# Bölüm 5

# NEW TREATMENT METHODS FOR ANAL FISTULES: CAN A FORWARD - LOOKING STANDARD ALGORITHM OCCUR?

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### LOGIN

Anal fistulas; It is a troubling disease that doctors have struggled with since the time of Hippocrates. Ideal treatment is based on 3 basic principles: (1) Control of sepsis; (2) closure of the fistula; and (3) maintaining continence. Against this difficult disease, treatment options continue to evolve. Despite the multiple approaches currently used for anal fistula treatment, there is a need for an algorithm with high quality data to guide decision making.

In the multi-center meta-analysis reports, the patients are generally not operated by a single doctor; The different surgical preferences of many doctors, the wide variety of treatment methods applied especially in complex fistulas, the scarcity of randomized controlled prospective studies, the wide range in the success rates of the studies prevent the formation of standard treatment methods.

Over time, it was deemed necessary to make modifications to the anal fistula classification described by Parks (figure 1). One of the most clinically useful classification systems for perianal fistulas has been defined by the American Gastroenterology Association. This classification separates anal fistulas into two groups as simple and complex. This also facilitates operative decision making (1).

Simple fistulas are low, meaning they contain a small portion of the internal and external sphincter complex. Sometimes they don't have any. These fistulas include subcutaneous, low intersphincteric, or low trans-sphincteric fistulas. At the same time, the connection between the anal canal and the skin occurs through only one canal.

In contrast, complex fistulas are anatomically longer and higher. The sphincter contains important parts of the musculature and may have more than one pathway. They may include neighboring organs (ie, the vagina). They may have developed secondary to radiotherapy or inflammatory bowel disease, specific infection. Recurrent fistulas also usually fall into this category.

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### **Simple Fistules**

Simple fistulas are easy to treat. By definition, they are superficial or simple fistulas that do not cross any (or an insignificant part) of the sphincter musculature. This group includes subcutaneous (anodermal), intersphincteric and low transsphincteric fistulas.

### Superficial (Subcutaneous, Anodermal) Fistules

Anal fistula can develop from the deepening of the anal fissure. It is not clear how many of the "cryptoglandular fistulas" arise from the fissure. Fistulas due to posterior fissures are significantly more common than fistulas due to anterior fissures. In their study, Garg et al.(2) reported that 34 (11.6%) of 294 patients had a history of anal fissure at the site of fistula development.

It can be treated with an open fistulotomy. These procedures include deroofing the fistula tract and curettage and cauterization of the tunnel epithelium. It has a success rate approaching 100%, with little or no effect on continence(3). Lateral internal sphincterotomy (LIS) can be applied at the fistula-fissure line, after fistulo-tomy, in the same session for anal fissure treatment.

### **Intersphincteric Fistules**

It is usually a simple fistula type. Sometimes it can be long and multi-channel, in the form of a complex fistula. The distance from the external orifice to the anus is less than 3 cm. Since the primary site of origin of anal abscesses is the intersphincteric fistula has a pathway that traverses the internal sphincter and then goes out of the anus. It can be treated with simple fistulotomy or post-seton, fistulotomy. Post-operative conservative wound care with sitz baths and analgesics is usually all that is required. There is some evidence to suggest that healing is faster with marsupialization of the pathway (4). Although the reported rates of incontinence after fistulotomy are very variable, the rate of incontinence appears to be less than 10% (5). Intersphincteric fistulas are the most common type of fistula, accounting for 50-80% of all cryptoglandular fistulas(6).

# **Transphincteric Fistules**

A trans-sphincteric fistula is a fistula that involves both sphincter as it passes to the other side of the external sphincter. If it contains <30% of the external anal sphincter, it is defined as low transsphincteric, and if it contains >30% of the external anal sphincter, it is defined as high transphincteric. Transsphincteric fistulas therefore pose a challenge to management and often require more complex or gradual treatment. However, the use of a seton to gradually "lower" the pathway and make

the pathway less involved with the external sphincter may allow migration of the pathway and fistulotomy at a later date while maintaining patient continence. The degree of involvement of the external sphincter determines the probability of post-operative incontinence, as a partial sphincterotomy will usually be tolerated(7).

# **Complex Fistules**

# **High Transphincteric Fistules**

High transfincteric fistulas involving > 30% of the external anal sphincter are complex. The risk of incontinence is greater. For this reason, gradual treatment and the use of new modern methods are required.

# **Suprasphincteric Fistules**

This fistula tract passes over the external sphincter, first through the puborectal muscle and then through the internal sphincter. Again, because of their high tracts, the use of seton before fistulotomy can be considered in these cases. Fistulectomy involves the sharp or cautery removal of the entire fistula tract. In many studies, no difference was found between fistulotomy and fistulectomy(7).

# **Extrasphincteric Fistules**

The internal orifice of these fistulas, rather than the dentate-line, arise in the proximal rectum and are sequelae of another frequently performed procedure. Its external openings are in the perianal region, and the tractus runs upward to enter the anal canal above the dentate line. More morbid surgeries such as lowering the level of the fistula, canal ligation, canal laser ablation, fistulectomy are required(7).



Figure 1. Parks classification: 1) Intersfincteric, 2) Transsfincteric, 3) Suprasfincteric, 4) Extrasfincteric, 5) Superficial

#### **Current Management Options For Anal Fistules**

#### **Fistulectomy and Fistulotomy**

Fistulectomy; It is a comprehensive treatment that includes the complete excision of the fistula tracts, thus providing complete excision of the tissue for histopathological examination and eliminating the risk of secondary pathway formation (8,9). With complete removal of the fistula tract, the recurrence rate is greatly reduced. However, because the residual wound is larger than other procedures, it has a higher rate of incontinence. The operation time and recovery period are longer (10).

Fistulotomy; The fistula exposes its tract. Facilitates drainage to ensure complete cure and reduce recurrence. At the same time, marsupialization results in faster recovery (11). Therefore, combined fistulotomy and marsupialization may be an excellent choice for patients with anal fistula.

Most surgeons; it is known that he believed the classical fistulotomy technique to be the gold standard for correct treatment (12). However, the problems associated with fistulotomy are numerous, including postoperative pain, bleeding, and delayed wound healing (8,13). The negative effects of this technique can be modified by the addition of marsupialization. Marsupialization of the open fistula facilitates the drainage of the existing wound and shortens the healing time. It helps to provide continence better by minimizing anal deformities (14).

#### **Seton Application**

Seton use; It increases inflammation by causing a foreign body reaction. Thus, it causes perisphincteric fibrosis(15). The treatment of anal fistula with Seton was first described by Hippocrates, who used horse hair as a seton (16). The technique has been improved over time and the variety of seton has increased. The main purpose of the seton application is to close the secondary canaliculi coming out of the main canal. However, a recurrence rate of 22-39% was reported in different studies using seton(17,18). Depending on the structure of the seton material, the placement technique, and the seton mechanism of action, many seton-related techniques have been described in the management of anal fistula.

Regarding their mechanism of action, setons are considered loose or cutting. Loose Seton acts as a drain that can stay in place for a long time. Sometimes it makes the fistula permanent by stimulating the fibrosis around it. Tight Seton has its own complications. After the operation, it needs to be tightened several times. Also, after the tight Seton is cut, the sphincter needs some time to heal. Therefore, it can cause severe pain, fecal or gas incontinence (19). Some studies admit that for any seton type, incontinence may be between 0-5% (20).

# Ligation of Intersphincteric Tract (LIFT)

The LIFT procedure was first described in 2007 by Rojanasakul et al. Method; It involves identifying the internal and external openings of the fistula, followed by careful dissection of the portion of the fistula tract within the intersphincteric space. It is ligated and cut from the part of the intersphincteric tract close to the inner orifice. Finally, the external orifice entrance is widened to facilitate drainage (21).

The LIFT procedure can be considered to have recovery rates of up to 75%(22). This technique is specific for trans-sphincteric fistula tracts. It can also be used for complex fistulas such as horseshoe or supra-sphincteric fistulas.

Some disadvantages of LIFT are the high recurrence rates of up to 40% reported in studies (23). The benefits of the LIFT procedure are that it can be operated in patients who have had fistula surgery before, providing continence and a small incision. It is a method compatible with re-operation when necessary. Patients who have a history of multiple fistula surgery, have a longer fistula tract, smoke or have obesity have a higher risk of failure of the surgery (24).

# Video-Assisdet Anal Fistula Treatment (VAAFT)

The most important feature of VAAFT is the visualization of the fistula tract and its internal opening with a camera. Failure to identify the fistula internal orifice, false internal orifice, is important for recurrence. VAAFT; It allows real-time visualization of the canal, precise definition of anatomy by fistuloscopy, and fulguration of the pathway under direct vision. Secondary branching tracts and abscess spaces that hinder successful treatment of anal fistula can also be identified and treated appropriately. Allows the fistula channel to be brushed and cauterized. Further, the inner opening can be conveniently closed by suturing or using a stapling device. Adoption of fistuloscopy combined with closure of the internal opening with a suture or stapling device allows effective treatment of complex anal fistulas with preservation of anal sphincters. The recurrence rate reported by Meinero and Mori was approximately 26.5%(25). Kochhar et al(26), reported the recurrence rate as 18.5% in their study.

# Fistule Laser Closure (FiLAC)

The use of laser in the treatment of anal fistula was first described by Wilhelm in 2011 (27). For this new sphincter sparing technique; It uses a laser probe [Fistula laser closure (FiLaC<sup>™</sup>), Biolitec, Germany] that destroys the fistula epithelium and simultaneously the remaining fistula tract. The main cause of surgical failure is the result of persistent fistula tract or remnants of unexcised fistula epithelium. The

benefit of this newly designed radial emitting laser probe is considered to eliminate fistula epithelium or any granulation tissue in a circular fashion. After the procedure, it closes the fistula tract with its shrinkage effect. Simple diathermy has no shrinking effect on tissues. Adjusting for potential thermal damage to sphincter muscles is more difficult. The fiber laser gives its energy 360° homogeneously and while it is withdrawn at a speed of 1 mm/s by applying energy continuously, the path of the wick is closed. Depending on the width of the path, a 980 nm or 1470 nm diode laser can be deployed, providing different wavelengths.

Giamundo et al.(28) performed the FiLaC<sup>™</sup> procedure on 35 patients with cryptoglandular and Crohn's disease-associated fistulas. The overall success rate at 20-month follow-up was 71%. Öztürk et al.(29) reported a success rate of 82% at 12-month follow-up in 50 patients treated for intersphincteric and transsphienteric fistulas.

This procedure has some advantages. It does not affect continence, applies controlled hyperthermic energy to tissues, has a short learning curve and shortens postoperative hospital stay compared to endorectal advancement flap or LIFT. However, it also has some disadvantages. Because direct visualization of the fistula tract or any secondary pathway is not possible, it is a "blind" procedure and can result in recurrence. The method may fail to close, especially in very short and long distance fistulas. The process may need to be repeated. It requires expensive equipment, especially when compared to other sphincter sparing techniques. Therefore, randomized studies comparing FiLaC<sup>T</sup> with the most common sphincter sparing procedure are needed(30).

### **Advancement Flep**

Advance flap; It is defined to close the internal opening of the fistula, thereby removing the fistula from the source of sepsis and allowing secondary healing of the tract. An endoanal advancement flap involves advancing a healthy rectal wall over the debrided internal opening and suturing the flap distal over the internal opening. It is based on a large pedicled flap dissected from the healthy proximal rectum. Additionally, this procedure involves creating a large defect in the previously undamaged rectum and carries the risk of devascularization and loss of a much larger portion of the rectal wall. Failure or ischemia of these flaps may result in the formation of a defect much larger than previously existed. Dissection in a chronically inflamed setting can compromise the sphincter. The success rates of this approach vary greatly in the literature and range from 0% to 63%(31,32,33).

### Anal Fistula Plug (AFP)

Anal fistula plug (AFP); It is a simple repair based on the application of semisynthetic material along the canal between the inner and outer orifice. For this reason, it was found very attractive at first. The plug is withdrawn from the fistula tract and secured in place at the inner opening (the larger part of the plug is at the inner opening) and sutured, leaving the outer opening open.

Although initial reports documented a very high success rate, overall success over time turned out to be low. Johnson's(34) first statements documented nearly 80% success. This was supported by a study of Champagne(35), which documented an 83% success rate. However, with more studies, it has been shown that the overall success rate is lower and some studies report a 20% success rate. A recent meta-analysis by Jacob and Keighley reported success rates ranging from 35% to 85%(33,36).

### **Fibrin Glue**

Fibrin glue injection was seen as a promising development in sphincter sparing approaches to complex fistulas. This method is based on the injection of liquid fibrin, which will facilitate healthy tissue growth and fistula closure, in the fistula tract. The biggest advantage is that the approach is extremely easy and non-in-vasive. Regardless of the anatomy or complexity of the fistula tract, it does not require any dissection of the sphincter musculature. However, despite early hopes, long-term results have resulted in low success rates of up to 16%(37,38).

### **Treatment in Crohn Patients**

Anal fistula is very difficult to treat in Crohn's patients. However, early diagnosis is critical for effective treatment. These patients should be referred to a gastroenterologist and receive anti-TNF alpha therapy as primary therapy for fistula disease. If the fistula persists after medical treatment, setons are the most commonly used primary surgical option in these patients, with reasonable recovery rates after anti-TNF alpha therapy(39). A few studies have retrospectively demonstrated effective cure rates of approximately 67–90% of combined seton and anti-TNF alpha therapy in patients with Crohn's disease(40).

Infliximab should be added for treatment in the delayed diagnosis group. In patients receiving infliximab treatment, an increase in recovery rates was found depending on the increase in the drug dose (41.42).

### Results

There are many technical differences in the surgical treatment of anal fistula, making it difficult to reassess and compare treatment outcomes between different centers. In Ratto et al's 2019 survey study:

Fistulotomy and fistulectomy are the most common operations performed by more than 40% of surgeons (> 20 per year). Overall, 82% of surgeons apply fistulotomy as the gold standard treatment for simple fistula only.

Less than half of surgeons routinely perform marsupialization or emergency sphincter reconstruction (primary sphincteroplasty) after fistulotomy for intersphincteric and inferior transsphincteric fistulas.

Most of them prefer and use loose setons (90%). Most surgeons (77%) consider the use of seton as part of a stepwise surgical approach. They leave the seton in place for an average of 8 (6-12 weeks) to create a fistula tract before trying any other treatment.

Nearly three out of four surgeons said they had experience doing LIFTs. OTSC was the least used technique, with only 1% of surgeons interviewed using this technique. One in four surgeons reported their experience with plug placement. Less than 15% of surgeons had experience using fibrin glue injection.

Overall, 10% of surgeons used FiLaC. Surgeons' experience with currently available surgical techniques explains the chronological evolution of new techniques, with less than 10% of respondents applying the latest approaches (ie, VAAFT, FiLaC, and OTSC).

The algorithm defined by Garg et al in 2021(44) (table 1) seems to be the most appropriate treatment protocol, which should be up-to-date.

New classification of perianal fistula with treatment guidelines recommended by Garg(44).

Category Level Description Treatment guidelines

### Simple

I *Low linear intersphincteric and transsphincteric fistulas* (less than 1/3 of external sphincter involvement):

Suggetion: In almost all of these fistulas (>95%), fistulotomy should be possible.

**II** *Low intersphincteric and transsphincteric fistulas* (less than 1/3 of external sphincter involvement): Suggetion: In most of these fistulas (>90%), fistulotomy should be possible.

### Complex

**III** *High linear transsphincteric fistula* (>1/3 external sphincter involvement): (or fistula associated with Crohn's disease, sphincter injury, post-radiation exposure, or anterior fistula in women)

Suggetion: Fistulotomy should not be attempted. FPR or sphincter sparing procedures (LIFT, VAAFT, AFP, TROPIS, OTSC clip or FiLaC laser) IV Complex high (>1/3 external sphincter involvement) transsphincteric fistula: IV-A: abscess IV-B: multiple path IV-C: horseshoe

Suggetion: Fistulotomy should not be attempted. FPR or sphincter sparing procedures are recommended (LIFT, VAAFT, AFP, TROPIS, OTSC clip, FiLaC laser). FPR and AFP should be avoided in abscess. Preferably refer these fistulas to a fistula specialist.

V *Transsphincteric with intersphincteric supralevator extension* (>1/3 sphincter involvement): Suggetion: Fistulotomy should not be attempted. Sphincter sparing procedures are recommended (LIFT, VAAFT, AFP, TROPIS, OTSC clip). Preferably tertiary referral centers.

Table 1 Garg's suggetion

FPR, fistulectomy with primary sphincter reconstruction; LIFT, ligation of the intersphincteric fistula tract; VAAFT, video-assisted anal fistula treatment; AFP, anal fistula plug; TROPIS, transanal opening of the intersphincteric space; OTSC, comprehensive clip proctology; FiLaC, fistula tract laser closure.

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