

Fibrin glue and transanal rectal advancement flap for high transsphincteric perianal fistulas; is there any advantage?

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Abstract

Backgrounds and aim In recent decades, fibrin glue has appeared as an alternative treatment for high perianal fistulas. Early results seemed promising, with high success rates being reported. However, with increasing follow-up, the enthusiasm was tempered because of disappointing results. The aim of this retrospective study was to assess the additional value of fibrin glue in combination with transanal advancement flap, compared to advancement flap alone, for the treatment of high transsphincteric fistulas of cryptoglandular origin.

Materials and methods Between January 1995 and January 2006, 127 patients were operated for high perianal fistulas with an advancement flap. After exclusion of patients with inflammatory bowel disease or HIV, 80 patients remained. A consecutive series of 26 patients had an advancement flap combined with obliteration of the fistula tract with fibrin glue. Patients were matched for prior fistula surgery, and the advancement was performed identically in all patients. In the fibrin glue group, glue was installed retrogradely in the fistula tract after the advancement was completed and the fistula tract had been curetted.

Results Minimal follow-up after surgery was 13 months [median of 67 months (range, 13–127)]. The overall recurrence rate was 26% ($n = 21$). Recurrence rates for advancement flap alone vs the combination with glue were 13% vs 56% ($p = 0.014$) in the group without previous

fistula surgery and 23% vs 41% ($p = 0.216$) in the group with previous fistula surgery.

Conclusion Obliterating the fistula tract with fibrin glue was associated with worse outcome after rectal advancement flap for high perianal fistulas.

Keywords Rectal fistula · Surgery · Recurrence · Fibrin glue · Advancement

Introduction

Perianal fistulas of cryptoglandular origin cause considerable discomfort and arise from infections in anal glands lying in the intersphincteric space [1]. To delineate the fistula tract, magnetic resonance imaging (MRI) and anal endosonography are nowadays readily available and are increasingly used for fistula imaging [2]. The essence of surgical treatment of perianal fistulas is to eradicate the fistula tract and at the same time preserve continence. Low fistulas, where the fistula tract is submucosal, intersphincteric or located in the lower third of the external anal sphincter can be treated by fistulotomy with low recurrence rates and relatively little impact on continence [3]. In patients with high perianal fistulas, the fistula tract is located in the upper two-thirds of the external sphincter. Fistulotomy performed on high fistulas results in loss of sphincter function in a considerable number of patients due to the interference of the external sphincter complex [4, 5]. There are various alternative surgical options for high fistulas, namely, rectal advancement, fibrin glue, and seton drainage.

In 2006, Johnson et al. [6] reported a new biologic anal fistula plug to treat high transsphincteric perianal fistulas. The anal fistula plug is biologic absorbable and consists of

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lyophilized porcine intestinal submucosa. In their series of 46 patients treated with the anal fistula plug, a success rate of 83% was achieved at a median follow-up of 12 months [7]. After this publication, several authors have reported their experience with the anal fistula plug, resulting in success rates ranging from 41–88% [8–10].

Currently, the transanal rectal advancement flap (AF) remains the “gold standard” in the treatment of high transsphincteric perianal fistulas of cryptoglandular origin. The rationale behind the AF is that the open internal opening is the cause of the persisting fistula tract. By advancing the tissue over the internal opening, it would be impossible for fecal material to be forced into the fistula tract during defecation. However, recurrence rates of the advancement flap found in literature vary considerably and extend up to 63% [11–15]. Roughly, one out of every four patients requires multiple surgical interventions to close the fistula tract successfully.

In recent decades, fibrin glue has appeared as an alternative treatment for high perianal fistulas. As a result of the obliteration of the fistula tract and the closure of the internal opening, the fistula might heal. Early results seemed promising, with high success rates being reported. However, with increasing follow-up, the enthusiasm was tempered because of disappointing results [16–20]. Recently, Zmora et al. [21] conducted a retrospective study including 37 patients with high perianal fistulas. In a subset of 13 patients with fistulas of various etiologies, the advancement flap was used in addition to the fibrin glue installation. The results showed a recurrence rate of 46%.

The aim of this study was to assess the additional value of fibrin glue to the transanal rectal advancement flap in a well-defined group of patients with high transsphincteric fistulas of cryptoglandular origin. Patients with previous fistula surgery are a surgically more challenging group as the result of scar tissue and sometimes anal stenosis. Therefore, patients were matched for the presence of a history of fistula surgery.

Materials and methods

Patient characteristics Between January 1995 and January 2006, a consecutive series of patients were treated by AF. Only patients with high transsphincteric perianal fistulas of cryptoglandular origin were analyzed. High perianal fistulas were defined as patients with fistulas running through the upper two thirds of the external sphincter complex, which is confined by the puborectal sling and the end of the anal canal. Patients in whom the internal fistula opening was not detectable and patients with perianal fistulas as a result of Crohn’s disease, HIV, and other causes were excluded.

Patients over 18 years of age were included. A consecutive series of patients were operated on with fibrin glue (Tissucol Duo®, Baxter International) in addition to the AF in an attempt to decrease the recurrence rate of the AF. This series of patients were treated on between February 2003 and January 2006. Patients were matched for previous surgery and divided into two groups; one group with previous fistula surgery and the other without. Preoperatively, no routine imaging was performed. Only in selected case when the fistula was complex and/or recurrent, MRI or anal endosonography was used to outline the fistula tract. In The Netherlands and Belgium, non-experimental clinical case series of patients treated with a CE-approved device do not require approval of the local Medical Ethics Commission. A subset of patients from this series were also included in a study where the aim was to assess the long-term functional outcome and identify risk factors for the development of recurrence in patients surgically treated for cryptoglandular fistulas [22].

Surgical technique On the day of surgery, an enema was administered to the patient to clean the proctum. All procedures were performed under general or locoregional anesthesia in the lithotomy position, and broad spectrum antibiotics were administered perioperatively. Subsequently, the internal opening was located by probing the external opening. During surgery, the amount of sphincter involved was judged by palpation of the puborectal sling and the inferior edge of the external sphincter complex. In cases where the internal opening was not found by probing, hydrogen peroxide was injected to locate the internal opening. In case of active sepsis, a seton was placed for a period of at least 3 months insuring adequate drainage. In the group that was operated with the AF, the internal opening was excised followed by mobilization of the mucosa, submucosa, and a small amount of muscular fibers from the internal sphincter complex. The rectal flap was mobilized to sufficiently cover the internal opening with overlap. Hemostasis was performed to prevent a hematoma under the flap. The base of the advancement flap was kept wide enough to ensure adequate circulation in the flap. The internal opening was not closed before advancing the flap over the internal opening. This was followed by suturing the flap in the distal anal canal with Vicryl 2/0 after the fistula tract had been curetted. In the AF + G group, the identical procedure was carried out. In addition to the advancement procedure, fibrin glue was installed retrogradely in the fistula tract after the AF was completed and the fistula tract had been curetted. Installation of the fibrin glue was performed via the external opening, under direct vision of the advancement flap to prevent flap dislocation and subsequent failure. No specific postoperative instructions were given to the patients.

Data collection Chart review was performed on age, gender, tertiary referral, previous fistula surgery, smoking habits, complications, and fistula recurrence. All patients visited the outpatient's clinics on a regular basis (every 2–4 weeks) until full 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, it was considered as a persistent or recurrent fistula. No routine postoperative imaging or proctoscopy was performed to confirm the closure of the fistula tract. The data was collected retrospectively and the outcome was compared between groups.

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-square test or Fisher's exact test were used when appropriate to compare groups in case of categorical or dichotomous variables. All reported *p* values are two-sided. A *p* value of 5% or less was considered as statistical significant. Statistical analysis was done using the SPSS v.12.0 package (SPSS, Chicago, IL, USA).

Results

In the study period, a total of 127 patients were operated for high perianal fistulas. Inflammatory bowel disease ($n = 30$), HIV ($n = 12$), or no internal opening found during surgery ($n = 5$) were the reason of exclusion in 47 patients. In total, 80 patients were analyzed in this comparative study. Of these, 54 patients were treated with the AF and 26 patients underwent AF combined with the installation of fibrin glue. Furthermore, patients were matched for a history of fistula surgery. Patient characteristics for both groups are shown in Tables 1 and 2. The groups were comparable for patients' characteristics as sex, age, smoking, seton drainage, and number of tertiary referrals.

Table 1 Characteristics of patients with high anorectal fistula without previous fistula surgery

Variable	AF ($n=32$) ^a	AF+G ($n=9$) ^b	<i>p</i> value
M/F (<i>n</i>)	18:14	6:3	0.711
Age (median, in years)	42 (21–67)	41 (29–55)	0.653
Tertiary referral	26 (81%)	7 (78%)	1.000
Smoking	43%	71%	0.232
Seton drainage	18 (56%)	6 (67%)	0.711

^a Rectal advancement group

^b Rectal advancement group with fibrin glue

Table 2 Characteristics of patients with high anorectal fistulas with previous fistula surgery

Variable	AF ($n=22$) ^a	AF+G ($n=17$) ^b	<i>p</i> value
M/F (<i>n</i>)	18:4	11:6	0.282
Age (median, in years)	43 (22–62)	47 (35–72)	0.136
Tertiary referral	15 (68%)	8 (47%)	0.209
Smoking	53%	50%	1.000
Seton drainage	10 (46%)	12 (71%)	0.193

^a Rectal advancement group

^b Rectal advancement group with fibrin glue

Clinical outcome All patients were operated in day case setting. There were no intraoperative complications. In two patients out of the AF group, a postoperative complication was encountered, consisting of a minor bleeding ($n = 1$) and a bradycardia for which the patient was observed overnight ($n = 1$, patient with cardiac history). In the AF + G group, there were no postoperative complications recorded. The minimal follow-up after surgery was 13 months with a median of 67 months (range, 13–127). There were no patients lost to follow-up. The overall recurrence rate was 26% ($n = 21$; Table 3.). In 17% of the patients, the fistula persisted in the AF group compared to 46% in the AF + G group ($p = 0.05$). In the matched group without previous fistula surgery, the result was significantly worse for the AF + G group compare to the AF group ($p = 0.014$). The recurrence rates were 56% ($n = 5$) and 13% ($n = 4$), respectively. In the group with a history of fistula surgery, the recurrence rate was 23% ($n = 5$) compared to 41% ($n = 7$) in the AF and the AF + G group, respectively ($p = 0.216$).

Discussion

High perianal fistulas remain a surgical challenge. There are various treatment options for treating high transsphincteric fistulas, e.g., the rectal and anodermal advancement flap, loose and cutting seton, fibrin glue, and potentially the newly developed anal fistula plug [3]. However, the results from these therapies vary. Transanal rectal advancement

Table 3 Recurrence rates for the matched group analysis

Group	AF ^a	AF+G ^b	<i>p</i> value
Overall ($n=80$)	9/54 (17%)	12/26 (46%)	0.050
No previous fistula surgery ($n=41$)	4/32 (13%)	5/9 (56%)	0.014
Previous fistula surgery ($n=39$)	5/22 (23%)	7/17 (41%)	0.216

^a Rectal advancement group

^b Rectal advancement group with fibrin glue

flap is nowadays the treatment of choice because of its sphincter-saving approach. Due to the low recurrence rate of only 30%, which leaves a lot of room for improvement [11, 14], fibrin glue has been widely studied. Fibrin glue was developed to obliterate the fistula tract by stimulating fibroblasts, which leads to permanent closure of the fistula tract. Unfortunately, the long-term results were not as good as expected [19, 20]. In the present series, an attempt was made to decrease the recurrence rate of the surgical treatment of high transsphincteric perianal fistulas of cryptoglandular origin by combining the two methods, i.e., fibrin glue and the rectal advancement flap in a consecutive series of patients. Overall, although not significant, a clear trend was found consisting of a worse outcome for patients from the AF + G group. The recurrence rate was 46% compared to 17% in the AF + G and AF group, respectively. In the group without a history of fistula surgery, patients in the AF + G group did significantly worse than the AF group. In the group with a history of fistula surgery, no significantly different recurrence rates were found.

In 2003, Zmora et al. [21] described a small retrospective series of 13 patients with perianal fistulas of different origins treated with fibrin glue in combination with the AF [14]. In their series, a recurrence rate of 46% was found after a mean follow-up of 12.1 months. The group contained patients with fistulas of cryptoglandular origin and fistulas associated with Crohn's disease or surgical trauma. In addition, two patients with rectovaginal fistulas were included. More recently, Ellis and Clark [23] reported on a series of 58 patients randomized into advancement flap repair alone or advancement flap repair combined with fibrin glue. Selected were patients with perianal fistulas where the fistula tract comprised more than 30 to 50% of the sphincter complex. Furthermore, patients were included when the fistula was located anteriorly in women or when the patient had a history of incontinence. In two thirds of the patients, the mucosal advancement flap was used and the remaining patients were treated by anodermal advancement flap. The recurrence rate was significantly higher in the group where fibrin glue was combined with the advancement flap compared to the group treated only by advancement (46% vs 20%). Two techniques, i.e., mucosal advancement flap and anodermal advancement flap, were used. Furthermore, no information was provided on the distribution of causes of the fistulas in both groups making the results difficult to interpret.

The effectiveness of the AF is the result of the closure of the internal opening [24]. The reason why addition of fibrin glue fails to decrease the recurrence rate and even seems to worsen the result is still unclear. After AF, the fistula tract acts as a drainage canal for any remaining sepsis, with the external opening left open. With the installation of the fibrin glue, a temporary closure of the fistula tract is theoretically

achieved. After a few weeks, when the clot resolves, the fibroblasts activated by the matrix should provide collagen syntheses for a definitive closure of the tract [25]. A possible explanation to why the AF + G group does worse is that the closure of the fistula tract with the fibrin glue leads to a situation where insufficient drainage from the primary and eventual secondary fistula tracts occurs.

Sentovich reported on a prospective series of 48 patients (75% of cryptoglandular origin) treated with fibrin glue [20]. In their technique of using the fibrin glue, the procedure was combined with closure of the internal opening with only a figure eight suture without an advancement flap. After a median follow-up of 22 months, a recurrence rate of 31% was found. Surprisingly, the patients with longer fistula tracts did significantly worse than those with short fistula tracts. Loungnarath et al. [26] reported on 39 patients with perianal fistulas treated with fibrin glue. The overall recurrence rate was 69%. In 6 of the 39 patients, the internal opening was closed using a figure eight suture to avoid clot extrusion because of high pressure from the anal canal during defecation. Four of these patients had a recurrence (33%).

This retrospective study, in contrast to earlier studies [21, 23], assessed the additional value of fibrin glue to the transanal rectal advancement flap of only patients with high transsphincteric fistulas of cryptoglandular origin with a long follow-up. The rectal advancement flap combined with fibrin glue installation was associated with a significantly higher recurrence rate, compared to the advancement flap treatment alone, in patients without previous fistula surgery. This observation must be interpreted carefully because of the small sample size of the AF + G group. As the costs of the fibrin glue are considerable and the therapeutic effect very doubtful, it cannot be recommended routinely in the adjunct of transanal rectal advancement flap treating high perianal fistulas. The rectal advancement flap remains the treatment of choice for high transsphincteric perianal fistulas of cryptoglandular origin until novel methods like the anal fistula plug are studied sufficiently in randomized trials.

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