Surgical treatment of perianal and rectal fistula
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Chapter 3

Outcomes of surgical treatment for perianal fistulas in Crohn’s disease

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ABSTRACT

Background
The aim of this study was to assess recurrence rates and long term functional outcome after surgical treatment of anal fistulas in Crohn’s disease.

Methods
Between 1995 and 2006, a consecutive series of patients were treated for perianal fistulas as a result of Crohn’s disease. Only patients without proctitis or active sepsis underwent fistulotomy or advancement. The following risk factors for recurrence were examined: gender, seton usage, use of infliximab, prior fistula surgery, history of segmental resection, and smoking. Continence was assessed by Vaizey and COREFO (colorectal functional outcome) questionnaires. Results were compared with institutional data for cryptoglandular fistulas.

Results
Sixty-one patients were included. Follow-up duration was 79 months (range 13-140). Patients were treated with a seton (n=24), fistulotomy (n=28) or mucosal advancement (n=9). For low fistulas the fistulotomy was used more frequently compared to the seton. This was the other way around in higher more complex fistulas where seton drainage was used in the majority of the cases. Recurrence occurred following fistulotomy and advancement in 5/28 and 5/9 respectively. Half of the patients treated by seton reported soiling compared to two thirds and three quarters of those treated by fistulotomy and mucosal advancement respectively. Functional outcomes were worse for all patient groups compared to patients with simple cryptoglandular fistula disease. No potential risk factor reached significance in the regression analysis.

Conclusions
The outcome of surgical treatment of complex and high fistulas in Crohn’s disease remains disappointing and recurrence is unpredictable.
INTRODUCTION

Crohn’s disease is complicated by the development of anal fistulas in approximately one third of patients.\textsuperscript{1,2} The goal of fistula surgery for patients with Crohn’s disease is to relieve symptoms and to achieve closure in selected cases.\textsuperscript{3} Surgical treatment for fistulas in Crohn’s disease consists of abscess drainage, loose-setons, fistulotomy, and mucosal advancement.\textsuperscript{4-6} The success rate after fistulotomy is around 80\% compared to a success rate of about 55\% for high fistulas treated by advancement flap.\textsuperscript{7,8} These fistulas are often refractory to surgery and associated with recurrent sepsis, discomfort, and impaired quality of life.\textsuperscript{9} In most papers no distinction is made between cryptoglandular fistulas and fistulas in Crohn’s disease confusing true outcome data for surgically treated Crohn’s fistula. Furthermore, continence is rarely assessed using validated questionnaires. The aim of this study was to assess the recurrence rates and long term functional outcome after surgical treatment of anal fistulas in Crohn’s disease.

METHODS

Patients

Between May 1995 and January 2006, a consecutive series of patients operated for anal fistulas in Crohn’s disease were retrospectively analyzed. Patients with cryptoglandular fistulas, human immunodeficiency virus, pouch fistulas, rectovaginal fistulas, as well as patients aged under 18 were excluded.

Treatment protocol

Patients were primarily treated by surgical drainage through incision and drainage of abscesses and seton drainage in case of insufficiently drained fistulas. Subsequently, optimization by medical therapy was pursued. Only in selected patients without proctitis or active Crohn’s disease definitive closure by surgical intervention was attempted. For the definitive surgical treatment these patients were divided into two groups. The first group comprised of patients in which the fistula tract was submucosal, intersphincteric or located in the lower third of the anal sphincter.
This group was treated by fistulotomy. The second group treated by advancement flap consisted of patients with high fistulas in which the fistula tract was located in the upper two-third of the sphincter complex. The advancement flap was done according to a technique described herein. All procedures were performed under general or locoregional anesthesia in the lithotomy position.

**Follow-up**

All patients visited the outpatient’s clinics following surgery. The fistula was considered closed if the external opening was closed and no discharge or pain were experienced. Patients were contacted by telephone using a standard questionnaire to assess fistula recurrence, abscess development, and use of infliximab. Furthermore, patients, including the patients with loose setons, were sent a postal survey to assess functional outcome. Functional outcome was evaluated using the Vaizey scale and the COREFO questionnaire. The validated Vaizey scale consists of items on the type and frequency of incontinence and change in lifestyle. The total score on the Vaizey scale ranges from zero (complete continence) to 24 (complete incontinence). The COREFO questionnaire is a validated questionnaire with 27 questions to assess colorectal functional outcome. Five categories and a calculated total score were assessed and these scores ranged from zero to 100. A higher score represents an increased level of continence disturbance. Follow-up was calculated from the clinical notes when the patient could not be contacted successfully by phone.

**Statistical analysis**

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 case of categorical data. Cox proportional hazard models were used to examine the association between potential risk factors and the time until fistula recurrence. The following risk factors were examined: gender, seton usage, use of infliximab, prior fistula surgery, history of segmental resection, and smoking. Statistical analysis was performed using the SPSS version 15.0.1 for Windows (SPSS, Chicago, Illinois, USA).
RESULTS

A total of 61 patients with anal fistulas were included. Anal fistulas due to HIV, ulcerative colitis, and rectovaginal and cryptoglandular fistulas were excluded (n=301 patients) (Figure 3.1). Patient characteristics are shown in Table 3.1. The median follow-up duration was 79 months (range 13-140).

Figure 3.1 – Flow chart of patients with anal fistula in Crohn’s disease.

**Surgical treatment**

Figure 3.1 demonstrates how patients were treated surgically. Twenty-four patients (39%) were treated with loose seton drainage. In 37 of the 61 patients definite closure was attempted. In the low fistula group six patients were treated by seton drainage before fistulotomy. In the group with the high fistulas three patients underwent
Table 3.1 – Characteristics of 61 patients low and high fistulas in Crohn’s disease.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Low fistulas (n=39)</th>
<th>High fistulas (n=22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M:F</td>
<td>24:15</td>
<td>9:13</td>
</tr>
<tr>
<td>Age (median in years)</td>
<td>33 (19-70)</td>
<td>36 (21-70)</td>
</tr>
<tr>
<td>Previous fistula surgery</td>
<td>11 (28%)</td>
<td>12 (55%)</td>
</tr>
<tr>
<td>Duration of Crohn’s disease (years)</td>
<td>7 (0-37)</td>
<td>8 (3-25)</td>
</tr>
<tr>
<td>Segmental resection*</td>
<td>17 (44%)</td>
<td>8 (36%)</td>
</tr>
<tr>
<td>Smoking</td>
<td>9 (23%)</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>Fibrin glue addition</td>
<td>-</td>
<td>16 (23%)</td>
</tr>
<tr>
<td>Recurrence</td>
<td>5/28 (18%)</td>
<td>5/9 (56%)</td>
</tr>
<tr>
<td>Follow-up (months, range)</td>
<td>79 (13-140)</td>
<td>82 (17-132)</td>
</tr>
</tbody>
</table>

*Patients that underwent segmental bowel resection prior to the fistula surgery.

Seton drainage before performing the advancement. Recurrence rates in patients that were treated by fistulotomy and advancement were 18% and 56% respectively. In all patients with a fecal diversion that were operated the ostomy was still present during the assessment of closure.

None of the potential risk factors reached significance in low or high fistulas. None of the factors were analyzed in the multivariate model as result of the low amount of patients in the subgroups. There were no postoperative complications in either group.

Follow-up

Fifty patients were contacted successfully (82%). The patients in the different groups are presented in Table 3.2. From the 11 patients that could not be contacted, two had deceased, four underwent a complete proctectomy, and the five remaining were lost to follow-up. In the group that was contacted four patients had undergone surgery for an anal abscess in the low anal fistulas group compared to four in the high group. Two patients in the group with high fistulas underwent a proctectomy because of recurrent anal fistulas and anal stenosis.

Functional outcome

The results of the continence questionnaires were presented in Table 2.2. There were no statistically significant differences between the seton drainage, fistulotomy, and the advancement group in either the COREFO (p=0.714) or the Vaizey score.
Surgical treatment of perianal fistulas in Crohn’s disease

Table 3.2 – Vaizey scale and colorectal functional outcome (COREFO) for patients treated by fistulotomy or rectal advancement.

<table>
<thead>
<tr>
<th>Scale, mean (SD)</th>
<th>Fistulotomy (crypto)*</th>
<th>Advancement Seton drainage (crypto)*</th>
<th>Fistulotomy (n=23)†</th>
<th>Advancement flap (n=8)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaizey§</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incontinence</td>
<td>2.0 (±2.5)</td>
<td>2.3 (±2.8)</td>
<td>3.8 (±3.5)</td>
<td>4.7 (±4.8)</td>
</tr>
<tr>
<td>Social impact</td>
<td>4.5 (±1.7)</td>
<td>3.9 (±2.5)</td>
<td>5.5 (±1.6)</td>
<td>4.9 (±1.4)</td>
</tr>
<tr>
<td>Total</td>
<td>6.5 (±3.5)</td>
<td>6.2 (±4.0)</td>
<td>7.4 (±2.5)</td>
<td>8.7 (±4.4)</td>
</tr>
<tr>
<td>COREFO¶</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incontinence range</td>
<td>9.2 (±12.8)</td>
<td>11.8 (±13.6)</td>
<td>25.9 (±7.5)</td>
<td>30.2 (±21.6)</td>
</tr>
<tr>
<td>Social impact</td>
<td>9.7 (±13.9)</td>
<td>12.3 (±12.3)</td>
<td>31.3 (±11.0)</td>
<td>24.5 (±21.1)</td>
</tr>
<tr>
<td>Frequency</td>
<td>7.7 (±12.9)</td>
<td>6.4 (±6.4)</td>
<td>16.7 (±8.8)</td>
<td>26.1 (±24.7)</td>
</tr>
<tr>
<td>Stool-related aspects</td>
<td>14.4 (±9.9)</td>
<td>12.6 (±12.6)</td>
<td>28.5 (±12.9)</td>
<td>16.7 (±15.4)</td>
</tr>
<tr>
<td>Medication</td>
<td>8.2 (±18.0)</td>
<td>5.9 (±14.9)</td>
<td>24.3 (±15.6)</td>
<td>15.2 (±21.2)</td>
</tr>
<tr>
<td>Total</td>
<td>9.8 (±12.4)</td>
<td>10.8 (±11.2)</td>
<td>27.2 (±7.0)</td>
<td>24.6 (±15.4)</td>
</tr>
</tbody>
</table>

*Perianal fistulas of cryptoglandular origin treated by fistulotomy and mucosal advancement flap in the same institution. †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.

(p=0.451). In the seton group 54% of the patients reported soiling compared to 61% and 75% in the fistulotomy and the mucosal advancement group respectively.

In Table 3.2 results from an institutional series of cryptoglandular fistulas were included. The recurrence rates in these series were 7% and 21% for cryptoglandular fistulas treated by fistulotomy and mucosal advancement flap respectively. Soiling was seen in 40% of the patients in both groups.

DISCUSSION

In the present series, surgically treated patients with anal fistulas in Crohn’s disease were described. Surgical treatment options were chronic seton drainage, fistulotomy, and advancement flaps. Attempted definitive closure by surgical intervention was only done in a selected group excluding those with active Crohn’s disease or proctitis.

In the group in which definitive closure was attempted, low and high fistulas were treated by fistulotomy and advancement flap respectively which resulted in 18% and 56% recurrence rates. There were no significant continence differences between the groups treated by loose seton drainage, fistulotomy and advancement flap.
Active Crohn’s disease, especially proctitis, interferes with wound healing and fistula closure. The aim of the treatment protocol was to limit the amount of inflicted surgical damage in terms of anal scarring, incontinence, and recurrent fistulas. Despite patient selection, patients in the current series treated surgically for Crohn’s anal fistula did worse both in terms of recurrence rates and incontinence compared to patients operated for cryptoglandular disease treated in our institute. The recurrence rates found for fistulotomy were worse compared to recurrence rates of cryptoglandular fistulas treated by fistulotomy (18% vs. 7%). The recurrence rates following advancement flap were also worse (56% vs. 21%). Possibly, as the flap is constructed with rectal mucosa affected by Crohn’s disease wound healing might be compromised. A recurrent Crohn’s anal fistula could be a true recurrence or a newly developed fistula. This could not be discriminated in the present study.

The continence results were significantly worse compared to data from a series of patients operated in the same hospital for cryptoglandular fistulas. In the different groups of the cryptoglandular fistulas the reported soiling was around 40%. In the present series between 54% and 75% of the patients reported soiling. Incontinence following fistula surgery in Crohn’s disease in literature ranges from low to very high. Often a mixed group of patients consisting of both cryptoglandular and Crohn’s disease fistulas were reported. It could only be speculated whether surgery has contributed to the incontinence, since preoperative data were lacking. Probably the incontinence has multiple causes. It could result from previous sphincter damage, scarring, diarrhea and impaired rectal reservoir function resulting from long standing proctitis.

Disappointing results in closure of anal fistulas in Crohn’s disease lead to much interest for novel techniques. Nowadays, infliximab has an important role in the treatment of anal fistula due to Crohn’s disease. It is effective in closing the fistula but the fistula often recurs after stopping the medication. Currently, the anal fistula plug has been used extensively in various studies. The anal fistula plug, a bioabsorbable xenograft made of porcine intestinal submucosa, is placed in the fistula tract. The plug is replaced by own tissue within several weeks. The anal fistula plug has been used in a series of 20 patients with Crohn’s disease leading to 80% closure. These results are not confirmed yet by other groups.

An interesting technology is the use of stem cells to treat fistulas in Crohn’s disease.
Mesenchymal adipose stem cells are harvested by liposuction and used to stimulate fistula closure. Garcia-Olmo et al. performed a randomized clinical trial comparing adipose derived stem cells and fibrin glue with only fibrin glue in the treatment of anal fistulas.\textsuperscript{21} Cryptoglandular (n=35) and Crohn’s disease (n=14) fistulas were included in the study. The stem cells were isolated by liposuction and after preparation of the material the cells were injected into the rectal mucosa. The fistula closed in 71\% in the stem cell group compared to 16\% in the fibrin glue group. Currently a multinational trial is being conducted in Europe assessing the value of stem cell therapy.\textsuperscript{21}

In conclusion, only in selected patients with Crohn’s disease treatment aiming for fistula closure was possible. The majority were treated with loose setons. Recurrence rates in patients with Crohn’s fistula were higher compared to similarly treated patients with cryptoglandular fistulas after fistulotomy and particularly advancement flaps respectively. Functional outcome in terms of continence was worse compared to cryptoglandular fistulas.

REFERENCES


