistulas are the most common type of fistulas in fistulising CD. The cumulative incidence of perianal fistulas was estimated at 23%–26% after 20 years of CD [1,2]. Patients with perianal fistulas can present with symptoms such as constant anal pain or pain after defecation, (painful) swelling around the anus, continuous (malodourous) discharge of pus and/or blood from the external opening with skin irritation around the anus, fever and even incontinence [3]. In 20–45% of the CD patients a perianal fistula developed before or at the time of diagnosis CD [1,2]. Patients with colonic and active rectal disease have more frequently perianal fistulas compared to patients with isolated ileal or ileocolonic disease [1,2,4–6]. Male gender, age at diagnosis of CD and smoking are other risk factors although data are conflicting [1,2,5,7–9]. The formation of perianal fistulas in CD is based on the presence of a penetrating ulcer in the rectal or anal mucosa resulting in an abnormal granulating connection between the epithelial lining of the rectum or anal canal and the perianal skin [10,11]. However, most perianal fistulas are cryptoglandular fistulas (90%) and are not associated with CD. They originate from the intersphincteric anal glands due to a local infection with abscess formation [12]. Normally the internal sphincter is a barrier for bacterial overgrowth, only chronic infection, CD inflammation or local

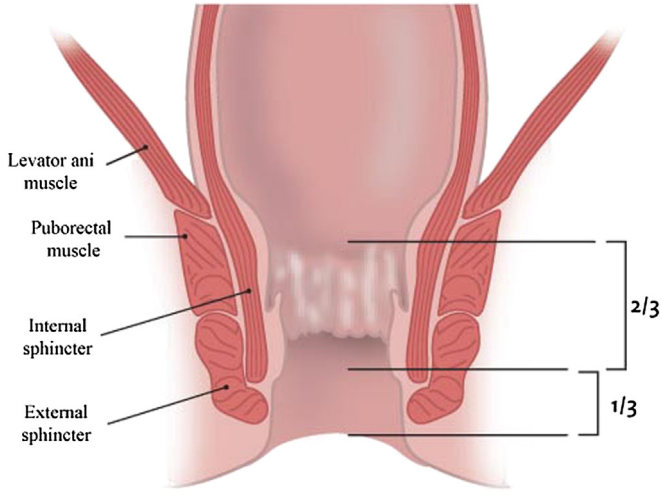


Fig. 1. Anatomy of the muscles surrounding the rectum and anal canal. A fistula tract through the lower third of the external muscle is classified as a low perianal fistula; fistulas in the two-thirds above as high perianal fistulas. Figure reproduced with permission from Bemelman from van Koperen et al [93].