DISEASES OF THE COLON & RECTUM

ORIGINAL CONTRIBUTION

Long-Term Functional Outcome and Risk Factors for Recurrence After Surgical Treatment for Low and High Perianal Fistulas of Cryptoglandular Origin

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PURPOSE: This study assessed long-term functional outcome and explored risk factors for fistula recurrence in patients surgically treated for cryptoglandular fistulas.

METHODS: Three hundred ten consecutive patients were surgically treated for perianal fistulas. After exclusion of patients with inflammatory bowel disease or HIV, 179 patients remained. Patients were divided into two groups: those who received fistulotomy for low perianal fistulas and those who received rectal advancement flap for high perianal fistulas. Time to fistula recurrence was the main outcome and Cox proportional hazard models were used to assess the importance of various risk factors. Functional outcome was assessed using the Vaizey and colorectal functional outcome (COREFO) questionnaires.

RESULTS: The median follow-up duration was 76 months (range, 7–134). The 3-year recurrence rate for low perianal fistulas treated by fistulotomy (n=109) was 7 percent (95 percent confidence interval, 1–13 percent). In high transsphincteric fistulas treated by rectal advancement flap (n=70), the recurrence rate was 21 percent (95 percent confidence interval, 9–33 percent). In both groups, soiling was reported at 40 percent. None of the seven potential risk factors examined were statistically significant.

CONCLUSIONS: Fistula recurrence rate after fistulotomy was low. No clear risk factors were found. Overall functional outcome in terms of continence was good. However, a substantial amount of patients reported soiling.

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INTRODUCTION

The aim of fistula surgery is to eradicate the fistula tract by closing the internal opening, without jeopardizing continence. In general, patients with perianal fistulas in the lower one-third of the external sphincter complex are easily treated by fistulotomy with low recurrence rates and relatively little impact on continence.[1,2] For perianal fistulas in the upper two-thirds of the external sphincter complex, the rectal advancement flap is considered the standard surgical treatment. Various treatment options have emerged in recent years for the treatment of high perianal fistulas. During the last decades, fibrin glue appeared as an attractive alternative. Reported long-term outcomes vary considerably between the different studies and recurrence rates range from 0 to 100 percent.[3] Inconsistent reports of recurrence rates are likely a result of heterogeneous research designs. Often patients with Crohn's disease and HIV were included, various classifications of perianal fistulas were used, alternative treatment protocols were used, and sufficient follow-up was lacking.

This study examined long-term functional outcome and assessed possible risk factors for the development of fistula recurrence in patients surgically treated by fistulotomy or rectal advancement flap according to a standardized treatment protocol. As the recurrence rate and the continence are the most important factors in the treatment of perianal fistulas, these measures were specifically studied.

PATIENTS AND METHODS

Patient Characteristics

Between January 1995 and May 2003, a consecutive series of patients operated for perianal fistulas of cryptoglandular

origin were analyzed. Patients in which the internal fistula opening could not be detected and patients with fistulas caused by Crohn's disease or human immunodeficiency virus (HIV) were excluded, as well as patients aged less than 18 years and patients with rectovaginal fistulas.

Treatment Protocol

Patients were divided into two groups. These groups were operated on according to a standardized treatment protocol. The first group comprised patients in which the fistula tract was submucosal, intersphincteric, or located in the lower third of the external anal sphincter and were treated by fistulotomy (fistulotomy group). The second group comprised patients with perianal fistula in which the fistula tract was located in the upper two-thirds of the external sphincter and who were treated by rectal advancement flap (rectal advancement flap group). In cases of acute sepsis, patients were treated with three months of seton drainage before definitive surgery. The anal canal was defined on the proximal side by the puborectal sling and the distal side by the lower margin of the external sphincter. On the day of surgery, an enema was administered to the patient to clean the rectum. All procedures were performed under general or locoregional anesthesia in the lithotomy position. Broad spectrum antibiotics were administered perioperative. The rectal advancement flap was performed according to a technique described herein. The internal opening was excised followed by mobilization of the mucosa, submucosa, and a small amount of muscular fibers from the internal sphincter. A rectal flap with a 2-cm to 3-cm broad base was mobilized. The rectal flap was mobilized sufficiently to cover the internal opening with overlap. Hemostasis was performed to prevent a hematoma under the flap. The fistula tract was curetted. The internal opening was not closed before advancing the flap over the internal opening. Finally, the flap was sutured in the distal anal canal with interrupted Vicryl 2–0 sutures (Ethicon Endo-Surgery, Cincinnati, OH). In a consecutive series of patients, fibrin glue was added to the procedure in an attempt to decrease the recurrence rate. No specific postoperative instructions or bowel regimens were given to the patients.

Data Collection

Retrospective chart review collected information on demographic data, tertiary referral, previous fistula surgery, smoking, surgical treatment (fistulotomy or rectal advancement flap), complications, and fistula recurrence rate. Prior fistula surgery was defined as surgery aimed to permanently repair the fistula. Drainage of abscesses and seton placement were not considered as prior fistula surgery. All patients visited the outpatient clinic until closure of the fistula tract was achieved. The fistula was considered closed if the external opening was closed and no discharge or pain was experienced. Otherwise, the fistulas were considered persistent or recurrent. Follow-up was calculated from the clinical notes when the patient did not respond to the postal survey and to multiple attempts to contact them by telephone. In the questionnaire, patient's complaints indicated a recurrent fistula. Patients were asked if they had been operated on elsewhere after their visits to our clinic.

Functional Outcome

To assess functional outcome of treatment, a postal survey was undertaken. Patients who did not respond were contacted by telephone. If patients had moved, the general practitioner was contacted for their address and telephone number. Continence was evaluated using the Vaizey scale and the colorectal functional outcome (COREFO) questionnaire.[4,5] The validated Vaizey scale consisted of items on the type and frequency of incontinence. Also, changes in lifestyle were assessed. Patients are asked on their use of pads or plugs, constipation medication, and the lack of ability to postpone defecation for 15 minutes. The total score on Vaizey scale ranged from 0 (complete continence) to 24 (complete incontinence). The COREFO questionnaire is a validated questionnaire with 27 questions to assess colorectal functional outcome. Patient's were asked to consider the two weeks prior before filling out the questionnaire. Five categories were assessed: incontinence, social impact, defecation frequency, stool-related aspects (questions on pain during bowel movements, blood loss, and local skin problems), and use of medication. Scores ranged from 0 to 100. A total score was calculated from these categories, also ranging from 0 to 100. A higher score represents an increased level of continence disturbance. In the same survey, patients were asked about smoking habits and whether they had fistula surgery in another hospital after discharge.

Statistical Analysis

Data are presented as median values with ranges unless otherwise specified. Categorical data are presented as frequencies or percentages. Differences between groups were tested using Mann-Whitney *U* test for continuous data. Chi-squared test was used to test for differences between groups in cases of categorical data. Fistula recurrence-free survival was estimated using the Kaplan-Meier method. Cox proportional hazard models were used to examine the association between potential risk factors and the time until fistula recurrence. Hazard ratios (HR) with 95 percent confidence intervals were used to quantify the strength of these associations.[6] The following potential risk factors were examined: gender, age, tertiary referral, prior fistula surgery, and smoking. For the rectal advancement flap group, the factors seton drainage and the use of fibrin glue were also examined. Natural cubic splines (4 knots) graphical analysis were used to examine the functional form of continuous variables in relation to the

outcome.[7,8] Based on these graphic analyses, an appropriate transformation or categorization was chosen if the relationship was clearly nonlinear. $P<.05$ was considered as statistically significant. Statistical analysis was done using the SPSS v.12.0 package (SPSS, Chicago, IL).

RESULTS

Between January 1995 and May 2003, 310 patients were operated on for perianal fistulas in the study period. Patients were excluded (N=131) for the following reasons: no internal opening found during surgery (n=8), HIV (n=23), rectovaginal fistulas (n=22), or inflammatory bowel disease (n=78) (Fig. 1). Of the remaining 179 patients, 109 patients had low fistulas and were treated by fistulotomy. The remaining 70 patients had high perianal fistulas and were treated by rectal advancement flap. The majority of patients had outpatient surgery. The minimum observed follow-up for all patients after surgery was 7 months with a median of 76 months (range, 7–134). Seventy-nine of 179 patients could not be contacted by mail or telephone because they had moved without informing their general practitioner or because they were deceased. These patients were censored at their date of last clinical contact at which they had no sign of recurrence. The response rate for 100 patients successfully contacted by mail or telephone was 95 percent.

FIGURE 1. Patient flow chart.

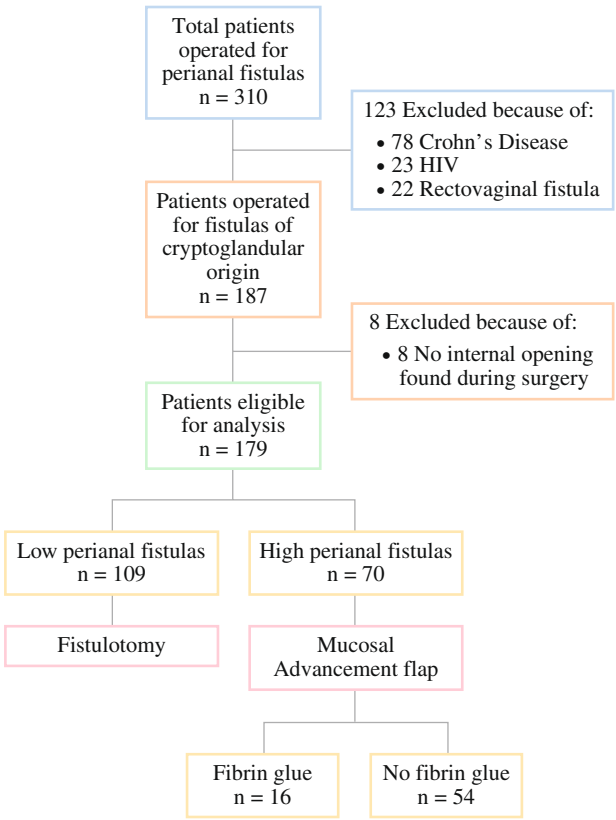

Table 1. Characteristics of patients with low and high perianal fistulas

Variable	*Fistulotomy (n=109)**	*Rectal advancement flap (n=70)†*
Male: Female, n	71:38	47:23
Age, years, median (range)	39 (19–69)	42 (21–67)
Tertiary referral n (%)	14 (13%)	27 (39%)
Prior fistula surgery, n (%)		
0	87 (80%)	37 (53%)
1	13 (12%)	17 (24%)
2	5 (5%)	6 (9%)
3 or more	4 (4%)	10 (14%)
Smoking, %	32%	43%
Preop incontinence (n)		
gas	1	4
soiling	2	3
Fibrin glue addition, n (%)	–	16 (23%)
Seton drainage, n (%)	–	37 (39%)
Recurrence, n (%)	8 (7%)	15 (21%)
Follow-up, months, median (range)	77 (7–134)	70 (22–127)

* Low perianal fistulas • † High perianl fistulas

Fistulotomy Group

The median age was 39 years (range, 19–69) (Table 1). Seventy-one patients were male (65 percent). Prior fistula surgery was performed in 22 patients (20 percent). Fourteen patients (13 percent) were referred from other hospitals mainly because of complex and or recurrent fistulas. The median number of previous surgical procedures was 1 (range, 0–5). Patients had fistula-related complaints for a median of 6 months (range, 0–240). Preoperative continence was impaired in three patients and varied from incontinence of flatus to soiling, determined by medical history on the initial visit to the outpatient clinic. At the time of surgery, 32 percent of the patients smoked. A postoperative complication was encountered in 2 patients: minor bleeding (n=1) and urinary tract infection (n=1). The 3-year recurrence rate was 7 percent (n=8, 95 percent CI, 1–13 percent, Fig. 2) The data on the continence questionnaires completed by 63 patients are presented in Table 2. The median follow-up duration of patients with completed questionnaires was 74 months (range, 7–134). The mean total Vaizey score was 6.5 (SD, 3.5) and 18 of 63 (29 percent) had perfect continence (Vaizey score=0). The mean total score for the COREFO questionnaire was 9.8 (SD, 12.4). The mean incontinence scale was 9.2 (SD, 12.8). Soiling was reported in 26 of 63 patients (41 percent). Only three patients reported having lost solid stool unintentionally. None of the potential risk factors for fistula recurrence reached statistical significance in the univariate or in the multivariate analysis (Table 3). In male patients that smoked and were referred to a tertiary center, the estimated risk for fistula recurrence was more than doubled, but the associated confidence intervals were wide.

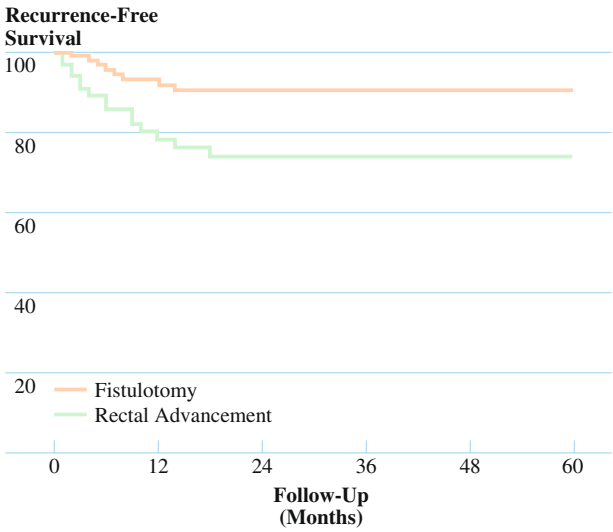

FIGURE 2. Fistula recurrence-free survival after fistulotomy (n=109 patients) and rectal advancement flap (n=70).

Rectal Advancement Flap Group

The median age at the time of surgery was 42 years (range, 21–67). Forty-seven patients were male (67 percent). Twenty-nine patients (41 percent) had undergone prior fistula surgery (Table 1). Twenty-seven patients (39 percent) were referred from other hospitals because of complex and/or recurrent fistulas. The median number of previous surgical procedures was 2 (range, 0–8). Patients had fistula-related complaints for a median of 12 months (range, 1−144). Preoperative continence was disturbed in seven patients. Four of these patients were incontinent for flatus and the three others had soiling. At the time of surgery, 43 percent of patients smoked. Before performing the rectal advancement flap procedure, 37 patients (39 percent) were treated by seton drainage. In 16 patients, fibrin glue was added to the procedure. In two patients a postoperative complication was encountered: minor bleeding (n=1) and bradycardia for which the patient was observed overnight (n=1, patient with cardiac history). The recurrence rate for fistulas treated by rectal advancement flap was 21 percent (n=15, 95 percent CI, 9–33 percent, Fig. 2). The outcome of patients with seton drainage did not significantly differ from the patients without. In the patients that underwent seton drainage, the recurrence rate (24 percent) was similar to patients without seton drainage (18 percent, $P=0.53$). In the group of patients that underwent rectal advancement flap combined with fibrin glue, the fistula recurrence rate was 31 percent similar to the advancement only group at 17 percent ($P=0.31$). A median of 2 operations was necessary in these patients to close the persistent fistulas (range, 2–4). In 37 of 39 successfully contacted patients, the continence questionnaires were completed (Table 2). The median follow-up duration of patients with completed questionnaires was 64 months (range, 22–126). The mean total Vaizey score was 6.2 (SD, 4.0). Of 37 patients, 2 (5 percent) had a perfect continence (Vaizey score=0). The mean total score for the COREFO questionnaire was 10.8 (SD, 11.2). The mean incontinence scale was 11.8 (SD, 13.6). Sixteen of 37 (43 percent) patients reported soiling. Only two patients reported problems with losing solid stool unintentionally. In the rectal advancement flap treatment group, none of the potential risk factors reached statistical significance, neither in the univariate nor in the multivariate analysis (Table 4).

DISCUSSION

This retrospective study assessed the long-term results of surgical treatment of a large consecutive series of patients with low or high perianal fistulas of cryptoglandular origin treated according to a standardized treatment protocol. In the present series of patients treated by fistulotomy or rectal advancement flap, the observed recurrence rate was 7 and 21 percent respectively at a median follow-up of 76 months. The overall functional outcome measured by the COREFO and the Vaizey scale was not significantly different from normal patients.[5] However, around 40 percent of the patients in both groups were found to have problems with soiling, which is considerable. No significant risk factors for the development of a recurrent perianal fistula were found in either the fistulotomy or the rectal advancement flap treatment group with either univariate or multivariate analysis.

Table 2. Vaizey scale and colorectal functional outcome (COREFO) for patients treated by fistulotomy or rectal advancement flap

Scale, mean (SD)	*Patients without complaints**	*Fistulotomy (n=63)†*	*Rectal advancement flap (n=37)‡*
Vaizey§			
Incontinence	1.9 (3.4)	2.0 (2.5)	2.3 (2.8)
Social impact	9.5 (3.5)	4,5 (1.7)	3.9 (2.5)
Total	5.6 (2.8)	6.5 (3.5)	6.2 (4.0)
COREFO¶			
Incontinence range	5.6 (7.5)	9.2 (12.8)	11.8 (13.6)
Social impact	9.2 (11.0)	9.7 (13.9)	12.3 (12.3)
Frequency	6.2 (8.8)	7.7 (12.9)	6.4 (6.4)
Stool-related aspects	7.7 (12.9)	14.4 (19.9)	12.6 (12.6)
Medication	6.1 (15.6)	8.2 (18.0)	5.9 (14.9)
Total	7.2 (7.0)	9.8 (12.4)	10.8 (11.2)

* Group of control patients after right-sided hemicolectomy or laparoscopic cholecystectomy[5] • †Low perianal fistulas (amount returned questionnaires), ‡High perianal fistulas (amount returned questionnaires). §Mean score ranging from 0–24 (complete continence-complete incontinence) for the total score. Both subscale scores range from 0–12. • ¶Mean score per category after linear transformation to a score from 0–100, higher score represents an increased level of continence disturbance. As the total score, all subscales range from 0–100.

Table 3. Fistulotomy group: possible risk factors for fistula recurrence

	Simple model HR (95% CI)	*P-value*	*Multivariate HR (95% CI)*	*P-value*
Male sex	3.74 (0.46–30.47)	0.22	3.83 (0.46–32.21)	0.22
Age (per 10 years increase)	0.73 (0.33–1.58)	0.42	0.83 (0.39–0.18)	0.61
Tertiary referral	3.85 (0.92–16.12)	0.07	2.81 (0.51–15.35)	0.23
Prior fistula surgery	1.54 (0.37–6.44)	0.55	1.40 (0.32–6.18)	0.66
Smoking	2.20 (0.53–9.21)	0.28	1.67 (0.31–9.15)	0.55

HR = Hazard Ratio • CI = Confidence Interval

The recurrence rate found in the present study conforms with recurrence rates reported in the literature, which range from 0 to 39 percent.[9,10] This wide range is a result of the heterogeneous population selected for fistulotomy in the different studies, which makes it difficult to compare the different outcomes. In a recent series from Van de Hagen *et al.*, 62 patients with a fistula tract originating from the lower third of the anal sphincter were treated by simple fistulotomy. At a median follow-up of 75 months, a cumulative recurrence of 39 percent was found. In the series, patients with Crohn's disease also were included. These nine patients with Crohn's disease had a cumulative recurrence rate of 60 percent at a follow-up of 48 months.[10] Patients with perianal fistulas caused by Crohn's disease should therefore be assessed separately because of the origins of the disease and because outcome depends on the presence of proctitis.[11]

The recurrence rate found in the present study for the rectal advancement flap is relatively favorable to the literature, in which success rates are reported between 40 and 90 percent.[12–14] These results account for a select patient group where patients with HIV, Crohn's disease, and inability to find the internal opening were excluded. These recurrence rates however remain relatively high. In our study, 1 in 5 patients needed multiple operations to successfully treat high fistulas. In this series of patients treated with fibrin glue in addition to the rectal advancement flap, no significant differences in procedure success rate were observed. However, several other authors found the addition to be deleterious for the closure of the fistula in combination with the advancement flap.[15,16]

Unfortunately, from a substantial number of patients, no questionnaires were received. To maximize the response rate all patients that failed to return the questionnaires were contacted by telephone. Furthermore, if the patients had moved, their general practitioner was contacted for their address and telephone number. This effort resulted in only five patients that refused to respond by telephone. Since our response rate was only 53 percent and no detailed preoperative data on continence was available, there is a potential error in the outcome and conclusions drawn.

Disruption of the sphincter complex leads to incontinence.[17] The COREFO questionnaire and Vaizey scale were used in this study for the continence assessment. In both groups, overall continence outcomes were not significantly different from normal. The scores found were comparable to the scores reported by Bakx *et al.* for a group of control patients without complaints after right-sided hemicolectomy or laparoscopic cholecystectomy.[5] In the subscales, stool aspects and incontinence, our sample had slightly worse scores than in the control group.[5] The subscale, stool aspects, contains questions on blood loss during bowel movement and having irritated perianal skin. Around 25 percent of the patients who received fistulotomy or rectal advancement flap reported problems in stool aspects. The subscale, incontinence, implies patients having problems ranging from having to use pads to protect underwear to unintentionally passing stools. When looking in detail at soiling, a considerable amount of patients had problems postsurgery. This finding was surprising given the rectal advancement flap is considered a sphincter-saving procedure. These data indicate that soiling is a considerable problem after

Table 4. Rectal advancement flap group: possible risk factors for fistula recurrence

	Simple model HR (95% CI)	*P-value*	*Multivariate HR (95% CI)*	*P-value*
Male sex	1.16 (0.40–3.39)	0.79	1.35 (0.44–4.12)	0.60
Age (per 10 years increase)	0.70 (0.39–1.28)	0.25	0.67 (0.35–1.27)	0.16
Tertiary referral	1.66 (0.60–4.58)	0.33	1.60 (0.50–5.11)	0.39
Prior fistula surgery	1.16 (0.41–3.28)	0.77	1.38 (0.38–5.03)	0.87
Smoking	1.52 (0.54–4.26)	0.43	1.15 (0.39–3.44)	0.69
Seton drainage	1.54 (0.53–4.51)	0.43	1.58 (0.52–4.78)	0.42
Fibrin glue	1.55 (0.55–4.36)	0.41	1.35 (0.42–4.31)	0.61

HR = Hazard Ratio • CI = Confidence Interval

surgery for fistula, although it is not clear whether the soiling problem was solely the result of surgery since no preoperative data on soiling were available for comparison. Furthermore, the number of prior surgical procedures was high in the rectal advancement flap treatment group.

The question arises as to what extent this relatively young population will develop continence problems in the future. In the literature, many different criteria are used to report incontinence and as a consequence the continence outcome varies substantially between different publications.[18,19] Further prospective research is needed to assess long-term outcome of continence after different treatments for perianal fistulas using validated questionnaires before and after surgery.

In the risk factor analysis, tertiary referral in the fistulotomy group showed a trend toward significance ($P=0.065$) and displayed a clinically significant absolute effect size (HR=3.74). However, the confidence interval is large, possibly because of a small sample size, which limits the interpretation of these results. An explanation for this large effect size seen for tertiary referral may be that most patients requiring simple fistulotomy are not referred to tertiary centers. Possibly these patients had complex fistula which were expected by their physician to lead to recurrence. Unfortunately, as a result of the retrospective nature of this study, further data were not available.

Garcia-Aguilar *et al.* described risk factors for recurrence in a series of patients with anorectal fistulas of cryptoglandular origin with the use of a mailed questionnaire. Prior fistula surgery was not found to be significantly associated with recurrence, however a clear trend was described.[20] In a retrospective study of 106 advancement flap procedures by Mizrahi *et al.*, prior attempts at fistula repair were not associated with recurrence. However, Crohn's disease appeared to be correlated to fistula recurrence.[21]

Smoking is well known to influence wound healing in various patient groups.[22,23] In the literature, smoking was assessed as a possible risk factor and discrepancies exist as to whether smoking has an effect on the outcome of surgical treatment for anorectal fistulas. Zimmermann *et al.* described smoking to be associated with a high risk for fistula recurrence in 105 patients with perianal fistulas of cryptoglandular origin treated with a rectal advancement flap. A reduced blood flow in the flap was noted as a possible contributing factor.[24] Recently, Gustafsson *et al.* did not find any relationship between smoking and a lower healing rate in their randomized trial of 83 patients surgically treated by rectal advancement flap for high anorectal fistulas.[25] In the present study, no significant relationship could be found between smoking and fistula recurrence as well.

CONCLUSION

This study assessed long-term outcome of two distinctive groups of patients with perianal fistulas of cryptoglandular origin. The recurrence rate was low in the group treated by fistulotomy. In patients treated with rectal advancement flap procedure for high perianal fistulas, a considerable number of recurrences occurred. No clear risk factors for the development of a recurrent perianal fistula were found in the fistulotomy nor in the rectal advancement flap treatment group. Overall, continence disturbances were infrequent and similar in both groups. However, a reasonable number of patients in both groups reported soiling. Further research is warranted to develop new techniques to deal with high perianal fistulas of cryptoglandular origin and to solve the probable high incidence of soiling.

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