



## Current State of Anal Fistula Surgery Worldwide and in Germany

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### Abstract

Surgery for anal fistulas and abscesses is as old as humankind. Procedures were performed more than 2000 years ago, described in ancient manuscripts. In modern times, anal fistulas remain a significant issue for colorectal surgeons. Only surgery can heal the patient. A septic process starts within an anal cryptogland, forming an abscess in the acute phase and a fistula in the chronic phase. Patients with recurrent abscesses will only have relief when the underlying fistula has been dealt with. Most fistulas are superficial: fistulotomy results in a low recurrence rate with only minor problems concerning fecal continence. Complex fistulas are those in which fistulotomy produces fecal incontinence. Therefore, sphincter-saving procedures have been developed. These techniques are described, and the pros and cons are discussed. In German guidelines, rectal advancement flap and fistulectomy with primary anal sphincter repair have found their place. In the last 30 years, many new techniques have been developed; some are still being used, while others have been abandoned. Surgery for anal fistula is demanding: recurrence and fecal incontinence rates should be low. On the other hand, the more recurrences a patient has, the higher the chance of a new recurrence and the higher the chance of fecal incontinence. Every new septic process in the anal region may worsen anal and pelvic floor function. The colorectal surgeon dealing with a complex anal fistula should have more than one option to offer and discuss with the patient.

**Keywords:** Anal fistula, Fistulotomy, Rectal advancement flap, Anal fistula plug, Ligature of the intersphincteric tract

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### Introduction

Surgery for anal fistulas is as old as humankind, with ancient Persian manuscripts describing certain anorectal operations (1). Nowadays, fistula surgery remains a hot topic for surgeons and patients as well. Because patients fear adverse effects of the surgery (fecal incontinence), sphincter-saving techniques have been developed, mostly in the past

30 years. Most anal fistulas are superficial, referred to previously as “low anal fistulas,” because fistulotomy would not lead to complete fecal incontinence. For a “high” anal fistula, several techniques have been developed. In this review, only cryptoglandular fistulas are dealt with—fistulas of other origins, especially Crohn’s disease, are not considered.

Recurrences and fecal incontinence are the big issues concerning surgeons and patients. The

papers by Lunniss et al.(2) and van Koperen et al. (3) suggest that the epithelium at the bottom of the fistula tract might play a role in recurrences. If part of the epithelial fistula tract is left in the wound, this might be the origin of the next recurrence. Another factor in recurrent anal fistulas might be epithelial-mesenchymal transition (EMT) (4). Inflammatory factors (cytokines interleukin [IL]-1 beta and IL-8) might also be involved in the etiology of anal fistulas and their recurrence after surgery.

## Selection of the Technique

### History

The surgeon should take the medical and surgical history of the patient. Previous surgeries are important. Concomitant diseases (especially IBD), vaginal births, and medications should be asked. A continence score should be filled in. Concerning the continence score, it should be considered that some patients perceive secretions out of the fistula as fecal incontinence, which might be why some patients achieve a better score after fistulotomy. Ideally, a quality of life questionnaire should be filled in. For studies, it is vital to consider the Anal Fistula Core Outcome Set (AFCOS, 5)

### Examination

At best, the operating surgeon should examine the patient before surgery. The examining finger of an experienced surgeon is better than manometry. Endoanal ultrasound (EUS), if available, should be performed. An MRI might be useful in certain cases (multiple previous operations with recurrence, IBD, etc.). The information gathered with the patient's history and examination will guide the surgeon and patient to the different options for surgery.

### Examination Under Anesthesia (EUA)

The preoperative examination findings should be confirmed by EUA, specifically identifying the inner and outer fistula openings. If in doubt, toluidine blue solution and EUS are further options.

Most methods described in the following section should not be used for an acute abscess. Only superficial fistulas found after drainage of an abscess might be simultaneously dealt with by fistulotomy. All other fistulas found when draining an abscess should be dealt with a loose seton.

### Fistulotomy/fistulectomy

- a. Preparation: enema to have a clean rectum.
- b. Antibiotic prophylaxis: only in selected (immunosuppressed) patients.
- c. Steps: A probe is inserted into the fistula tract. If it shows a superficial fistula, the overlying tissue (with only minimal sphincter tissue) is divided and laid open. Out of this split wound, a shallow ditch should be made by excising the edges that exist after splitting the fistula. This prevents adhesions between

the wound edges. If a fistulectomy is performed, the epithelial bottom of the divided fistula tract is also excised. In doing a fistulotomy, this remains in the wound.

d. Achilles' heel: If too much EAS is divided and sphincter repair is not done, there is a risk of incontinence.

e. Postoperative regime: Healing is by secondary intention. Wound healing after fistulectomy might be longer compared to fistulotomy (5).

f. Recurrence: In papers with at least 100 patients with anal fistula, recurrence rates vary from zero up to 24% (6, 7). In a recent systematic review, the weighted average healing rate by fistulotomy was 93.7% (8).

g. Fecal continence: In the above-mentioned papers with at least 100 patients with anal fistulas, up to 36% had at least minor problems with continence. In the above-mentioned systematic review, "continence impairment was reported in 12.7% of patients." (8)

h. Quality of life: A Spanish paper (9) reported on 49 patients who underwent a fistulotomy declared "a median length of 41% of the external anal sphincter and 32% of the internal anal sphincter was divided during fistulotomy. Significant differences in mild symptoms of anal continence were found with increasing length of external anal sphincter division." However, "there was no significant deterioration in continence, soiling, or quality of life scores at the 1-year follow-up".

i. Remarks: The technique of the cutting seton, which is actually a "slow motion" fistulotomy, is not recommended because of the protracted pain for the patient caused by the elastic band or the necessity of putting the seton under tension repeatedly.

j. Ideal indication: Superficial fistulas, in which less than one-third of the EAS is divided.

k. German guideline (10): Fistulotomy/fistulectomy is a good option for superficial fistulas.

l. In Germany, fistulotomy and fistulectomy are usual options for treating superficial anal fistulas.

### Rectal Advancement Flap (RAF)

a. Preparation: Enema to achieve a clean rectum or oral bowel preparation identical to a prep for colonoscopy. In some patients with multiple previous operations, a stoma to divert bowel movement might be considered.

b. Antibiotic prophylaxis: Single-shot, broad-spectrum antibiotics are given at the start of the operation.

c. Steps: Circular excision of the outer fistula opening and dissecting/excising the fistula tract conically up to the external anal sphincter (EAS), followed by excision of the inner fistula opening and excision of the intrasphincteric part of the fistula tract. Next, the excision trapezoidal flap out of the rectum is developed proximal to the inner fistula opening. The flap may consist of mucosa and submucosa only; many surgeons also dissect part of the rectal wall.

The flap should be dissected proximally so far that the (elastic) flap can cover the inner opening without any tension. The inner fistula opening, a defect in the anal sphincter after excision of the fistula tract, is closed with adapting, not-tight sutures. Then, the flap is advanced and sutured distally to these sphincter muscle sutures. The wounds lateral to the flap are also closed. A tampon might be inserted to prevent hematoma formation underneath the flap. The outer wound is left open for secondary healing, though some surgeons close this wound.

d. Achilles' heel: Side tracts might be overlooked and therefore not excised. There is no test to check whether all fistula tissues have been excised.

e. Postoperative scheme: With normal wound care, the wound should heal by secondary intention. Feeding after the operation varies considerably (normal feeding up to complete resorbable feeding).

f. Recurrence: Soltani and Kaiser (11) reported in a review of 35 studies of limited quality on cryptoglandular and Crohn's fistulas that the "weighted success rate was 80.8% for cryptoglandular fistulas". A recent review (12) reported 70-80% healing rates for RAF; it was not lower compared with "minimally invasive surgery" (MIS; e.g., plug or laser). In the report by Chaveli Diaz et al., the recurrence rate after 10 years of follow-up was 23.8%, most occurring in the first year after surgery (13).

g. Fecal continence: The weighted incontinence rate has been reported at 13.2% for cryptoglandular fistulas (11). In the above-mentioned review by Garcia-Olmo et al. (12), continence was worse compared with MIS. In a recent study by Kumar et al. comparing ligation of the intersphincteric tract (LIFT) with RAF, after two years, there were no patients with incontinence in either group (14). In the above-mentioned study by Chaveli Diaz et al., continence "showed a mild deterioration over time" (13).

h. Quality of life (QoL): The study by Garcia-Olmo et al. mentions two studies that showed no differences in QoL pre- and post-operatively after surgery for anal fistula (12). Bondi et al. found in their randomized trial (comparing plug versus RAF) no differences in QoL after six months (15).

i. Remarks: Smoking might have a negative influence on the recurrence rate. Zimmerman et al. (16) reported a 60% healing rate for patients who smoked and 79% healing for non-smokers. This finding was confirmed by Ellis et al. (17). However, in a report by Mei et al. (18), there was no significant association between recurrence and smoking.

j. Ideal indication: High, complex fistulas without side tracts and previous surgery.

k. German guideline (10): RAF is a well-established option for high anal fistulas.

l. In Germany, RAF is a procedure to treat anal fistulas, especially in departments specialized in anorectal surgery.

### *Fistulectomy and Primary Anal Sphincter Repair (FPR)*

a. Preparation: Enema to have a clean rectum or oral bowel preparation identical to a prep for colonoscopy. In some patients with multiple previous operations, a stoma to divert bowel movement might be an option.

b. Antibiotic prophylaxis: Single-shot broad-spectrum antibiotics are given at the start of the operation.

c. Steps: Over the probe that is inserted into the anal fistula, the overlying tissue (with sphincter) is completely divided. After this fistulotomy, the fistulous tissue (septic, inflammable, scar-prone) and side tracts should be excised completely. After excising the fistula, the divided sphincter parts should be adapted as in anal sphincter repair. Mucosa and anoderm should also be adapted. The outer, perianal part of the wound is left open to heal by secondary intention.

d. Achilles' heel: The sphincter repair should heal without dehiscence of the sutures. If dehiscence shows up, this might be deleterious for continence.

e. Postoperative scheme: With normal wound care, the wound should heal by secondary intention. Feeding after the operation varies considerably (normal feeding up to complete resorbable feeding).

f. Recurrence: In the German guideline (10), recurrence rates of up to 10% are described. In the paper by Sørensen et al. (19), FPR was compared with video-assisted anal fistula therapy (VAAFT). The study was terminated because recurrence rates were high in both groups (27% in the FPR group). In the study by Farag et al. (20), the recurrence rate after one year was 9.1%. In a review by Ratto et al. (21), the overall success rate was 93.2%.

g. Fecal continence: In the German guideline (10), the incontinence rate is reported as up to 21%. In the paper by Sørensen et al. (19), FPR was compared with VAAFT. There was an improvement in continence in both groups. In the study by Farag et al. (20), the incontinence rate after one year was 2.28%. In the review by Ratto et al. (21) on FPR, the overall postoperative worsening continence rate was 12.4% (mainly post-defecation soiling).

h. Quality of life: In the review by Ratto et al. (21), the quality of life, when evaluated, improved significantly. An improvement in QoL was also reported by Sørensen et al. (19).

i. Remarks: The advantage of FPR is the opportunity of excising all visible fistulous tissues. If left, this could be the source of recurrence. FPR might prevent the development of a keyhole deformity (22).

j. Ideal indication: High, complex fistulas with multiple side tracts.

k. German guideline (10): FPR is a well-established option for high anal fistulas with a success rate of up to 90%. Variable incontinence rates have been reported; this should be discussed with the patient.

l. In Germany, FPR has become a procedure to



treat anal fistula in the last 10-15 years, especially in departments specialized in anorectal surgery.

### *Fistula Plug*

a. Preparation: Mechanical bowel preparation or enema to have a clean rectum or oral bowel preparation identical to a prep for colonoscopy.

b. Antibiotic prophylaxis: 2 g of metronidazole in the evening before surgery; broad-spectrum antibiotics on induction of anesthesia.

c. Steps: After identifying the primary opening with a conventional probe, all fistula tracts are cleaned with hydrogen peroxide and brushed/curetted. After rehydrating the plug, a suture is put through the tip of the plug. After pulling this suture into the fistula tract via the internal opening, the plug is pulled tip-first through until the plug is wedged snugly. Excess material is excised, and the plug is secured by a figure-of-eight-suture to the internal anal sphincter (IAS). In the beginning, the outer part of the plug is also secured with a suture. The plug is modified to obtain a disc at the base of the plug. This disc should be secured to the IAS.

d. Achilles' heel: Side tracts might be overlooked and therefore not excised, and there is no test to check whether all fistula tissues have been excised.

e. Postoperative scheme: With normal wound care, the wound should heal by secondary intention.

f. Recurrence: In a randomized controlled trial comparing plug versus RAF, recurrence rates after 12 months were 68 vs. 38% (15).

g. Fecal continence: In the trial mentioned above, there was no difference between the groups in regard to anal continence.

h. Quality of life: The same applies regarding QoL.

i. Remarks: The use of plugs adds to the cost of surgery. One manufacturer (Gore) stopped producing their bioprosthetic plug.

j. Ideal indication: A short, transsphincteric fistula that has not been operated before, and the plug might be an option in patients with reduced anal continence.

k. German guideline (10): The plug procedure has broadened the options for high fistulas but has low success rates compared with RAF and FPR.

l. In Germany, treating anal fistulas with a plug was frequently done at the beginning of the century. Nowadays, plugs are seldom used for anal fistulas because of the disappointing long-term results.

### *Ligation of the Intersphincteric Tract (LIFT)*

a. Preparation: Enema to achieve a clean rectum; drainage of the fistula tract with a seton is at the surgeon's discretion.

b. Antibiotic prophylaxis: Only in selected (immunosuppressed) patients.

c. Steps: A curvilinear skin incision is made lateral to the intersphincteric groove overlying the site of the intersphincteric fistula tract. The incision is deepened by electrocautery, and the intersphincteric space is subsequently exposed. The intersphincteric

fistula tract is exposed to the internal and external sphincter. At the site of the internal anal sphincter, the fistula tract is ligated with an absorbable suture. The external opening and the remnant fistulous tract are then curetted, and suture ligation is performed to close the fistula opening on the external sphincter complex in the intersphincteric plane. The internal and external sphincter muscles are approximated, and the intersphincteric incision is closed by interrupted absorbable sutures. The outer wound is left open for secondary healing.

d. Achilles' heel: Because of scarring (previous surgery) or the fistula tract's high course, dissecting in the intersphincteric space might be tedious, especially in patients with a funnel-shaped pelvic floor.

e. Postoperative scheme: With normal wound care, the wound should heal by secondary intention. In the original paper by Rojanasakul et al. (23), all patients received oral ciprofloxacin and metronidazole for two weeks.

f. Recurrence: Rojanasakul et al. (23) reported a recurrence rate of 6% after a follow-up of 6 months or less. If follow-up was longer and more patients were operated on, the recurrence rates increased: 43 up to 68 (24, 25) and 32 up to 61 (26, 27).

In a recent meta-analysis of LIFT vs. RAF, both procedures "had similar odds of healing, recurrence, and complications" (28).

g. Fecal continence: Incontinence rates are low or nil after LIFT (28).

h. Quality of life: Kumar et al. (14) reported a better QoL with LIFT than RAF after six months. Madbouly et al. (29) found no difference in QoL between LIFT and RAF. QoL is diminished if a recurrence develops after LIFT (30).

i. Remarks: LIFT can be combined with the interposition of biomaterial (BioLIFT), with a plug, and with platelet-rich plasma (PRP). Epithelium left in the external fistula tract or cavities might be the origin of a recurrence. If the ligature on the side of the IAS resolves, an intersphincteric fistula or abscess might develop because of the dissecting of this plane.

j. Ideal indication: Transsphincteric fistula, not too high in the intersphincteric plane, with no previous surgery.

k. German guideline (10): LIFT is a new option to treat high anal fistulas with results comparable to RAF.

l. In Germany, experience with LIFT is limited to selected departments and is quite low.

### *Fistula Laser Closure (FiLaC)*

a. Preparation: Enema to achieve a clean rectum or oral bowel preparation identical to a prep for colonoscopy.

b. Antibiotic prophylaxis: Broad-spectrum antibiotics only at induction of anesthesia or multiple doses on the day of the operation and the day after (31).

c. Steps: The inner and outer openings of the fistula should be identified. The tract should be debrided with a curette. The laser probe is introduced over the external opening up to the (closed) internal opening. This is followed by continuous delivery of laser energy (usually a wavelength of 1470 nm and 13 W) circumferentially within the fistula (32) tract while withdrawing it at a rate of 1 cm per 3 s. Some authors close the internal opening; one author combines the FiLaC with a flap.

d. Achilles' heel: Long fistula tracts might be a problem (33); the same applies to curved tracts, where the rigid laser probe might not be introduced or coagulate the complete wall. Side tracts or cavities alongside the tracts might be problematic as well.

e. Postoperative scheme: With normal wound care, the external wound should heal by secondary intention.

f. Recurrence: In a review from 2020 (comprising 454 patients), the healing rate after FiLaC was 67.3% (34). In the narrative review by Adegbola et al. (35), the healing rates varied from 20 to 89%; in four papers with more than 100 patients, healing rates varied from 40 to 64%.

g. Fecal continence: Elfeki et al. (34) reported "a weighted mean rate of continence affection of 1% in the form of soiling." In the review by Adegbola et al. (35), there were "no reports of any deterioration in fecal continence."

h. Quality of life: In the review by Frountzas et al. (32), it was concluded that FiLaC "preserves quality of life."

i. Remarks: The laser probe used for endovascular varicose treatment is for single use only, and a processor is needed. This augments the cost for FiLaC.

j. Ideal indication: A straight short fistula.

k. German guideline (10): Because of the limited number of papers on FiLaC, no recommendation is given.

l. In Germany, FiLaC has been made popular by Wilhelm in Cologne; up to now, he is the only German surgeon reporting on FiLaC.

### *Fibrin Glue, Cyanoacrylate, or Collagen*

a. Preparation: Enema to achieve a clean rectum or oral bowel preparation identical to a prep for colonoscopy.

b. Antibiotic prophylaxis: Broad-spectrum antibiotics only at the anesthesia induction or multiple on the day of the operation and the day after.

c. Steps: After identifying the internal and external openings, the tract is curetted, brushed, or flushed with saline. The internal opening might be sutured or covered by a flap. After introducing a catheter through the external opening up to the internal opening, fibrin glue (or cyanoacrylate) is injected into the tract by slowly retracting the catheter until sealing the whole tract with the glue. For the collagen paste, a catheter is not needed; the paste is injected

into the whole tract. To prevent leakage of the paste, the external opening is closed.

d. Achilles' heel: There is no test to confirm that all side tracts and cavities are filled up with fibrin or paste.

e. Postoperative scheme: With normal wound care, the external wound should heal by secondary intention.

f. Recurrence: In the review by Pommaret et al. (36), success rates with fibrin glue vary from 25 to 69%. For cyanoacrylate (only small numbers published), success rates vary from 85% after six months to 68% after 34 months of follow-up (37). For the collagen paste, healing rates vary from 20 to 77.4% (38).

g. Fecal continence: Continence is not compromised by the use of fibrin glue, cyanoacrylate, or collagen paste.

h. Quality of life: in a paper comparing platelet-rich plasma (PRP) with fibrin glue, QoL was better with PRP (39).

i. Remarks: Fibrin glue, cyanoacrylate, and collagen paste increase the costs.

j. Ideal indication: Anal fistula in patients that already have or are afraid of fecal incontinence.

k. German guideline (10): Fibrin glue should be used only in selected cases. For collagen paste, no definitive recommendation could be given. There is no recommendation on cyanoacrylate.

l. In Germany, as to the authors' knowledge, there is limited experience in treating anal fistulas with fibrin glue, cyanoacrylate, or collagen paste.

### *Video-assisted anal Fistula Therapy (VAAFT)*

a. Preparation: Enema to achieve a clean rectum or oral bowel preparation identical to a prep for colonoscopy.

b. Antibiotic prophylaxis: Broad-spectrum antibiotics only at induction of anesthesia.

c. Steps: I. Diagnostic Phase: the rigid fistuloscope (with obturator) is inserted into the external opening. A glycine-mannitol solution is sent through the scope and fills up to the opening of the fistula tract. The scope is introduced slowly under direct vision up to the inner fistula opening. This maneuver straightens the tract. After identifying the inner opening, sutures should be placed alongside the opening but not tied yet.

II. Therapeutic phase: After the removal of the obturator, an electrode is inserted into the scope. Under direct vision, the whole fistula tract with all the side tracts and cavities is cauterized. After that, the tract is cleaned by flushing, brushing, curetting, etc. Then, the internal opening should be closed with a stapling device or, in the case of difficulty, by a mucosal or cutaneous flap. Over the external opening, a small catheter is introduced and inserted up to the inner opening. 0.5 ml of synthetic cyanoacrylate is instilled to reinforce the closure and ensure the complete closure of the inner opening (40).

d. Achilles' heel: Because the fistuloscope is rigid, the risk of breaking up the fistula (via falsa) is possible. Because of the breakage, the flushing solution might get into the soft tissues of the ischioanal region. Tracts that go distally off the main tract may be overlooked; with the scope, inspecting these side tracts is impossible.

e. Postoperative scheme: With normal wound care, the external wound should heal by secondary intention.

f. Recurrence: Healing rates after VAAFT vary from 22 (41) to 93% (42). Follow-up times vary.

g. Fecal continence: Most papers reporting on VAAFT report no negative influence on fecal continence. In the reviews by Emile et al. (43) and Tian et al. (44), results on fecal continence are not mentioned.

h. Quality of life: Papers that report on QoL report no change or a better QoL after VAAFT. In the above-mentioned reviews (43, 44) QoL is not mentioned.

i. Remarks: Closing the internal opening with a stapling device seems to have better results compared to direct sutures or flaps (43, 44). Using a stapling device adds to the costs of surgery.

j. Ideal indication: A straight short fistula.

k. German guideline (10): There is no evidence yet favoring VAAFT over traditional methods.

l. In Germany, to the authors' knowledge, there is only limited experience with VAAFT. There are no reports with results with VAAFT from Germany.

#### *Platelet-rich Plasma (PRP), Platelet-rich-fibrin (PRF), and Stem Cells*

"Platelet-rich plasma (PRP) is defined as a portion of one's own plasma with above-baseline platelet and growth factor levels as obtained with centrifugation. Platelets have alpha granules that contain a number of proteins (PDGF, FCT- $\beta$ , IL-1, FADP, VEGF, ECGF, osteocalcin, osteonectin, fibrinogen, fibronectin, and thrombospondin) with multiple actions on the various aspects of tissue repair" (45).

Platelet-rich-fibrin: Fibrin enriched with growth factors derived from platelets (46).

Stem cells: Autologous or allogeneic stem cells derived from adipose tissue. The stem cells are supposed to have "intrinsic immunomodulatory properties, with the secretion of some anti-inflammatory molecules and paracrine signaling to nearby cells to maintain the local anti-inflammatory environment" (47). The cells are supposed to repair damaged tissue and achieve long-term healing of the fistula (47).

a. Preparation: Enema to achieve a clean rectum or oral bowel preparation identical to a prep for colonoscopy. The fistula should be drained by a loose seton for a couple of weeks.

b. Antibiotic prophylaxis: Single-shot broad-spectrum antibiotics are given at the start of the operation.

c. Steps: I—PRP/PRF: After identifying the internal

and external openings, the tract is curetted, brushed, or flushed with saline. The internal opening might be sutured. After production of the PRP out of the patient's own venous blood, it is injected into the tissue surrounding the fistula tract (48) or injected into the fistula using a catheter inserted through the external opening up to the internal opening. The PRP is then injected while retracting the catheter until PRP pours out of the external opening (45). De la Portilla et al. (39) used PRF and combined both methods (injecting part of the PRF into the surrounding tissue and injecting the other fibrin-rich part into the fistula tract). Some authors combined PRP with other methods (advancement flap, VAAFT, LIFT, etc.) (49).

Steps: I—Stem cells: After identifying the internal and external openings, the tract is curetted, brushed, or flushed with saline. The stem cells are injected around the internal opening and around the fistula tract from the internal up to the external opening. The internal opening is closed with a suture (47). Some authors combined stem cells with other methods (fibrin glue, flap, plug).

d. Achilles' heel: All authors described the preparation of the fistula tract by curettage, brushing, and/or flushing. If epithelium or cavities are left behind, these might be the origin of a recurrent fistula or abscess.

e. Postoperative scheme: With normal wound care, the external wound should heal by secondary intention.

f. Recurrence: In the latest meta-analysis by Wang et al. (49), the healing rate of PRP alone was 62.9%. If PRP was used in combination with other methods, the cure rate was 83%. For stem cells, healing rates vary from 20 to 74% (47).

g. Fecal continence: No paper described impairment of continence after using PRP/PRF or stem cells.

h. Quality of life: In the report by Moreno-Serrano et al. (45), 80% had a "satisfactory" QoL. De la Portilla et al. (39) concluded that PRP-treated patients had a "better reported QoL." For stem cells, no papers were found that report on QoL.

i. Remarks: The preparation of venous blood in Germany underlies the regulations for blood products, and the department has to be licensed for this procedure. Stem cell preparation as autologous or allogeneic underlies regulative restrictions because it is regarded as a therapeutic substance.

j. Ideal indication: An anal fistula that has not been operated on or patients with impaired fecal continence.

k. German guideline (10): Because of lacking evidence, no definitive recommendation can be made.

l. In Germany, there is limited experience with PRP, PRF, and stem cells, probably due to the overriding legislative regulations. There are no reports from Germany with results on treating anal fistulas with these substances.



### Over-the-scope Clip (OTSC)

a. Preparation: Ideally, the fistula should be drained at least six weeks with a seton; oral bowel preparation identical to a prep for colonoscopy.

b. Antibiotic prophylaxis: Broad-spectrum antibiotics only at induction of anesthesia.

c. Steps: Mucosa and anoderm around the inner opening are excised, so an area of 1 cm diameter of the IAS is exposed. The fistula tract is brushed and flushed. Two U-shaped sutures are placed through the IAS, and the long ends are tied together and pulled through the channel of the clip applicator. Under slight tension of these sutures, the applicator with the premounted clip is pressed on the exposed IAS, and the clip is released, grasping the IAS and tightening the inner opening with a constant pressure that should last for healing/closing the internal fistula opening (50).

d. Achilles' heel: There is no test to confirm that all side tracts and cavities are curetted/brushed/flushed. If the sphincter part of the fistula tract still has epithelial tissue, by pressing epithelium to epithelium, the clip will not result in the closure of the wound. If the patient does not tolerate the clip, it has to be removed.

e. Postoperative scheme: With normal wound care, the external wound should heal by secondary intention.

f. Recurrence: The authors only found six papers reporting on OTSC, with recurrence rates varying from 7 to 74% (51, 52).

g. Fecal continence: Continence is not compromised by the use of OTSC.

h. Quality of life: QoL after OTSC has not been reported.

i. Remarks: The OTSC equipment increases the costs.

j. Ideal indication: Anal fistula with a draining seton in patients with no previous surgery.

k. German guideline (10): Because of lacking evidence, no definitive recommendation can be made.

l. In Germany, as to the authors' knowledge, experience with OTSC is concentrated around the surgeon Prosst, who developed this technique.

### Miscellaneous

Surgery for anal fistulas has been done over the ages. After Hippocrates's horse hair for drainage, the braided silk seton was used. Nowadays, silicon setons are used for drainage and preparation of fistula tracts. Although a loose seton is actually no therapy for the fistula, some patients prefer the seton for the rest of their life if they fear fecal incontinence or already had multiple unsuccessful surgeries for their complex fistulas. Permanent loose seton drainage (in the authors' opinion) seldom leads to healing of the fistula.

The cutting seton in complex fistula often results in fecal incontinence, and because of the pain caused

by the strangulating seton, the cutting seton is no option in Germany.

In India, *Ksharasutra* (cotton seton coated with Ayurvedic medicines) is used for therapy with reasonable success. The formula for the fluid used in this method is very variable and unstable, so FDA or EMA cannot license the method. The papers that described the method come almost all from India.

Silver nitrate: Silver nitrate is an old solution that cauterizes infective tissue. It is also used for anal fistulas (1, 5, and 20% solutions). It is injected into the fistula tract. Some patients need more than one treatment session. In the latest paper on silver nitrate by Attaallah et al.(53), the healing rate was 44% (follow-up 50 [7-64] months)).

Many different instruments have been developed to facilitate the curettage of the fistulous tract or excision of the fistulous tissue. However, reports are restricted to case series.

### Discussion

Many methods have been developed to operate anal fistulas. Some are quite old, like the "old-fashioned" fistulotomy/fistulectomy and the cutting seton treatment. Rectal advancement flap was described at the beginning of the 20<sup>th</sup> century, and fistulectomy with primary sphincter repair was described more than 50 years ago. Fibrin glue, FiLaC, anal fistula plug, LIFT, stem cells, FRP/FRF, VAAFT, collagen paste, and OTSC were developed within the past 30 years. A 2010 Cochrane study (54) could only find 10 (TEN) randomized controlled trials on anal fistula surgery. The authors found "no major difference between the various surgical interventions for anorectal fistula as far as recurrence rates are concerned." Furthermore, there was "a paucity of good quality data that compares various types of operative treatment for anorectal fistula," with further trails needed in this field.

Since this Cochrane review, there have more trials. A review from 2023 on RCTs for anal fistula treatment found 36 trials and checked them for robustness. The results indicated that "studies demonstrating superiority of one treatment over another in the management of fistula may be less robust than studies that do not demonstrate such superiority" (55).

The main issues in these studies are the healing or recurrence rate and rate of incontinence impairment. Because many papers have different endpoints, it is essential that future studies publish identical outcome issues. The paper of Iqbal et al. (56) proposed a core outcome set (AFCOS) to implement in any study on anal fistulas. By reporting the AFCOS, studies may be compared, and the power of evidence increases. In the AFCOS, QoL is a main issue, especially for the individual patient with a fistula. The fistula itself reduces QoL. Fecal incontinence may reduce QoL as well. Having a recurrent fistula also reduces QoL.

The surgeon must discuss the different methods to operate the patient's fistula. He has to consider many factors: the type of fistula, anal and pelvic function of the patient, patient's wishes and expectations, age, births, previous surgery, etc. The surgeon has to counsel the patient about the options the surgeon has for the fistula the patient shows up with. The surgeon has to take into account also the personal setting of the patient and the clinical setting of his office and hospital. In low-income countries, FRF/FRP, stem cells, fibrin glue, collagen paste FiLaC, VAAFT, OTSC, etc., might not be an option because of the costs or failing instruments. It might be better to offer procedures like RAF, FPAR, and LIFT in these settings. For these procedures, however, the surgeon needs some dexterity and experience. If the surgeon is not experienced in these procedures, it should be advised to refer the patient with a high or complex fistula to a colorectal surgeon familiar with the procedures. "Simple" fistulas might be laid open if the surgeon feels comfortable with that; otherwise, they should put a seton into the fistula and refer the patient to a center.

The colorectal surgeon, to whom the patient with a high, complex, or recurrent anal fistula is referred, should have a repertoire of methods to offer the patient. These can include plugs, glues, etc.

Three papers report on factors related to recurrence and anal incontinence after surgery for anal fistula (57-59). Previous surgery is a factor related to both recurrence and anal incontinence. Corman's textbook says: "The surgeon who is fortunate enough to have the opportunity to treat the patient initially is the one most likely to effect a cure, to limit morbidity, and to minimize disability" (60).

In many papers dealing with anal incontinence, other pathologies are mentioned for the etiology: vaginal birth, rectal prolapse, pudendal neuropathy, internal sphincterotomy for anal fissure, etc. Most

patients with fecal incontinence have never had surgery for anal abscesses or fistulas.

Despite being well-established for anal fistulas, RAF and FPR need craftsmanship and expertise. Some new procedures seem to be quite simple to perform. The newer methods often showed promising results on short-term follow-up and were applied by many surgeons after the publication of these results. If patients were followed up for a much longer term, results worsened, as shown for fibrin glue, plug, OTSC, VAAFT, etc. The same applies to LIFT. This often led to modification and addition of new elements to the procedure (glue with flap, Bio-LIFT).

## Conclusion

Plug, glue, OTSC, and so on are "crutches" for a surgeon inexperienced in fistula surgery (61). Rectal advancement flap and fistulectomy with anal sphincter repair are operations that demand surgical mastery. For the less experienced surgeon, the differentiation between low and high anal fistulas is crucial: the low ones can be divided, while the high ones should be drained with a seton and then referred to an experienced center. The experienced surgeon should have multiple methods to tackle the high ones, particularly for recurrent cases. If a patient has a recurrent fistula, the chance is high that he will have another recurrence, and the more operations a patient has, the higher the chance of having problems with fecal continence!

## Declaration on Ethics

Both authors declare that the manuscript did NOT involve any studies on human beings or animals.

**Conflict of interest:** None declared.

## References

1. Amir Hossein Faghihi Kashani GH, 2,\* Seyde Sedighe Yousefi,3 Rasool Choopani,2, Mohamad Kamalinejad SKV, 5 and Seyed Hamdollah Mosavat6. Effects of "Satureja hortensis L." on Improving Adult Gastroesophageal Reflux Disease: A Double-Blinded, Randomized, Controlled Clinical Trial. *Iran Red Crescent Med J.* 2018;20(2).
2. Lunniss PJ, Sheffield JP, Talbot IC, Thomson JP, Phillips RK. Persistence of idiopathic anal fistula may be related to epithelialization. *The British journal of surgery.* 1995;82(1):32-3.
3. van Koperen PJ, ten Kate FJ, Bemelman WA, Slors JF. Histological identification of epithelium in perianal fistulae: a prospective study. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland.* 2010;12(9):891-5.
4. Ratto C, Litta F, Lucchetti D, Parello A, Boninsegna A, Arena V, et al. Immunopathological characterization of cryptoglandular anal fistula: a pilot study investigating its pathogenesis. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland.* 2016;18(12):O436-o44.
5. Shahbaz M, Musa O, Ansari NA. Study on Comparative Analysis on Fistulotomy and Fistulectomy in the Management of Low Anal Fistula %J *Iranian Journal of Colorectal Research.* 2023;11(1):-.
6. Bennett RC. A review of the results of orthodox treatment for anal fistulae. *Proceedings of the Royal Society of Medicine.* 1962;55(9):756-7.
7. S K. Continence following splitting of an anorectal fistula. *Chirurg.* 1966;37(2):64-6.
8. Litta F, Parello A, De Simone V, Grossi U, Orefice R, Ratto C. Fistulotomy and primary sphincteroplasty for anal fistula: long-term data on continence and patient satisfaction. *Techniques in coloproctology.* 2019;23(10):993-1001.
9. García-Botello S, Garcés-Albir M, Espi-Macias A, Moro-Valdezate D, Pla-Martí V, Martín-Arevalo J, et al. Sphincter damage during fistulotomy for perianal fistulae and its relationship with faecal incontinence. *Langenbeck's archives of surgery.* 2021;406(7):2497-505.
10. Ommer A, Herold A, Berg E, Farke S,



- Fürst A, Hetzer F, et al. S3-Leitlinie: Kryptoglanduläre Analfisteln. *coloproctology*. 2017;39(1):16-66.
11. Soltani A, Kaiser AM. Endorectal advancement flap for cryptoglandular or Crohn's fistula-in-ano. *Diseases of the colon and rectum*. 2010;53(4):486-95.
  12. García-Olmo D, Gómez-Barrera M, de la Portilla F. Surgical management of complex perianal fistula revisited in a systematic review: a critical view of available scientific evidence. *BMC surgery*. 2023;23(1):29.
  13. Chaveli Diaz C, Esquiroz Lizaur I, Marzo Virto J, Oteiza Martínez F, Gonzalez Álvarez G, de Miguel Velasco M, et al. Fistulectomy and endorectal advancement flap repair for cryptoglandular anal fistula: recurrence and functional outcome over 10 years of follow-up. *International journal of colorectal disease*. 2021;36(4):841-6.
  14. Kumar P, Sarthak S, Singh PK, Mishra TS, Sasmal PK. Ligation of Intersphincteric Fistulous Tract vs Endorectal Advancement Flap for High-Type Fistula in Ano: A Randomized Controlled Trial. *Journal of the American College of Surgeons*. 2023;236(1):27-35.
  15. Bondi J, Avdagic J, Karlbom U, Hallböök O, Kalman D, Šaltytė Benth J, et al. Randomized clinical trial comparing collagen plug and advancement flap for trans-sphincteric anal fistula. *The British journal of surgery*. 2017;104(9):1160-6.
  16. Zimmerman DD, Gosselink MP, Mitalas LE, Delemarre JB, Hop WJ, Briel JW, et al. Smoking impairs rectal mucosal bloodflow--a pilot study: possible implications for transanal advancement flap repair. *Diseases of the colon and rectum*. 2005;48(6):1228-32.
  17. Ellis CN, Clark S. Effect of tobacco smoking on advancement flap repair of complex anal fistulas. *Diseases of the colon and rectum*. 2007;50(4):459-63.
  18. Mei Z, Wang Q, Zhang Y, Liu P, Ge M, Du P, et al. Risk Factors for Recurrence after anal fistula surgery: A meta-analysis. *International journal of surgery (London, England)*. 2019;69:153-64.
  19. Sørensen KM, Möller S, Qvist N. Video-assisted anal fistula treatment versus fistulectomy and sphincter repair in the treatment of high cryptoglandular anal fistula: a randomized clinical study. *BJS open*. 2021;5(5).
  20. Farag AFA, Elbarmelgi MY, Mostafa M, Mashhour AN. One stage fistulectomy for high anal fistula with reconstruction of anal sphincter without fecal diversion. *Asian journal of surgery*. 2019;42(8):792-6.
  21. Ratto C, Litta F, Donisi L, Parello A. Fistulotomy or fistulectomy and primary sphincteroplasty for anal fistula (FIPS): a systematic review. *Techniques in coloproctology*. 2015;19(7):391-400.
  22. De Hous N, Van den Broeck T, de Gheldere C. Fistulectomy and primary sphincteroplasty (FIPS) to prevent keyhole deformity in simple anal fistula: a single-center retrospective cohort study. *Acta chirurgica Belgica*. 2021;121(5):308-13.
  23. Rojanasakul A, Pattanaarun J, Sahakitrungruang C, Tantiphlachiva K. Total anal sphincter saving technique for fistula-in-ano; the ligation of intersphincteric fistula tract. *Journal of the Medical Association of Thailand = Chotmaihet thangphaet*. 2007;90(3):581-6.
  24. Bleier JI, Moloo H, Goldberg SM. Ligation of the intersphincteric fistula tract: an effective new technique for complex fistulas. *Diseases of the colon and rectum*. 2010;53(1):43-6.
  25. Wallin UG, Mellgren AF, Madoff RD, Goldberg SM. Does ligation of the intersphincteric fistula tract raise the bar in fistula surgery? *Diseases of the colon and rectum*. 2012;55(11):1173-8.
  26. Aboulian A, Kaji AH, Kumar RR. Early result of ligation of the intersphincteric fistula tract for fistula-in-ano. *Diseases of the colon and rectum*. 2011;54(3):289-92.
  27. Liu WY, Aboulian A, Kaji AH, Kumar RR. Long-term results of ligation of intersphincteric fistula tract (LIFT) for fistula-in-ano. *Diseases of the colon and rectum*. 2013;56(3):343-7.
  28. Emile SH, Garoufalia Z, Aeschbacher P, Horesh N, Gefen R, Wexner SD. Endorectal advancement flap compared to ligation of intersphincteric fistula tract in the treatment of complex anal fistulas: A meta-analysis of randomized clinical trials. *Surgery*. 2023;174(2):172-9.
  29. Madbouly KM, El Shazly W, Abbas KS, Hussein AM. Ligation of intersphincteric fistula tract versus mucosal advancement flap in patients with high transsphincteric fistula-in-ano: a prospective randomized trial. *Diseases of the colon and rectum*. 2014;57(10):1202-8.
  30. Vander Mijnsbrugge GJH, Felt-Bersma RJF, Ho DKF, Molenaar CBH. Perianal fistulas and the lift procedure: results, predictive factors for success, and long-term results with subsequent treatment. *Techniques in coloproctology*. 2019;23(7):639-47.
  31. Wilhelm A, Fiebig A, Krawczak M. Five years of experience with the FiLaC™ laser for fistula-in-ano management: long-term follow-up from a single institution. *Techniques in coloproctology*. 2017;21(4):269-76.
  32. Frountzas M, Stergios K, Nikolaou C, Bellos I, Schizas D, Linardoutsos D, et al. Could FiLaC™ be effective in the treatment of anal fistulas? A systematic review of observational studies and proportional meta-analysis. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2020;22(12):1874-84.
  33. Lauretta A, Falco N, Stocco E, Bellomo R, Infantino A. Anal Fistula Laser Closure: the length of fistula is the Achilles' heel. *Techniques in coloproctology*. 2018;22(12):933-9.
  34. Elfeki H, Shalaby M, Emile SH, Sakr A, Mikael M, Lundby L. A systematic review and meta-analysis of the safety and efficacy of fistula laser closure. *Techniques in coloproctology*. 2020;24(4):265-74.
  35. Adegbola SO, Sahnun K, Pellino G, Tozer PJ, Hart A, Phillips RKS, et al. Short-term efficacy and safety of three novel sphincter-sparing techniques for anal fistulae: a systematic review. *Techniques in coloproctology*. 2017;21(10):775-82.
  36. Pommaret E, Benfredj P, Soudan D, de Parades V. Sphincter-sparing techniques for fistulas-in-ano. *Journal of visceral surgery*. 2015;152(2 Suppl):S31-6.
  37. Qeralto M, Portier G, Bonnaud G, Chotard JP, Cabarrot P, Lazorthes F. Efficacy of synthetic glue treatment of high cryptoglandular fistula-in-ano. *Gastroenterologie clinique et biologique*. 2010;34(8-9):477-82.
  38. Vollebregt PF, Vander Mijnsbrugge GJ, Molenaar CBH, Felt-Bersma RJF. Efficacy of Permacol injection for perianal fistulas in a tertiary referral population: poor outcome in patients with complex fistulas. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2021;23(8):2119-26.
  39. de la Portilla F, Muñoz-Cruzado MVD, Maestre MV, García-Cabrera AM, Reyes ML, Vázquez-Monchul JM, et al. Platelet-rich plasma (PRP) versus fibrin glue in cryptogenic fistula-in-ano: a phase III single-center, randomized, double-blind trial. *International journal of colorectal disease*. 2019;34(6):1113-9.
  40. Meinero P, Mori L. Video-assisted anal fistula treatment (VAAFT): a novel sphincter-saving procedure for treating complex anal fistulas.

- Techniques in coloproctology. 2011;15(4):417-22.
41. Chase TJG, Quddus A, Selvakumar D, Cunha P, Cuming T. VAAFT for complex anal fistula: a useful tool, however, cure is unlikely. *Techniques in coloproctology*. 2021;25(10):1115-21.
  42. Zarin M, Khan MI, Ahmad M, Ibrahim M, Khan MA. VAAFT: Video Assisted Anal Fistula Treatment; Bringing revolution in Fistula treatment. *Pakistan journal of medical sciences*. 2015;31(5):1233-5.
  43. Emile SH, Elfeki H, Shalaby M, Sakr A. A Systematic review and meta-analysis of the efficacy and safety of video-assisted anal fistula treatment (VAAFT). *Surgical endoscopy*. 2018;32(4):2084-93.
  44. Tian Z, Li YL, Nan SJ, Xiu WC, Wang YQ. Video-assisted anal fistula treatment for complex anorectal fistulas in adults: a systematic review and meta-analysis. *Techniques in coloproctology*. 2022;26(10):783-95.
  45. Moreno-Serrano A, García-Díaz JJ, Ferrer-Márquez M, Alarcón-Rodríguez R, Álvarez-García A, Reina-Duarte Á. Using autologous platelet-rich plasma for the treatment of complex fistulas. *Revista española de enfermedades digestivas*. 2016;108(3):123-8.
  46. Pérez Lara FJ, Hernández González JM, Ferrer Berges A, Navarro Gallego I, Oehling de Los Reyes H, Oliva Muñoz H. Can Perianal Fistula Be Treated Non-surgically with Platelet-Rich Fibrin Sealant? *Journal of gastrointestinal surgery : official journal of the Society for Surgery of the Alimentary Tract*. 2019;23(5):1030-6.
  47. Eberspacher C, Mascagni D, Ferent IC, Coletta E, Palma R, Panetta C, et al. Mesenchymal Stem Cells for Cryptoglandular Anal Fistula: Current State of Art. *Frontiers in surgery*. 2022;9:815504.
  48. Cwaliński J, Hermann J, Paszkowski J, Banasiewicz T. ASSESSMENT OF RECURRENT ANAL FISTULAS TREATMENT WITH PLATELET-RICH PLASMA. *Arquivos de gastroenterologia*. 2021;58(2):185-9.
  49. Wang Y, Rao Q, Ma Y, Li X. Platelet-rich plasma in the treatment of anal fistula: a systematic review and meta-analysis. *International journal of colorectal disease*. 2023;38(1):70.
  50. Prosst RL, Joos AK, Ehni W, Bussen D, Herold A. Prospective pilot study of anorectal fistula closure with the OTSC Proctology. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2015;17(1):81-6.
  51. Mascagni D, Pironi D, Grimaldi G, Romani AM, La Torre G, Eberspacher C, et al. OTSC® Proctology vs. fistulectomy and primary sphincter reconstruction as a treatment for low trans-sphincteric anal fistula in a randomized controlled pilot trial. *Minerva chirurgica*. 2019;74(1):1-6.
  52. Prosst RL, Joos AK. Short-term outcomes of a novel endoscopic clipping device for closure of the internal opening in 100 anorectal fistulas. *Techniques in coloproctology*. 2016;20(11):753-8.
  53. Attaallah W, Uprak TK, Kara B, Sen A, Tuney D, Yegen C. Chemical Ablation for Treating Anal Fistulas without Surgical Intervention: Long-Term Results. *Surgical innovation*. 2021;28(6):731-7.
  54. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. *The Cochrane database of systematic reviews*. 2010(5):Cd006319.
  55. Placer-Galán C, Enriquez-Navascués JM, Lopetegui AE, Ansorena YS. An analysis of randomized controlled trials on anal fistula conducted between 2000 and 2020 based on the Fragility Index and Reverse Fragility Index. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2023;25(8):1572-7.
  56. Iqbal N, Machielsen A, Kimman ML, Kane G, Woodcock R, Grossi U, et al. AFCOS: The Development of a Cryptoglandular Anal Fistula Core Outcome Set. *Annals of surgery*. 2022;277(5):e1045-50.
  57. Sainio P, Husa A. Fistula-in-ano. Clinical features and long-term results of surgery in 199 adults. *Acta chirurgica Scandinavica*. 1985;151(2):169-76.
  58. Garcia-Aguilar J, Belmonte C, Wong WD, Goldberg SM, Madoff RD. Anal fistula surgery. Factors associated with recurrence and incontinence. *Diseases of the colon and rectum*. 1996;39(7):723-9.
  59. Sygut A, Zajdel R, Kedzia-Budziewska R, Trzeciński R, Dziki A. Late results of treatment of anal fistulas. *Colorectal disease : the official journal of the Association of Coloproctology of Great Britain and Ireland*. 2007;9(2):151-8.
  60. ML C. *Colon and Rectal Surgery*. In: Lippincott WW, Philadelphia., editor. 5th ed 2005. p. 295.
  61. Bordeianou L. Bad news on glues: fibrin glue success rates in the treatment of anal fistulas. *Inflammatory bowel diseases*. 2008;14(1):134-5.