Full-thickness endoanal advancement flap repair (EAFR) in patients with IBD and fistulas-in-ano

---Long-term outcomes for healing and continence

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**Purpose:** The purpose of this study was to assess primary healing, recurrence and continence after endoanal advancement flap repair in patients with IBD compared to those with cryptoglandular disorders. **Patients and Methods:** 71 patients with fistulas-in-ano received endoanal advancement flap repair between 1997 and 2009. This is a prospective, non-randomized, single-centre study. **Results:** Follow up data was available for 63 patients. In 46% the fistulas were due to chronic inflammatory bowel disease. 54% had cryptoglandular fistulas. Primary healing was observed in 37 cases (58.7%). The median time to recurrence was 27 months (mean: 45 ± 50.31) and differed significantly across the patient groups: Inflammatory bowel disease 11 months (mean: 23.65 ± 32.47), cryptoglandular origin 51 months (mean: 63.20 ± 55.84) (P < 0.01). Preoperatively, 31 (49.2%) of the patients had impaired continence versus 30 (47.6%) postoperatively. In IBD there was no significant difference between pre- and postoperative CCIS values (pre 4.05 ± 4.12 vs 3.61 ± 4.78, P = 0.4) **Conclusions:** Full-thickness endoanal advancement flap repair is a successful treatment option for IBD patients. Fistulas associated with chronic inflammatory bowel disease were found to have a significantly higher rate of recurrence and a shorter time to recurrence at long-term follow-up. Repeat interventions do not negatively impact postoperative continence.

**Keywords:** inflammatory bowel disease; fistula-in-ano; continence; long-term follow up


**Introduction**

Perianal lesions occur in 25-80% of patients with Crohn’s disease [1]. The course of the disease varies from straightforward to complex and destructive. Perianal Crohn’s lesions are signs of an aggressive form of Crohn’s disease, especially if these symptoms are found at initial diagnosis. If systemic or local therapy fails, creation of a stoma may be needed in some cases to control symptoms [2]. The reversal rates are reported at 10 - 51%. In 25 - 68% a proctectomy with definitive stoma is unavoidable [3, 4, 5].

A number of non-fistulous perianal lesions associated with Crohn’s disease (skin tags, ulcers, hemorrhoids, fissures, strictures) may also require surgical intervention. The pre-condition is a remission of the underlying disease at the time of surgery. If there is sepsis, incision and percutaneous drainage of the abscess may be indicated.

Patients with M. Crohn and manifest perianal involvement develop fistulas in 14-38% of cases. These are generally secondary manifestations of the transmural inflammations typical of Crohn’s disease [6]. They may occur anywhere in the lower rectum or anal canal, but may also originate in the crypts [7]. Consequently, Crohn’s fistulas present an
impressive array of different forms. Simple fistulas can be addressed by fistulotomy and laying open. Healing rates range from 8-100%. [7].

Complex fistulas may require percutaneous drainage, fistulotomy, fistulectomy, biologicals and/or advancement flaps. The choice of procedure depends on the site of the fistula in the anal canal and the condition of the adjacent tissue. Transsphincteric fistulas extending to the vagina, so-called rectovaginal fistulas (RV) present a special challenge.

In general, it would seem that fistulotomy leads to a better healing rate for cryptoglandular fistulas, but fecal continence decreases as a function of the residual sphincter mass [8,9,10,11]. Regrettably, the majority of studies do not report on patient continence in the short and long-term. In contrast, sphincter-saving techniques seem to preserve fecal continence at the expense of higher recurrence rates [8].

Tissue-preservation should be the top priority of surgical intervention, especially because chronic inflammatory bowel disease (IBD) is associated per se with the risk of fecal incontinence [12]. Fistulas arising from IBD tend to recur and some patients have to undergo several operations before the fistulas are closed [13, 14].

Currently, there is an overall paucity of empirical data on the long-term healing outcomes and on postoperative continence after endoanal advancement flap repair for Crohn’s fistulas. Comparison with outcomes after EAFR for cryptoglandular fistulas has confirmed good performance of the procedure in IBD patients. The present study also analyzed the data of a prospective, non-randomized study, whereby the focus was on IBD and IBD fistulas [15].

Patients and Methods

This prospective, non-randomized, single-centre study describes a series of 71 patients with fistulas-in-ano of different etiologies who received EAFR between 1997 and 2009. All fistulas were either perianal fistulas (AF) or RVs. All AFs were type 2 (trans-sphincteric) fistulas according to Parks’ classification [16].

Etiologies included IBD and cryptoglandular inflammation (CGI). Patients with a preoperative Crohn’s Disease Activity Index (CDAI) > 150 were excluded [17,18]. Patient data were entered into a prospectively managed database. Demographic and surgical data as well as the Cleveland Clinic Incontinence Score (CCIS) [19] were retrieved from this database. Follow-up data (CCIS, fistula healing) were supplemented by patient information given on the telephone in reply to standardized questionnaires. The survey was conducted in 2010-2011 by a research assistant. The study was approved by the local ethics committee (No. 437/129). For 8 patients, follow-up data could not be collected since contact details were not available.

Statistics

Statistical analysis was performed with the STATA ® 11.0 statistical package. The data were recorded as whole numbers or percentages (categorical data) or as a mean with standard deviation (continuous data). The median was used when distributions were highly skewed. Group comparisons of categorical data were performed with the chi-squared test ($\chi^2$-Test), other group comparisons were performed with student’s t-tests. Multiple regression analysis was used to assess healing and incontinence (odds ratio (OR), confidence intervals and p-values of the Wald test). The time to recurrence after fistula closure was analysed using the Kaplan-Maier survival function and the log-rank test.

Operative Details

Patients with AF or RV were prepared for EAFR after assessment by an experienced colorectologist. Preoperative stomata were not created to protect the flap. However, in some patients, the stoma had been created to manage uncontrollable fistula symptoms. In some patients stomata had been created prior to EAFR in the context of a rectum resection, which then could not be reversed due to the fistula. Antibiotic prophylaxis was administered prior to surgery.
Flaps were formed according to a procedure described by Stone&Goldberg [20] and Belt&Belt [21] as follows. With the patient fully relaxed and in the Lloyd-Davies position, the internal fistula opening is identified, and any setons are removed. This is followed by careful exploration of the fistula tract in order to identify the real fistula opening on the dentate line [13]. A full thickness flap (containing the muscularis propria) is formed beginning at the internal opening and using a Schulze-Bergmann rectal speculum. Flap transposition over the fistula opening must be possible without causing tension. The internal sphincter is reconstructed in the region of the internal fistula opening using Vicryl ® sutures. The flap is then transposed distally and fixed with Vicryl ® sutures, thus cover the fistula opening with an overlap. Generally, a small ectropion forms in the anal canal [22]. The outer fistula opening is thoroughly excised, and the fistula tract is carefully abraded. The external opening is not closed to allow drainage. Patients remained in the hospital for postoperative treatment. On the second postoperative day, patients were started on a light diet. Plantago ovata husks were prescribed 1 - 3 times per day to regulate bowel activity. Postoperative antibiotic treatment was not routinely administered.

Results

Patient demographic data

71 patients received EAFR. Follow-up data were available from 63 patients (47 women (mean: 42 years - range: 18 to 79), 16 men (mean: 45.75 years - range: 20 to 77)) at a median postoperative time of 7.8 years (range: 2.5-12 years). There is an imbalance in favor of women, which is due to our clinical reality as a tertiary referral center.

In 29 patients (46%), the fistulas were due to IBD (27 Crohn’s disease / 2 colitis ulcerosa). Perioperative seven of the Crohn’s patients received steroids. Etiologically, 34 patients (54%) had CGI fistulas. Anatomically, 35 patients (55.6%, 19 women, 16 men) had AFs. In 28 women (44.4%), a RV had formed. Sixteen patients (25.4%) had already undergone fistula surgery (9 x fistulectomy, 4 x fistulectomy, 1 x AFPlugs, 2 x flaps). 22 patients had seton drains inserted preoperatively. On average, the seton had been inserted one year before the operation. The distribution of pre-treatments did not differ between IBD and CGI (previous fistula surgery: Chisq = 1.861, p = 0.761; seton drains: Chisq = 0.995, p = 0.319). 7 patients (11.1 %) had already received a stoma before the operation (Table 1).

Pre-existing stomata were reversed in all patients after successful fistula treatment. Three patients developed a postoperative urinary tract infection. None of the patients had to be re-hospitalized due to postoperative complications. Preoperatively, the median CCIS was 1 (mean: 3.577 ± 4.569).

Healing

Overall primary healing was recorded in 37 of the 63 cases (58.73%). 22 patients had to undergo more than one operation (a maximum of 4 operations were performed on
any one patient). Of these, 14 fistulas healed (22.22%). In 12 cases (19.05%), the fistula was not eliminated in the long term. There was no significant difference between men and woman in primary healing (Chi² 2.47, P = 0.12).

The etiologies had a clear tendency towards different primary healing rates (Chi² 5.1, P = 0.02).

IBD fistulas healed primarily in 45% compared to 82% of CGI fistulas.

AF and RV showed no significant difference in primary healing. (Chi² = 1.83, P = 0.17).

There was also no significant difference in primary healing between types of fistula with respect to their etiology (IBD: Chi² 0.09, P = 0.76; CGI: Chi² 0.34, P = 0.56).

Overall, 79.4% of all fistulas were successfully eliminated (IBD 66%, CGI 91%).

Looking, in the long term, at which patients were healed, we found a significant difference for the IBD patients. IBD patients experienced considerably more recurrences than patients whose disease was of cryptoglandular origin (Chi² 5.01, P = 0.03). If the type of fistula is also taken into consideration, this difference was apparent for AFs (Chi² 5.41, P = 0.02), but not for RVs (Chi² 0.45, P = 0.5). IBD patients underwent more operations than patients with CGI (mean: IBD 1.82 vs CGI 1.29, P < 0.05)

The median time to recurrence was 27 months (mean: 45 ± 50.31) and differed significantly across the etiological groups: IBD 11 months (mean: 23.65 ± 32.47), CGI 51 months (mean: 63.20 ± 55.84) (P < 0.01). (Figure 1)

Considered separately, the time to recurrence for the individual etiologies of AFs (IBD mean 34.83 ± 45.299 months vs CGI: mean 68.96 +/- 56.817 months, P = 0.02) and RVs (IBD mean 15.76 ± 16.570 vs CGI mean 51.18 ± 54.365 months, P = 0.01) was found to be significantly different. In multiple regression analysis, the risk of a fistula not healing was 5 times higher for patients with IBD than for other patients (OR 4.92, p < 0.05).

Neither age, nor gender, nor prior formation of stomata had an effect on fistula healing in the long term. In IBD patients, perioperative steroid medication was a risk factor for recurrence (OR 13.75, CI 0.972 - 194.648, p = 0.05).

Continence

Preoperatively, 31 (49.2%) patients had impaired fecal continence versus 30 (47.6%) postoperatively. Preoperatively, the median CCIS was 1. Women tended to obtain a worse CCIS (women: mean CCIS 4.20 +/- 4.651; men: mean CCIS 1.69 +/- 3.881, P = 0.086).

Multiple regression analysis showed that impaired preoperative fecal continence was associated with gender but not with age, type or etiology of the fistula or previous fistula surgery. Women have an approximately 9-fold increased risk of being incontinent compared to men (OR 9.12, CI 1.107 - 75.23, P = 0.04).

At follow-up, the overall median CCIS was 0. Overall, mean postoperative CCIS values improved significantly (preoperative 3.74 ± 4.56 vs postoperative 2.68 ± 4.75, p= 0.03).

Patients with primary healing of the fistulas following EAFR had lower CCIS values in the long term compared to patients with recurrent fistulas  (2.46 ± 4.63 vs 3.63 ± 4.96; P = 0.4).

Seven patients (6 women; 5 IBD patients; 3 RVs; 1.43 EAFR / patient) showed a CCIS increase postoperatively, but all except one had preoperative incontinence (preoperative 7.0 ± 4.397 vs. postoperative 10.571 ± 5.50, P = 0.01). In IBD there was no significant difference between pre- and postoperative CCIS values (pre 4.05 ± 4.12 vs 3.61 ± 4.78, P = 0.4)

Fistulas in CGI appeared to have improved postoperative CCIS values as compared to the preoperative values, the difference was significant for AFs (CCIS pre 2.75 ± 4.27 vs post 1.25 ± 3.31, P = 0.04), but not for RVs (pre 3.75 ± 5.092 vs 2.75 ± 6.65, P = 0.4). Postoperatively CCIS values differed significantly between IBD and CGI in the AF group (CCIS post 4.75 ± 5.19 vs 1.60 ± 3.43, P = 0.03), but not for the RVs. A possible explanation could be a different sex distribution between AF and RV. Other group comparisons did not yield any significant results.

Multiple regression analysis showed that postoperative continence disorder is determined by pre-existing preoperative incontinence (OR 10.84, P = 0.03). Patients with IBD had a significantly poorer CCIS at follow-up (OR 39.53, P = 0.03). Closure of RVs significantly improved the CCIS at long-term follow-up (OR 0.035, P = 0.02).

Importantly, fistula recurrence (OR 0.2, P = 0.45) or repeated interventions (OR 3.5, P = 0.6) had no effect on postoperative continence.

Discussion
The goal of surgery for fistulas-in-ano is to heal the fistula and to preserve fecal continence. The surgical strategy depends on the type of fistula and the underlying disease. The results of our study show that AFs and RVs can be successfully treated with the EAFR in IBD. However, there were significant differences in course of treatment and outcome between the groups analyzed.\cite{9,10}

While CGI fistulas responded well to surgical treatment, IBD fistulas were far more challenging to close. Overall, RVs were as likely to heal as anorectal fistulas. These results are comparable with data published by other groups \cite{13,23}.

We observed an overall EAFR healing rate of 80%. At long-term follow up, 91% of CGI fistulas had healed. IBD fistulas healed in 66% of cases. This is very similar to data presented in a systematic literature review by Soltani & Kaiser that analyzes 35 published studies with 1,654 relevant patients. The success rate for these patients was 80.8% for CGI and 64% for Crohn fistulas-in-ano \cite{22}.

IBD patients need surgery significantly more often, and recurrence after surgery is likely. Furthermore, immunosuppressive medication prior to surgery represents a risk factor for failure. In 2002, Sonoda et al. published data for primary repair of complex fistulas in a fairly balanced group of patients, which included roughly 50% of IBD patients. He found that IBD was associated with poorer treatment outcome and that prednisone was a risk factor for failure \cite{24}. Mizrahi, on the other hand, could not find a correlation of poor healing and perioperative steroid administration \cite{25}.

Our data show that repeat surgical intervention leads to closure in two-thirds of IBD fistulas.

Regarding continence, there is very little data on EAFR treatment. A study from 1990 reported that 7 out of 8 patients were continent after EAFR \cite{26}. Hyman performed 33 EAFRs with an 81% overall initial healing rate. All patients remained fully continent \cite{27}. Uribe analyzed healing rates and continence rates in 56 patients with complex fistulas-in-ano of mostly CGI origin after EAFR over a mean follow-up period of 43.8 months \cite{28}. He found a low recurrence rate of 7.1%. However, 21% of patients reported disturbed postoperative fecal continence. But the study was not able to identify risk factors for either recurrence or incontinence.

In 1997, VanTets clearly demonstrated the influence of Park’s anal retractors on continence after hemorrhoidectomy \cite{29}. In our opinion, the sphincter should never be stretched against resistance. The surgeon should ensure that the patient is fully relaxed. We use a Schultz-Bergmann speculum and change its position and tension during the operation. In general, we advocate avoiding any additional risk to continence and therefore avoid cutting through an intact anal sphincter. What might work well for simple fistulas in terms of healing, namely to open the fistula tract and to give it time to heal, has undesirable effects on continence when relevant masses of the sphincter are involved \cite{9,10}, even if the sphincter is reconstructed later \cite{30,31}. This is particularly true when a higher risk of incontinence exists for the individual patient, as is the case with IBD patients.

Importantly, continence can be preserved even when repeated treatments are necessary.

But, in multiple regression analysis, continence is significantly worse in IBD patients in the long term compared to CGI. One reason for this may lie in the nature of the disease itself.

Recently, Norton et al. found fecal incontinence in 74% of cases in a cohort of over 3000 IBD patients. Fecal incontinence was associated with age, gender and fistulizing disease \cite{12}. In published studies on patients with Crohn fistula-in-ano, continence appears to be associated with the degree of inflammatory activity. Anti-TNFα drugs may play a supportive role in continence recovery \cite{22}.

Prior to surgery, inflammatory activity should be at a minimum in order to increase the chances of success \cite{14}. Furthermore, careful patient selection is important in this etiological group due to the higher risk of recurrence. Our data suggest that in difficult situations, such as a recurrent Crohns fistula-in-ano, it may be better to provide symptomatic treatment (immunosuppressive medication and/or seton) or to leave a stoma rather than to perform an operation due to the higher risk of recurrence and fecal incontinence \cite{23}.

One of this study’s strengths was that all operations were uniform with regard to technique, and they were all performed by the same surgeon. The study also has the advantage of a long follow-up period of up to 12 years. The study includes different etiologies. This is unique as other published studies either compare a combination of methods and surgeons, or exclude etiologies like IBD, or fail to comment on continence.

Summary

Fistulas associated with IBD were found to have a significantly higher rate of recurrence and shorter flap durability at long-term follow-up as compared to other
etologies. However, even in this patient population, up to 66% of fistulas will reliably heal after repeat interventions. Importantly, repeat interventions do not negatively impact a patient’s continence postoperatively.

In this study, we demonstrate that fistula closure by full-thickness EAaFR is a successful treatment option for IBD fistulas. In comparison with fistula location, fistula etiology seemed to be prognostically more relevant.

Ethical Approval

The study was evaluated and approved by the local ethics committee (No. 437/129).

Conflicts of interest

The authors declare no competing interests.

Author contributions

GR performed surgery. All five authors drafted and revised the manuscript and gave their approval for publication.

Abbreviations

AF: Perianal Fistula; RV: Rectovaginal Fistula; CGI: Cryptoglandular inflammation; IBD: Fistula due to chronic Inflammatory Bowel Disease; Crohn’s disease or ulcerative colitis; CCIS: Cleveland Clinic Incontinence Score.

References


