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Updates in Fistula-in-Ano. A Narrative Review

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Abstract

Background: Anal fistula is a challenging disease with a high incidence that affects mainly young people. The aim of this narrative review is to evaluate the recent data regarding the pathogenesis, diagnosis, and treatment of anal fistula patients.

Data sources: The following databases were searched: MEDLINE, Pubmed, Scopus, Cochrane. Relevant articles were selected.

Conclusions: There is a need for better standardization of classifications, measurements, and outcomes. Fistulotomy and fistulectomy are simple and fast with good results in simple fistula. Modern sphincter-sparing techniques are more demanding, and sometimes costly, but there is less risk of incontinence.

Keywords: anal fistula treatment.

Introduction

Anal fistula is defined as a chronic abnormal communication between the epithelialized surface of the anorectal canal and, usually, the perianal skin. Hippocrates made the first reference for fistulous disease, and he was also the first to advocate the use of a seton (from the Latin *seta,* meaning "bristle") in about 430 BCE.[1]

With a variable annual incidence affecting 8.6-10/100 000 people and a prevalence for whole etiologies (cryptoglandular, Crohn's etc.) of 1.69 per 10,000 population in the European Union, fistula-in-ano (anal fistula, perianal fistula) is a common cause for surgery.[2-3] The condition, having a peak between the third to fifth decade of life is prevalent in males.[4]

Carrying the risk of recurrence and fecal incontinence, anal fistula negatively impacts the quality of life of the patient and is a challenge for the surgeon. There is no clear consensus about the optimal surgical procedure. There is also high heterogeneity in outcome selection, definition, and measurement in studies assessing the treatment of cryptoglandular anal fistula.[5] The aim of this narrative review is to evaluate the recent data in pathogenesis, diagnosis, and treatment of an anal fistula.

Method

A literature search of the last 5 years was performed. The following databases were searched: MEDLINE, Pubmed, Scopus, Cochrane. The search terms included:

"anal fistula," "anal fistula treatment," "fistula-in-ano," "VAAFT," "LIFT," and "Laser closure." Relevant articles were screened, and from a total of 144 titles, the selection included 59 observational studies and 19 randomized controlled trials. Relevant articles prior to the search period were also taken into review.

Pathogenesis

The etiology is not completely understood; however, the most accepted theory is the crypto-glandular theory, initially proposed by Parks.[4-5] According to this theory, glandular infections arise from the anal crypts communicating with anal proctodeal glands situated in the intersphincteric space. Dilated glands, which terminate deeper discharge between muscular fibers of the external anal sphincter, or through the external anal sphincter into the ischioanal fossa, will result with anal fistula. This may explain why some of perianal abscesses are associated with anal fistula from the beginning, although anal fistula is considered the chronic phase of intersphincteric anal gland sepsis.[7] Anorectal infection is responsible for 80-90% of the anal fistula.[7] Between 30-70% of the patients with anorectal abscesses present concomitantly with a fistula.[8] More than one third of those who do not present with this condition will be diagnosed with an anal fistula in a period of months or years after abscess drainage.[8-9] Less frequently, hemorrhoidectomy, foreign body perforation, and trauma are responsible. Other causes (e.g., Crohn's disease, radiation, tuberculosis etc.) should be thought in suspicious as well when looking at anal fistula, and are at the origin of the remaining 10-20% of the cases.

Some characteristics of anal fistulas cannot be explained by cryptoglandular theory (e.g., many abscesses do not result in a fistula, the prevalence in male patients, the absence of epithelization, and the presence of granulation tissue in most of the fistula tracts).[7-8]

Classification

The Parks classification is the one mostly utilized.[12-13] This system is based on the relationship of the fistula tract to the sphincter, which describes four types of anal fistula with various subtypes. Another two types of classification were added in the current classification (see below):

1. Intersphincteric - the fistula tract ramifies only in the intersphincteric plane; it is the most common of all types, accounting for 55-70% of the cases (45% in the study of Parks).[1,12,15] This can be further classified as:
   a. Simple intersphincteric, where the fistula tract in the intershincteric plane passes downward to the anal verge. It is the most frequent subtype of in- tersphincteric anal fistula; it is considered a low anal fistula.
   b. Intersphincteric fistula with a high blind tract.
   c. Intersphincteric fistula with a high tract opening into the lower rectum.
   d. High intersphincteric fistula without a perineal opening.
   e. High intersphincteric fistula with a pelvic extension.
   f. Fistula from pelvic disease.

2. Transsphincteric – the fistula tract passes from the intersphincteric plane through the external sphincter complex at varying levels into the ischiorectal fossa (25-30% of the cases). It can be:
   a. Uncomplicated
   b. With a high blind tract

3. Suprasphincteric - the tract passes in the intersphincteric plane over the top of the puborectalis muscle, then downwards again through the levator plate to the ischi- orectal fossa, and finally to the skin. Although this type was observed by Parks et al. in 20% of the cases in their series, it is rarely reported today (1-3%).[1,15] This is further subdivided into:
   a. Uncomplicated
   b. With a high blind tract

4. Extrasphincteric fistulas are very rare (1-5%). The fistula tract passes from the perineal skin through the ischiorectal fat and levator muscles into the rectum. It is usually the consequence of trauma or pelvic diseases (e.g., Crohn's). It can be further classified as:
   a. Secondary to transsphincteric fistula
   b. Secondary to trauma
   c. Secondary to anorectal disease (e.g., Crohn's disease)
   d. Secondary to pelvic inflammation

5. Combined

6. Horseshoe – which can occur in up to 4,4% of the cases.[16] It can be:
   a. Intersphincteric
   b. Transphincteric

Some authors add submucous (subanodermal) fistula as another type of anal fistula. In this case, the tract run under the anoderm or the rectal mucosa without any involvement of the sphincter.[18] Others consider this type a misnomer.[1,6]

In Japan, the Sumikoshi classification is more commonly used. In this classification, the space above the dentate line is referred to as high (H); below the dentate line is defined as low (L). Multiple or curved tracts are complex and the letter C is assigned; straight tracts are simple and signified by the letter S. The U letter is used for tracts that extend on one side (unilateral), whereas tracts on both sides are bilateral, and signified with the letter B.[14]

Anatomically, anal fistulas can be described as low or high depending on their relationship with the sphincter complex. There is some inconsistency in defining an anal fistula as high. In the classic study of Parks, a high anal fistula passes over the anorectal ring (puborectal muscle). In the consensus statement of the Association of Coloproctologists of Great Britain and Ireland (ACG-BI), a high intersphincteric fistula is defined as a fistula that passes deep to more than 50% of the length of the internal sphincter.[6] High transsphincteric, suprasphincteric, and extrasphincteric fistulas defined as such pass deep to more than 30% of the external sphincter.[4,8]

Fistulas that pose a high risk for incontinence are termed complex. A complex fistula- in-ano is defined by one of the following[18]:

- when the track crosses, > 30–50% of the external sphincter (high transsphincteric, suprasphincteric or extrasphincteric).
- is anterior in a female.
- is recurrent.
- has multiple tracts.
- the patient has pre-existing incontinence, local irradiation, or Crohn's disease.

Diagnostic

Clinical assessment

Pain, swelling, and discharge are the common complaints of patients with anal fistula. Many patients with fistula have a prior history of an abscess. Sometimes the discharge stops because the fistula opening is temporarily closed with a thin layer of epithelium. The fistula then reopens, with secretion occurring again. In rare cases, anal fistula may be seen in anorectal carcinoma, or an anal or rectal cancer can mimic a fistula[19-22]; although there are few cases reported, the examiner should be aware of the possibility.

The patient should be examined on a tilt table in the knee-chest position, or Sims. Visual inspection will generally identify the opening of the fistula. When the external opening is adjacent to the anal margin, it suggests an intersphincteric tract. A more laterally located opening would suggest a transsphincteric fistula. The further the distance of the external opening from the anal margin, the greater the chance of a complicated upward extension. Rectal examination with a bi-digital palpation may determine the primary opening and the fistula tract. Probing should be done gently, never forced, to avoid creating a false tract. Sometimes the angulation or stenosis of the tract precludes passing a probe. If infection/inflammation is present, the maneuver should be done under anesthesia where a therapeutic intervention will be performed (examination un- der anesthesia – EUA).

In general, the internal opening will be found at anoscopy at the level of the dentate line. Gentle pressure on the fistula track may result in discharge of pus from the primary opening. As Goodsall's rule states, when the external opening lies anterior to the transverse plane, the internal opening is located radially most of the time. When the external opening is posterior to the plane, the internal opening is generally (not always) in the posterior midline. A recent prospective study with a total of 188 patients found a predictive accuracy of 84.6% in case of a fistula with an anterior external opening.[23] In those with a posterior external opening, this was found to be 69.1% accurate with an overall predictive accuracy of Goodsall's rule of 77%.[23] As demonstrated, this rule should be used as guide to help the surgeon to find the tract and it is not absolute.[1,23]

Imaging

Most of the time, clinical examination is sufficient in primary anal fistula seen for the first time. Nevertheless, in complex fistulas, recurrent ones, or after multiple perianal procedures, imaging is necessary. From a practical standpoint, an imaging method should help in classifying the fistula, visualizing the tract and its secondary extensions, the relationship with the sphincter apparatus (its involvement), and to identify the internal opening. Historically, the following methods were used to attain the stated objectives:

- Fistulography – is a radiological study visualizing the fistula tract by injecting a few ml of a hydrosoluble contrast agent. It is seldom used today as it

does not give clear tridimensional anatomical information about the fistula tract in relationship with anatomical structures, mainly the sphincter. This method has a 10% rate of false-positive results, and an accuracy of only 16% in identifying the internal openings and secondary extensions. [24]

- Computed tomography (CT) - with administration of contrast intravenously, intrarectally, orally, or by injection through the fistula tract is helpful in high fistula (pelvic or supralevatorian) is superseded today by MRI or endoanal ultrasonography. With an accuracy rate between 24–60% and the burden of radiation, CT is rarely used today.[24] CT with intravenous contrast is sometimes still performed where MRI

and/or anal US is unavailable, or in an emergency setting.[25] In these acute situations, CT-scan may provide useful information about a pelvic infection.

- Ultrasonography - endo-anal ultrasonography (EUS) in anal fistulas was described first by Bartram et al. and the accuracy of the early studies was between 63-87%.[6,26-27] Using 3-D mode further improved the accuracy to 91-96% in experienced hands.[28-29] 3D-EUS is a reliable technique usually performed in left lateral decubitus position, although prone position or lithotomy position can also be used.[30-31] It can accurately classify fistulas and report the primary tract, the location of the internal opening, and the relation of the fistula to the anal sphincter muscles. In a prospective study of 196 cases with anal fistula comparing the clinical and functional outcome (incontinence), the usefulness of 3D-EUS was validated.[28] With a follow-up of up to one year in the two matched subgroups, one group with 3D-EUS and the other with clinical examination under anesthesia, Ding et al. demonstrated a statistical reduction of the recurrence rate in the EUS subgroup (8.8% vs. 13.8%).[28] The difference was even more signif icant in patients with complex fistulas (12.8% vs. 22.5%).[32] Additionally, a significant decrease in continence was found after one year in patients that were not evaluated with EUS.[32] Due to the high frequency used for EUS (between 7-10 MHz), the loss of resolution is important farther away from the transducer; this limits the value of EUS in visualizing secondary extensions, the ischioanal and ischiorectal region, and the supralevator area. Also, because of fibrosis and sclerosis encountered in recurrent fistulae, EUS is of limited help. Using hydrogen peroxide or a contrast agent injected through the fistula opening can enhance imaging in EUS thus better displaying the fistula tract.[25,27] In a very recent study, ultrasound with contrast media producing acoustic scattering of microbubble to enhance contrast was compared with standard MRI in 98 patients.[33] Both methods exhibited similar accuracy, but the accuracy of contrast perineal ultrasound was better than MRI for identifying an internal opening under 3 cm from the anal verge.[33] Still, hydrogen peroxide has the advantages of availability and cost as compared with any other contrast media. As an alternative to EUS, transperineal ultrasonography (TPUS) showed comparable, or even better than, EUS results in defining and classifying anal fistulae.[34] In an early study comparing EUS and TPUS in patients with perianal Crohn's disease, with EUS as the reference standard, TPUS had a sensitivity of 84.9% and a positive predictive value of 86.5% for anal fistulas and was of similar value as EUS for the diagnosis of anorectal abscess.[35] In another recent systematic review with a meta-analysis evaluating transperineal ultrasound (TPUS), the pooled results for perianal fistula identification showed a sensitivity of 98% and a positive predictive value (PPV) of 95% (95% CI 83–98%).[36] In the same review, the usefulness of TPUS for perianal fistulae classification has been found with a pooled sensitivity and a PPV of 92%.[36] The sensitivity for the classification of fistulae was higher when the comparator was examined under anesthesia (98%) rather than transrectal ultrasound or MRI (87%). A drawback of this review was the significant heterogeneity among the six studies included in the review.[36] TPUS has several important advantages in the diagnosis and classification of anal fistula, such as: relative ease of use, minimal discomfort, cost-effectiveness, relatively non-time consuming, and widely available in the clinical setting. Although recent data are encouraging, there is still no consensus about its use in perianal fistula. A common limitation for both EUS and TPUS is that they are both operator dependent.

- Magnetic resonance imaging - it is considered the "golden standard," and has the advantage of not being user-dependent for interpretation, as well as the ability to evaluate fistula tracts that course distant

(less than 4 weeks); and an associated stricture of the anorectum are relative contraindications to the rectal advancement flap.[47] Different forms of flaps (rhomboids, elliptical) are utilized by different authors without evidence of better results.[53] There is data showing that increasing the thickness of the flap improves the healing rates. The healing rate of endoanal advancement flap ranges between 68-87%.[54] In cases of failure, the procedure can be repeated.[7,47,55] Interestingly, patients with anal fistulas with and without Crohn's disease exhibit the same healing rate.[56]

Video-assisted anal fistula treatment (VAAFT)

Video-assisted anal fistula treatment is one of the sphincter-sparing procedures. VAAFT was described by Meinero and Mori in 2011, and has a diagnostic phase and a treatment phase.[57] Closing the internal opening is essential for success; it can be performed with a stapler, suture, or a flap (mucous or cutaneous). Initial results in 136 patients with anal fistula showed primary healing in 73 patients (73.5%) in the following 3 months after the procedure. No healing was found in 26 patients (26.5%).[57] Further reinterventions were executed and VAAFT was implemented again. At 12 months, the authors reported a healing rate of 87.1%.[57] Compared with FiLAC (Fistula Laser Closure (FiLaC™), the advantage of the procedure is that it is performed under direct vision.

During the reviewed period, 9 observational studies were found to meet the search criteria. Data from these studies is presented in tables 2 and 3. The healing rate of VAAFT was between 51-89.5%, and the recurrence rate was between 11.5 - 35% (tables 2 and 3). There were differences among the studies regarding the operative phase of the procedure, particularly the treatment of the internal opening (table 2). While heterogeneity of the studies is evident, the pooled healing rate was only 81.2%, and the reported rate of complications was 10.7%. Most complications were grade 1 on the Clavien-Dindo scale, although there were also grade 2 and even grade III type complications reported (table 3). Scrotal/perineal oedema or bleeding were the most severe reported complications.

In a very recent randomized control trial, Sorensen et al. compared VAAFT with fistulectomy and sphincter repair (FSR) in terms of wound healing, functional outcome, and quality of life.[58] Due to the high recurrence in both groups (65% for VAAFT and 27% for FSR), the study was terminated early.[58] It would seem that VAAFT fails to increase the healing rate in complex anal fistulas. It is also worth noting that in cases of VAAFT, there is a minimal risk of incontinence.

Fistula Laser Closure (FiLaC™)

FiLaC as a novel sphincter-preserving technique closure of the fistula tract using laser ablation was first published in 2011 by Wilhelm.[59] In this first study, healing occurred in 9 of the 11 patients involved the study (81.6%).[59] In the FiLaC procedure, the fistula tract is destroyed using a radial-emitting laser fiber. It can be combined with an additional method to close the internal orifice. Laser fistulectomy has increased in popularity due to its minimal safety issues, limited side effect profile, and short learning curve; however, the results are still subop timal in some studies (see table 4).

Ten studies were included in the present review (table 4). Overall, 623 patients were included, from which only 38 had Crohn's disease (6%) and 468 (74.5%) had previous surgery. The extremely variable primary healing rate was between 22-74.7% (table 4). The overall heal ing rate attained a maximum of 88% in the study of Wilhelm et al. with a follow-up of five years.[60] In the same study, a total rate of complication of 7.7% was also noted. Similar to other studies analyzing anal fistula treatment, the heterogeneity and the selection of the cases made interpretation of the results difficult. Moreover, there were differences in techniques among different groups in terms of power delivered (between 10-14 W), the speed of retracting the fiber, and the usage of different types of probes. Some authors consider that healing rates are better when the internal opening is closed, which tends to be the norm.[60] Others refut e this theory.[61] It may well be that the reason for such variety in the healing rates is the length of the fistula tract, as demonstrated by Lauretta et al.[62] In their retrospective observational study of 30 patients using a length of 30 mm as a cutoff, the shorter fistulas had a significantly better prognosis: 58.3% (7 out of 12) for fistulas shorter than 30 mm and 16.6% (3 out of 18) for fistulas longer than 30 mm.[62] In a recent systematic review and meta-analysis, the pooled success rate of the technique was 63%, and the pooled complication rate was 8%.[63] It can be concluded that FiLaC™ has success rates comparable to other sphincter-sparing techniques. The technique is safe with respect to adverse events and risk of incontinence, though it has no significant advantage over other methods that have been demonstrated up until now.

Ligation of the intersphincteric fistula tract (LIFT)

The LIFT technique starts with an incision along the intersphincteric groove, and meticulous dissection is performed to identify the fistula tract. This is ligated, and the fistula and the tissue of the fistula wall is cut and cleared in this way in order to eliminate the septic focus. It is considered appropriate for transsphincteric fistulas, including most complex anal fistulas, recurrent, and fistulas that fail after other surgical procedures.[51] Rojanasakul et al. introduced the LIFT technique as a cost-effective sphincter sparing method in 2007.[64] In a more recent study from the same center assessing the experience with LIFT over 10 years, the healing rate was 87.7%.[64] In a recent systematic review and meta-analysis, Emile et al. focused on a total of 1376 patients with a follow-up of one year and found an overall success rate of 78% (1075 patients) for LIFT and an incontinence rate of 1.4%, all but minor.[65] Horseshoe fistula, fistulas associated with Crohn's disease, and a history of previous fistula surgery were associated with a greater incidence of persistence or recurrence after LIFT.[65] It must be pointed out that, in the same study, the weighted mean complication rate was 13.9% higher than previously thought. The most common complications after LIFT were dehiscence and infection.[65] Leaving the wound open may avoid these complications. Based on their data, the conclusion of the system atic review concluded that LIFT had a better success rate and less complications than the rectal advancement flap technique.[66] In the recent randomized controlled trials presented in this review, the healing rate of LIFT was between 77.5-93.3% (table 5). Different modifications of the LIFT procedure were also proposed. Chen et al. used a lateral incision to access the intersphincteric groove in 10 patients.[67] In this modification, after dissection, the proximal end of the fistula was clamped above the external sphincter, and the distal portion was removed for pathological examination. The stump is ligated with a resorbable thread. The advantage of this approach is is a better view of the dissection.[67] Using the same approach, Kang et al. attained a healing rate of 75% (21 patients from 28).[68] One other modification of the LIFT procedure consisted of associating an advancement flap to the LIFT. The only report addressing this technique found a lower healing rate, primary or secondary to the original LIFT procedure.[69] Another modification focused on associating a bioprosthetic (resorbable) material in the intersphincteric plane to buttress the closure of the intersphincteric tract, also known as Bio-LIFT, originally described by Ellis et al.[70] Nonetheless, this procedure is expensive and requires a more extensive dissection in the intersphinc teric space than is usual for the LIFT. Another modification of LIFT plus plug was performed by Han et al. and involved the excision of a section of fistula tract in the intersphincteric space.[71] Then, the bioprosthetic plug (porcine small-intestine submucosa extracellular matrix plug) is placed into the fistula tract through an opening in the external sphincter to the external opening in the skin. In their randomized controlled trial, the rate of success for the modified procedure was 94% compared with 83.9% for simple LIFT.[71] In another retrospective cohort comparing BioLIFT with the LIFT procedure, Zwiep et al. found that the primary healing rate was 75% versus 58.7%, and the complication rate was 22.7% versus 17.3% in favor of the former.[72] Madbouly et al. recently combined injecting autologous platelet plasma rich with the LIFT procedure.[73] Their results showed a better healing rate for the modified LIFT procedure (77.5% vs. 59% - table 5). The LIFT procedure remains an adequate option as a sphincter-sparing procedure in anal fistulas. One advantage of LIFT could be understood as the downstaging of the fistula from transsphincteric to intersphincteric, which seems to take place in a proportion of failures.[47] This allows for a simpler treatment, thus preserving the external sphincter which would have been involved originally.

Anal fistula plug (AFP)

Another sphincter-sparing technique is an anal fistula plug. A variety of materials, bio-prosthetic or synthetic materials, are used to occlude the fistula track (human acellular dermal matrix, porcine dermal collagen etc.), by blocking the internal opening.[74] In this way, fecal material cannot enter the fistula tract to promote healing. Existing data do not demonstrate a better healing rate for this procedure. In a randomized controlled trial accruing a total of 304 patients, Jayne et al. found clinical healing rates associated with the fistula plug and surgeon's preference groups to be 54% and 55% at the 12-month follow-up, respectively.[75] Additionally, there were higher costs and highly uncertain quality-adjusted life-year (QALY) gains associated with the fistula plug.[75] In a systematic review comparing the rectal advancement flap and anal fistula plug procedure after pooling RCTs with long term follow-up, found that in the treatment of complex cryptoglandular anal fistulas, the RAF was superior to AFP in terms of heal ing and

recurrence rate.[76] Plug dislodgement or sepsis are the most common causes of fail ure. A variant of the plug for anal fistula is filling the fistula tract with material that will block communication of the fistula tract with the anorectum and promote healing. Fibrin glue was the first material to be used. The healing rates with fibrin glue are extremely variable, ranging between 14% to 94%.[47] Other filling materials were tried, including platelet-rich plasma, autologous cartilage, fat, autologous micro-fragmented adipose tissue, alginate, and allogeneic bone marrow-derived mesenchymal stromal cell.[51,77] There are high rates of recurrence with filling therapy, although there are differences among the different types of materials used. There is no strong evidence supporting these methods.

OTSC®(Over-the-Scope-Clip) Proctology Device

The OTSC™ Proctology system (Ovesco Endoscopy AG, Tuebingen, Germany) consists of a clip and applicator, and is a modification of the endoscopic OTSC™ clip, which is made of a super elastic shape memory alloy (Nitinol). When the opened clip is released from the applicator tip, it automatically closes and exerts constant pressure on the tissue between the jaws of the clip. When applied on the internal fistula opening, the clip compresses and seals the orifice. In this way, the fecal content from the rectum is blocked from entering the fistula tract maintaining the sepsis. It is considered a sphincter-sparing minimally invasive procedure. The possible migration of the clip and postoperative abscesses are the specific possible complications for this procedure.[78] In one of the first studies of this method reported that the healing rate was only 18%.[78] In another more recent study, the OTSC™ Proctology system attained a healing rate of 80%.[79] In the only review of this method (over 200 cases), the healing rate was 63% [80] Besides being a minimally invasive procedure and a sphincter sparing one, closing the fistula with this special clip has the advantages of repeatability as well as a short operative time; however, further studies are needed to determine the advatages.[80]

New procedures

New surgical treatments for anal fistulas were proposed by Garg et al.[15,81] The first procedure consisted of proximal superficial cauterization, regularly emptying fistula tracts and curettage of tracts (PERFACT, as was named by the author) procedure, and initially displayed a healing rate of 86%, which later dropped to 50%.[15] Subsequently, the same authors proposed transanal opening of intersphincteric space (TROPIS) for high complex fistulas.[15] Transanally, the internal opening and the intersphincteric portion of the fistula tract were both laid open into the anal canal. The resulting wound was left open to heal by secondary intention. The external tracts were curetted, and a drainage tube was placed in the cleaned tracts from the external opening up to the lateral border of the external sphincter. Healing occurred in 86% and recurrence in 14%.[15] The data was determined from a single center TROPIS procedure and was not replicated by others until now.

Conclusion

Further standardization of definitions, classifications, measurements, and outcomes in anal fistula are needed. Tailoring the treatment is still the best strategy to get optimal results. Fis tulotomy and fistulectomy are simple, fast, and provide adequate results in simple fistula, but with a higher risk of incontinence. Associating marsupialization improves the healing process. Sphincter-sparing techniques can be more technically demanding, and therefore operating time can be longer, but with less risk of incontinence. Despite technological advances and increasing cost of treatments, the search for the ideal treatment of anal fistula continues.

Conflict of Interest Disclosure Statement

The author reports no disclosures.

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Table legends

Table 1 – Recent studies assessing VAAFT in anal fistula (number of patients, type of fistula and internal opening closure type)

Table 2 – St James's University Hospital classification (42)

Table 3 – Recent studies assessing VAAFT in anal fistula (number of procedures and results)

Table 4 – Result of fistula laser closure (FiLaC) in recent studies

Table 5 – Recent randomized controlled trials (RCT) where LIFT procedure was compared or used as comparator.

Table 1

Fistula grade	Description
Grade I	Simple linear intersphincteric fistula
Grade II	Intersphincteric fistulas with abscess or secondary track
Grade III	Trans-sphincteric fistula
Grade IV	Trans-sphincteric fistula with abscess or secondary track within the ischiorectal fossa
Grade V	Supralevator and translevator fistula

Table 2

Authors	No. patients	Types of anal fistula	Patients with Crohn's disease	Previous surgery	Closure of the internal opening
Chase et al. (82)	84	complex	11 (13%)	66 (78%)	Vicryl suture or mucosal flap
Zhang et al. (83)	57	complex	-	24 (42%)	Anal fistula plug
Zhang et al. (84)	26	horseshoe	-	14 (54%)	Anal fistula plug
Zelic et al. (85)	73	complex	-	19 (26%)	17 - RAF 16 - matress suture 14 - LIFT
Giarratano et al. (86)	72	complex	-	18 (25%)	matress suture
Regusci et al. (87)	104	complex	-	25 (24%)	stapler
La Torre et al. (88)	28	high trans- sphincteric	-	3 (11%)	suture
Liu et al. (89)	64	complex	-	36 (53%)	suture
Jiang et al.	52	complex	1 (2%)	31 (60%)	Suture (2 with stapler)
Total	560		12 (2.1%	236 (42.1%)	

Table 3

Authors	No. of VAAFT	Repeat VAAFT	Complications Clavien-Dindo grade	Healing	No improvement / worse /recurrence	Follow-up
Chase et al. (82)	105	21	7 (6.7%) grd. II and IIIb	19 (23%) and 34 (38%) symptoms improvement	29 (38%)	6 months
Zhang et al. (83)	57	-	Not reported	51 (89.5%)	6 (10.5%)	6-50 months
Zhang et al. (84)	More than 26	2 patients needed more than 3 procedures	Not reported	23 (88.5%)	3 (11.5%)	6 months
Zelic et al. (85)	83	16	1 (1.4%) - grd. III	62 (85%)	11 (15%)	24 months
Giarratano et al. (86)	77	5	8 (11%) - grd. I	64 (86%)	8 (14%)	12 months
Regusci et al. (87)	120	16	9 (8.6%) - grd. I 4 (3.8%) - grd. II	80 (83.3%)	24 (16.7%)	36 months
La Torre et al. (88)	28	Not stated	4 (14%) - grd. I	24 (86%)	4 (14%)	1-6 months
Liu et al. (89)	64	-	2 (3%)	54 (84%)	10 (16%)	3 months
Jiang et al.	52	8 patients needed more than 3 procedures	25 (29%)	44 (85%)	8 (15%)	9 months
Total	586		60 (10.7%)	455 (81.2%)	103 (18.4%)	

Table 4

Author	No. patients	Crohn's disease patients	Previous surgery before FiLaC	Primary healing rate	Overall healing rate	Follow-up - months	Complications
Nordholm- Carstensen A et al. (90)	66	11 (16%)	28	64.7%	44.1%	26	1 (1.4%)
Giamundo P et al. (91)	175	-	150	117 (66.8%)	129 (73.7%)	4.8-87.6	17
Wolicki A et al. (92)	83	2 (2.4%)	76 (91.6%)	62 (74.7%)	64 (78.3%)	13-84	18
Brabender DE et al. (93)	18	4 (22%)	15 (83.3%)	22%	4 (22%)	18-46	3 (16%)
Serin KR et al. (61)	35	-	8 (38%)	na	15 (42.9%)	6-17.6	na
LaurettaA et al. (62)	30	-	22 (73.3%)	10 (33.3%)	12 (40%)	6-24	4 (13%)
Stijns J et al. (94)	20	-	4 (20%)	4 (20%)	6 (30%)	10	4 (20%)
Marref I et al. (95)	69	6 (8.7%)	37 (54.4%)		31 (45.6%)	4.2-9.3	na
De Hous N et al. (96)	10 (15 fistulas)	2	15 (100%)	10 (67%)	12 (80%)	4-26	na
Wilhelm A et al. (60)	117	13 (11.1%)	113 (96.6%)	75 (69.2%)	103 (88%)	25.4	1 (0.8%)
Total	623 (628)	38 (6%)	468 (74.5%)	324 (52%)	405 (65%)		48 (7.7%)

na - not available

Table 5

Authors	Type of fistula	Trial design	No. of patients	Comparator	Primary healing rate/overall healing rate LIFT	Healing rate comparator	Follow-up months
Wu et al. (97)	Parks type 2	RCT	60 (30/30)	Fistula thread closure	-/29 (97%)	27 (90%)	12
Madboulyet al. (73)	trans-sphincericfistulas involv- ing>50% of the sphincter	RCT	98 (49/49)	LIFT+ platelet-rich plasma	32/29 (65%/59%)	42/38 (85.7%/77.5%)	12
Dong X et al. (98)	Simple fistulas	RCT	100 (50/50)	fistulectomy	-/48 (95.56%)	42 (82.2%)	na
Han JG etal (71)	High transsphincteric fistulas (involv-ing>30% of theexternal sphincter	RCT	235 (118/117)	LIFT+ biopros-thetic anal fis-tula plug	98 (83.9%)	109 (94%)	9
Al Sebai et al. (99)	Transsphincteric fistulas	RCT	30 (15/15)	Fistulotomy	12 (80%)	14 (93.3%)	6

na - not available