Surgery and medical therapy in Crohn’s disease

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Complex fistulas and advanced soft tissue techniques

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Abstract

Perianal fistulas are categorized as “complex” under the following conditions: a high tract passing the upper two thirds of the external sphincter, presence of multiple fistula tracts, rectovaginal fistulas, previous local irradiation and association with the presence of an anorectal stricture or Crohn’s disease. Treatment of complex fistulas can be challenging and carries a high risk of poor wound healing, recurrences and incontinence. Therefore a detailed understanding of perianal anatomy, knowledge of the extent of the disease and its relation to the various structures is required for proper management. This chapter describes the technical approach of various advanced soft tissue techniques for complex fistula repair (i.e. the endorectal mucosal advancement flap, the anocutaneous advancement flap and the Martius flap) and discusses its indications, advantages and associated complications.

The reported success rates of endorectal advancement flaps in the literature is variable, but generally better for cryptoglandular (24-100%) compared to Crohn’s (33-92%) fistulas. The success rate in patients with Crohn’s disease appears to be slightly better under anti-TNF therapy. Sphincteroplasty following complete fistulotomy (episioproctotomy) can be an appropriate approach in a selected patient group.

In conclusion, treatment of complex perianal fistulas is challenging, and the advanced soft tissue techniques are an important option within the armamentarium of techniques that can be applied to treat this condition in a patient-tailored treatment approach.
Complex fistulas

Perianal fistulas can be classified according to several classification systems. Recently an empirical classification, as simple or complex fistulas, has been proposed by the American Gastroenterological Association Technical Review Panel.\(^1\) This classification provides a simplified but comprehensive approach to perianal fistulas. Simple fistulas are low (superficial, intersphincteric or low transsphincteric), have a single external opening, no undrained perianal abscesses, and are confined to the anal canal. Perianal fistulas are categorized as complex if the fistula tract is of intersphincteric or transsphincteric origin, with a high tract traversing the upper two thirds of the external sphincter, or if they are of extrasphincteric or suprasphincteric origin. In addition, the following risk factors also determine the complexity of a perianal fistula: presence of multiple fistula tracts, rectovaginal fistulas, previous local irradiation, the presence of an anorectal stricture or Crohn’s disease. From the surgical point of view, Parks’ classification is more descriptive as it can influence surgical decision making.\(^2\) Parks distinguished four fistula types in relation to the external anal sphincter: intersphincteric, transsphincteric, suprasphincteric and extrasphincteric fistulas. However, since this distinction is more difficult to use in daily clinical practice, nowadays most experts use the simple or complex subdivision classification.

Preoperative management

Careful patient selection is of crucial importance in any surgical attempt of fistula closure. In the case of Crohn’s disease with active rectal inflammation (proctitis), all procedures will be associated with a poor healing rate. Therefore, flap reconstruction should only be considered in selected Crohn’s patients with endoscopically demonstrated complete remission. Prior to any definite surgical repair, proper drainage of the primary tract and any secondary extensions should be performed to control perianal sepsis and prevent recurrent abscesses, since unresolved sepsis is, essentially, a guarantee for failure. Adequate imaging is crucial, since the findings might influence the therapeutic strategy. Magnetic resonance imaging (MRI) can identify the location of the internal opening, the presence of additional tracts and abscesses. It is considered to be the gold standard for complex fistulas (accuracy of 76-100%) and should be part of the initial diagnostic work-up in patients with more complex recurrent or Crohn’s perianal fistulas.\(^3\) Imaging
by endoscopic anorectal ultrasound is also an accurate technique (56-100%) when performed by experts in conjunction with hydrogen peroxide enhancement.\textsuperscript{3} In patients with Crohn’s disease, flexible sigmoidoscopy or other direct imaging is mandatory to assess the presence of proctitis.

Surgical exploration under anesthesia in the operating room with gentle probing and the ability to inject hydrogen peroxide into the fistula tract via the external opening to locate the internal opening is reported to be the most sensitive investigation for complex fistulas.\textsuperscript{3} In addition, it has the advantage of enabling concomitant surgery. Since complex fistulas are challenging to treat, surgery should be planned in several stages, starting with seton drainage. In patients with prior seton drainage, the success rate of advancement flap repairs has been reported to be significantly higher in a study by Sonoda et al. (73\% versus 51\%).\textsuperscript{4} In current practice, the seton is left in place for 6-12 weeks.

Preoperative patient work-up with respect to enema’s or dietary restrictions are eminence based. Although there are no data specifically for advancement flaps, perioperative antibiotics prophylaxis is generally accepted in the attempt of definite fistula closure.

\section*{Surgical options for complex fistulas}

While simple fistulas can be reliably treated with straightforward operative procedures such as fistulotomy with low recurrence rates, treatment of complex fistulas can be challenging according to the nature of the fistula. Advanced soft-tissue techniques carry a high risk of poor wound healing and incontinence. Proper management requires a detailed understanding of perianal anatomy, knowledge of the extent of the disease and it’s relation to the various structures. Therefore surgery should be performed by a colorectal surgeon with sufficient knowledge and experience in the management of complex fistulas.

The objective of complex fistula treatment is, essentially, to close the fistula tract in order to prevent recurrence and preserve continence. A number of techniques can be applied to approach the problem. Apart from advancement flaps, other options are the anal fistula plug, the LIFT (ligation of intersphincteric fistula tract) technique, VAAFT (video-assisted anal fistula treatment) and Over-The-Scope-Clip (OTSC; Ovesco\textregistered).
closure of the internal opening. Depending on the type of the fistula, the chronicity of the fistula and the scarring of the anus, the appropriate technique is chosen. There are several sphincter-sparing advanced soft tissue flap techniques that have been developed for the treatment of complex fistulas. Advanced soft tissue techniques aim to close of the high pressure end of the fistula with preservation of continence. By closing the internal opening, the fecal stream will not be able to enter the fistula tract with subsequent obliteration of the fistula tract and external opening over time. Closure of the internal fistula opening can be accomplished by the following surgical advanced soft tissue techniques: the endorectal (mucosal) advancement flap, the anocutaneous advancement flap and the Martius (bulbocavernosus) flap.

**Endorectal (mucosal) advancement flaps**

The rectal (mucosal) advancement flap was first developed and described in 1902 by Noble for the repair of rectovaginal fistulas following childbirth, and later modified and used for the treatment of cryptoglandular perianal fistulas. It entails mobilization of a broad based mucosal flap of rectum to cover the internal fistula opening after a period of sufficient preoperative seton drainage. Essential steps in this procedure are the creation of a broad based, well vascularized, tension free flap, and excision of the internal opening (figure 1 and 2). Therefore it should be extended proximal enough to fully cover the internal opening. The defect in the internal sphincter should be closed and proper drainage of the extrasphincteric tract is considered of significant importance. Although seton drainage prior to definite surgery has shown a higher success rate, it also carries the risk of epithelialization of both ends of the fistula tract. If the epithelialization is not excised, particularly at the internal opening, the tract is not able to close at that point. Studies have revealed that squamous epithelium in the fistula tract was found in a majority of patients following fistulotomy. Epithelium was predominantly found near the internal opening (81%) as compared to the mid (36%) and the distal canal (18%)\(^5\). There was no association between the amount of epithelialization present and the duration of fistula complaints or a history of fistula related surgery. Therefore curettage of the fistula tract and closing of the internal opening after excision of the epithelium should be performed. The free border of the flap should be sutured to the distal rectum or upper anal canal. In order
to ensure sufficient overlap of the flap, a small part of the epithelium must be excised caudad to the internal opening.

Figure 1 and 2: Endorectal advancement flap procedure steps.
Modifications to the flap introduced by Noble include the use of varying thicknesses and shapes of the flap, curved incisions and rhomboid flaps, with or without closure of the defect in and outside the external sphincter. Regarding the thickness, a flap can consist of tissue including the mucosa, the submucosa or even a portion of the circular muscle. These are more classically defined as a mucosal, a partial rectal wall or full thickness flap, respectively. With respect to the shape of the flap, this can be “tongue” like or “lip” like (horizontal). (figure 3 and 4)

Figure 3 and 4: “tongue” like and “lip” like shaped flaps.

The use of “tongue” flaps has not been compared with horizontal flaps, however horizontal flaps mobilized above and below the incision avoid the potential for a mucosal ectropion and subsequent leakage of mucus.

Relative contra-indications for the endorectal advancement flap, beside active Crohn’s disease, are malignant or radiation-related fistulas, a fibrotic anorectal canal, multiple internal openings of the fistula, severe perianal scarring due to previous fistula surgery,
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patients with pre-existing incontinence or a sphincter defect. In the latter case a sphincteroplasty may be considered.

Success rates & complications
The reported success rates of endorectal advancement flaps in the literature vary widely. In a recent systematic review by Soltani, in patients with cryptoglandular fistulas, the success rate is approximately 80% (range 24-100%).6 Unfortunately the results for Crohn’s fistulas are less favourable.6 The initial weighted success rate for this patient group is 64% (range 33-92%).6 It should be appreciated that a publication bias might be present providing more favourable results than in everyday practice. In patients with Crohn’s disease, even if they are in complete remission, the advantage of concomitant medical therapy with immunomodulators or biologics is currently under investigation. In a retrospective cohort series, the healing rate in patients with Crohn’s disease appeared to be slightly higher with anti-TNF therapy, with a success rate of 50% without and 65% with additional medical therapy.6

Endorectal advancement flap techniques can be complicated by poor wound healing, incontinence or soiling. Poor wound healing occurs mainly in patients with active Crohn’s disease in the rectum. Cigarette smoking is also well known to influence wound healing in various patient groups and can have a significant negative impact on the results of the flap repair. The observed healing rate in actively smoking patients with fistulas of cryptoglandular origin was 60%, compared to 79% in patients who did not smoke.7 Reduced blood flow in the flap directly caused by cigarette smoking has been noted as a possible contributing factor since it has been shown that the blood flow in normal rectal mucosa decreases temporarily after smoking a cigarette. However, flap necrosis is not often described in the literature.

A wide range of success in the rate of flap repair exists in the literature. Many factors may be responsible for this. The experience of the surgeon, technical details like de-epithelization of the internal opening, closure of the internal opening, drainage or excision of the extrasphincteric part of the fistula tract, perioperative administration of antibiotics, bowel preparation and bed rest and type of flap are all contributing factors to success.

Incontinence is described in 13% (0-35%) of patients with cryptoglandular fistulas and 9.5% (0-29%) in patients with Crohn’s fistulas after endorectal advancement flap repair.6 In addition, patients with two or more previous attempts at flap repair have less favorable success rates.
In the literature, soiling is frequently reported, however there is no significant difference between the amount of soiling before (36%) and after surgery (48%). In the case of soiling, it is important to distinguish what we are measuring: soilage may be due to purulent discharge from the fistula tract preoperatively or due to true fecal loss as a result of iatrogenic sphincter damage or anal canal deformity. It can be difficult for patients to differentiate between these two.

There are several mechanisms that may be responsible for the soiling. First, the resting anal pressure decreases in the lower part of the anal canal in the case of deliberate division and sacrifice of healthy anal sphincter muscle. Secondly, iatrogenic sphincter damage with the use of the Parks retractor has been reported in the literature. It is hypothesised that overstretching of the anal sphincters by a Parks retractor results in rupture of small nerve branches and consequently to denervation of muscle fibers. Therefore this type of retractor should not be used. Instead, the use of a proctoscope or a speculum is generally accepted. Furthermore, continence can be compromised by anatomic deformity of the anal margin due to the surgical incision, also referred to as a “keyhole” deformity. Keyhole deformity results from excision of excessive anoderm and perianal skin with excision of a portion of subjacent muscle. Finally, deterioration of continence may occur due to a mucosal ectropion if a flap advances mucosa beyond the fistula origin at the dentate line. This gives patients the false sensation of incontinence due to spontaneous discharge of mucus and soiling. Finally, chronic sepsis might jeopardize proper sphincter function due to scarring and damage to the anal sphincter.

Good data on the rate of healing relative to flap thickness is lacking. Although a better healing rate might be expected after either a partial or full-thickness flap, interestingly, this has not been borne out in the literature. In Soltani’s systematic review, correlation of success rates was not conclusive. However, they did report that full-thickness flaps were more frequently associated with recurrences when compared to studies using partial-thickness flaps. This is in contrast to the results of a single retrospective report comparing partial and full-thickness flaps, where higher success rates were suggested in full-thickness flaps as compared to mucosal rectal flaps. The one randomized controlled study directly comparing partial-thickness to mucosal advancement flaps showed a much higher rate of recurrence in the group with a mucosal advancement flap (10% versus 40% of the patients).

In the end, a significant group of patients, approximately 4.4%, eventually requires formation of a stoma to divert the fecal stream. Unfortunately, intestinal continuity is often not restored in patients with a diverting stoma.
Anocutaneous advancement flaps

In 1996, the Island anocutaneous advancement flap was introduced for the treatment of cryptoglandular perianal fistulas by Del Pino. This technique was initially developed to eliminate the risk of mucosal ectropion after endorectal mucosal advancement flaps or incontinence after fistulotomy. Since then, different shaped flaps have been described: the V-Y advancement, diamond, house, inverted or U-shaped flap. In current practice, the V-Y cutaneous advancement triangular flap, consisting of skin and subcutaneous tissue, is most frequently used. In this technique the crypt-bearing tissue around the internal opening of the fistula is excised, as well as the overlying anoderm (figure 5 and 6). The fistula tract is then de-epithelialized. Once sufficient mobility is obtained, the flap can slide easily into the anal canal. The proximal portion of the flap anoderm is then sutured to the anal mucosa and underlying internal sphincter.

Figure 5 and 6: Anocutaneous advancement flap procedure steps

Success rates & complications

Although short-term results in the literature were encouraging, with a reported low recurrence rate and only rarely observed deterioration of continence, variable success rates have been described in subsequent reports. Success rates range from 46% to 94%. Especially in patients with a history of previous fistula repair, outcomes are less favourable.

The main problem in flap advancement surgery is shrinkage of the flap. This is caused by inadequate blood supply, probably due to inadequate dissection, dimension of the flap or tension at the suture line. A flap containing the dermis and subcutaneous tissue allows medial and upward advancement of the flap without tension and does not jeopardize the blood supply to the flap. Another theory regarding the vitality of the flap is the influence of low internal sphincter spasms.
For this type of flap repair, cigarette smoking is also associated with an increased risk of fistula recurrence. Furthermore, the success rate is less favourable in patients with multiple previous attempts at repair.

In anocutaneous advancement flap repair, deterioration of continence is reported in 19% to 30% of patients. In this procedure it is also hypothesised that the decreased continence can be caused by overstretching of the sphincters, likely due to retractor injury during the deep intra-anal dissection.

It is not possible to comment on success rates of the various types of shapes of the anocutaneous flap due to small numbers in the literature.

**Martius flap**

Another technique in flap repair is the Martius, or bulbocavernosus, flap, first described by Heinrich Martius in 1928. It was originally used for urethra-vaginal fistulas repair and subsequently applied to cryptoglandular fistulae. This approach has been modified through the years and is also suitable for low anovaginal or rectovaginal fistulas. For low fistulas, this approach has the advantage of tissue transfer being in close proximity to the operative field with no functional and minimal cosmetic deficit of the donor site. The flap consists of the bulbocavernosus muscle and adipose tissue. The flap can be harvested from either labia, depending on local conditions, and any previous procedures. When performing the Martius flap repair, the internal rectal opening of the fistula must be closed. The bulbocavernosus muscle and the surrounding fibroadipose tissue are mobilised from the labial fat pad, preserving the postero-external vascular pedicle. A subcutaneous tunnel connecting the labial and perineal incisions is created and the graft is tunneled through. The graft is placed between the vagina and the rectum and sutured in place. The vaginal opening and the labial incisions are closed primarily, and the perineal wound is then closed loosely.

**Success rates & complications**

The success rate for Martius flap repair in cryptoglandular fistulas is higher (65%) when compared to Crohn’s fistulas (50%). The Martius flap is associated with a low morbidity rate, however deterioration of continence has been reported. Quality of life and sexual functions have not previously been studied after the Martius flap procedure.
Long-term outcomes & predictors of failure

Unfortunately, most studies reporting on advancement flap techniques are lacking long-term results. A retrospective study in 1996 did assess the long-term success, safety, applicability, and factors affecting recurrence in patients after endorectal advancement flap surgery. Overall, recurrences were seen up to 55 months after repair in 29% of patients, of which 75% occurred within the first 15 months. In 2008 van Koperen et al. reported a recurrence rate of 21% following advancement flap repair for cryptoglandular fistulas (median follow up of 76 months, range 7-134). The high percentages of recurrence reported in literature, even after initial reported success, can probably be explained by the lack of objectively confirmed closure with imaging. Most reports only use clinical healing with reduced fistula production as primary outcome parameter. However, closure of the internal and/or external opening is no guarantee for complete fistula healing. When part of the tract is not completely obliterated, the fistula can (clinically) recur.

Over the past decades several studies were aimed at identifying factors predictive of failure. In multivariate analyses, recurrence was not associated with the type of fistula, origin, antibiotic use, postoperative bowel confinement or preoperative steroid use. Regarding a history of previous repairs, studies show conflicting results. Ozuner et al. found that prior fistula related surgery was associated with higher failure rates, whereas other studies later on showed that previous attempts at repair were not related to less favorable outcomes. A negative influence of Crohn’s disease on flap healing rates was demonstrated in several studies. Furthermore smoking is a significant factor in failure rates as previously mentioned.

It has been hypothesised that by creating optimal circumstances for definite repair of complex fistulas, recurrence can be minimised. In 1995 Makowiec et al. found that a diverting stoma appeared to be an independent prognostic factor for symptomatic recurrence. However, multiple other multivariate analysis did not reveal a beneficial effect of fecal diversion on healing rates.

Soltani et al. reviewed several studies exploring anal sphincter function in patients after endorectal mucosal advancement flap surgery using manometry. Of these, only one study showed a reduction of resting and squeeze pressure after the advancement flap repair. However, in two other studies, no difference was found in the preoperative assessment as compared to postoperatively, or in comparison with fistulotomy and reconstruction.
**Sphincteroplasty**

For complex perianal fistulas, fistulotomy followed by primary sphincteroplasty (episio-proctotomy) is regarded with some reservation, mainly because of the risk of postoperative incontinence. Nevertheless, in some cases it may be an appropriate approach. Indications for sphincteroplasty include preoperative incontinence, an occult tear on ultrasound or the need of vascularised tissue. This technique, with end-to-end sphincteroplasty was first described by Parkash in 1985 for the treatment of complex perianal fistulas. In this approach, a complete fistulotomy of the primary tract of the fistula is performed with dissection of both the internal and the external anal sphincter. The primary tract is de-epithelialized, with excision of any secondary tracts or residual. After excision of the internal opening, end-to-end primary sphincteroplasty is performed. Thereafter both sphincters, the entire wall of the fistula tract and the anal submucosa and mucosa are closed. Again proper drainage of the external part of the fistula tract is a requirement.

Unfortunately solid evidence is lacking for results of this procedure. Therefore, careful patient selection for this type of procedure is important, and should probably only be considered in the presence of recurrent fistulas and fecal incontinence.

**Success rates & complications**

In a prospective observational study of 72 patients with complex anal fistulas of cryptoglandular origin treated with fistulotomy and primary end-to-end sphincteroplasty, the long-term success rate for healing of the fistula was 95.8%. In this study, the patient group consisted of a homogeneous group with complex fistulas with absence of acute perianal sepsis. A partial fistulectomy, limited to the fistula tract peripheral to the external anal sphincter, was performed. In order to minimize further possible damage of the anal sphincter, excision of the part of fistula tract passing through the sphincters was avoided.

De novo impairment of fecal continence occurred in 11.6% and major fecal incontinence occurred in 1.4%. A history of recurrent fistulas after previous fistula surgery significantly increased the risk of soiling post defecation.
Postoperative management

Advancement flap repair surgery can be performed in the ambulatory setting. The length of hospitalization does not influence healing rate. There is no consensus on the use of anti-diarrheal agents or antibiotics in the early postoperative period. Larger retrospective studies performing multivariate analysis did not demonstrate a beneficial effect on success rates in this regard. Clinical assessment of perfusion via capillary refill of the perianal skin should be performed by observation of color and gentle compression, since the main cause of failure is an inadequate blood flow in the flap.

Conclusions

Treatment of complex fistulas is challenging and carries a high risk of poor wound healing and continence impairment due to iatrogenic injury of the sphincter complex. Proper management requires a detailed understanding of perianal anatomy, knowledge of the extent of the disease and its relation to the various structures. In all sphincter-sparing advanced soft tissue flap techniques, controlling sepsis before any attempt at definitive repair is essential. Therefore, seton drainage prior to advancement flap repair is of significant importance. Furthermore, the creation of a broad based, well vascularized, tension free flap, de-epithelialization of the fistula tract and excision of the internal opening of the tract are essential steps in these type of procedures. Sphincteroplasty can be an appropriate approach in some cases, especially when preoperative incontinence is present. However patient selection should be prudent, and careful description and detailed informed consent in these advanced techniques is critical.
References


