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Review article

Anal Fistula of Crypto-Glandular Etiology: A Review of the Literature with a Step-by-Step Approach for Diagnosis and Surgical Management

Anestis Charalampopoulos [*1], George Bagias [1], Georgia Bompetsi [1], Kostantinos Nastos [1], Savvas Papagrigoriadis [2], Dimitrios Papaconstantinou [1]

[1]3rd Department of Surgery, Attikon University Hospital, National and Kapodistrian University of Athens, Athens,12462, Attiki, Greece.
[2]Department of Surgery, Metropolitan General Hospital, Athens, 15562, Attiki, Greece.

[*]Corresponding Author: Anestis Charalampopoulos; Associate Professor of General Surgery, National and Kapodistrian University of Athens, Medical School, 3rd University Surgery Unit, Attikon University Hospital of Athens, Greece; *achalaral@med.uoa.gr*

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Abstract

Background: Anal fistulas of crypto-glandular etiology, either simple or complex are common benign surgical conditions. The main treatment is surgery. There is a variety of surgical innovative anal sphincter- saving procedures that are used in the treatment of anal fistulas. ***Methods:*** We conducted an extensive review of the literature and tried to cite the most recent publications for anal fistulas. Pub Med and Google Scholar databases were searched for studies related to anal fistulas between 1970 and 2022.Clinical examination and MRI are the main assessment methods of the complexity of anal fistulas and the presence of risk factors related to fail of surgery. Surgical outcomes, complications, and recurrence rates for the most common therapeutic procedures were identified. ***Results:*** Simple fistulas are the most common fistulas, treated by fistulectomy or other sphincter sparing techniques with high healing rates of 90%, minor postoperative complications and low recurrence rates. Complex fistulas have more difficult management, optimal surgical outcomes are obtained in 30-80%, and rate of recurrence is higher than in simple fistulas, which results in many patients requiring a second operation. Transphincteric and suprashpincteric fistulas are the most common complex fistulas, more complex fistulas are the supralevator ones or those with long extraspincteric fistulous tracks. The latter are rare in the literature and present difficult surgical management and poor outcomes. ***Conclusions:*** Simple fistulas have excellent surgical outcomes. Complex fistulas present more recurrences, but several sphincter-sparing techniques may achieve eventual complete healing, despite recurrences and reoperations. Modern innovative sphincter- saving techniques play an important role in the treatment of simple and complex anal fistulas.

Keywords: ***anal, fistula, surgery, simple, complex***

Introduction

Anal fistula is a chronic anal condition, resulting from an either spontaneous or surgical drainage of an anal abscess. The formation of an anal abscess is caused by inflammation of the anal glands; this old theory is known in the literature as crypto-glandular theory. This is the most common etiology for the formation of an abscess/ fistula and the pathogenesis is under study [1]. Other causes are inflammatory bowel disease, radiation in the anal-perianal area and trauma. Anal fistula is considered an evolutionary stage in the natural history of the anal abscess and this evolution is not influenced by the use of antibiotics [2]. Anal fistula is characterized by; a) an external opening: located in the perianal skin, b) the fistulous track of various lengths and route affecting the anal sphincter system and c) the internal opening: located mostly at the dentate line and mainly when the anal fistula is crypto-glandular.

Anal fistula is considered a rare condition, and in recent reports presents a prevalence of 1.7-2.3 cases/10.000population [3], affecting middle age patients with a male to female ratio 2:1

Classification systems of anal fistulas

The first classification system was proposed by Parks AG et al. in 1976 [4], describing four main types of fistulas; intersphincteric, transphincteric, extrasphincteric and suprasphincteric with reference to other more complex conditions. It was a surgical classification attempting to associate the relation of fistulous tract with the anal sphincter system with emphasis to the coronal plane. The relationship of anal fistula with the anal canal is obtained by MRI imaging in axial and coronal planes and additional data regarding the existence of secondary tracks and anal abscesses may be obtained. The first MRI classification, was the St James's University Hospital classification modified from Spencer et al. in 1998 with predictive value of MRI for the postoperative outcomes [5] incorporating findings of abscess/sepsis in imaging MRI. This classification describes five grades of anal fistulas as follows; ***Grade 1:*** Simple linear intersphincteric fistula; located between internal and external anal sphincter. They are the most common; the external opening of the fistula is located next to the anal verge and the internal opening is located at the dentate line. The extrasphinteric area,

ischioanal or ischiorectal is without findings. ***Grade 2:*** intersphincteric fistula with abscess or secondary track; bounded also by the external sphincter, additional horseshoe tracks may exist. ***Grade 3:*** transphincteric fistula; starting from the dentate line, traversing the internal and the external sphincter and following a route in the extrasphincteric area in the ischiorectal/ischioanal fossa, terminating with an external opening at the perianal skin apart from the anal verge. ***Grade 4:*** transphincteric fistula with abscess or secondary track in the ischiorectal fossa; the abscess occupies the ischiorectal and ischioanal fossa and local or generalized clinic-laboratory signs of sepsis may exist.

Grade 5: supralevator and translevator fistulas; they are the less common fistulas, the former is formed from the expansion of an inter-sphincteric abscess, upwards, above the levator ani muscle and below the peritoneum, the abscess remains in the extra-peritoneal space and finally penetrates the levator ani muscle, following a long extra-sphincteric fistulous track in ischiorectal and ischio-anal fossa, terminating at the perineal skin quite far from the anal verge. The latter fistula known as translevator fistula originates from the intra-abdominal/pelvic areas and results from severe intrapelvic sepsis/abscess, this fistula is not of cryptoglandular etiology. Both entities present severe difficulties in surgical treatment.

Both systems of classification of anal fistulas refer to the crypto-glandular theory, where infection from the inter-sphincteric space may spread to other anatomical spaces of anal and perianal area. The Parks classification system, despite being old, is irreplaceable in the daily practice as it classifies the majority of fistulas. Simple local and superficial fistulas in the peripheral anal canal were not included, and thus a recent modification [6] incorporates superficial simple fistulas (or submucosal) of the anal canal, describing 4 types of fistulas; Parks type 1: this is the inter-sphincteric fistula. Parks type 2: this is the trans-sphincteric fistula containing a segment of internal and external anal sphincter. Parks type 3: this is a supra-sphincteric fistula and a long fistulous tract which affects the entire anal sphincteric system; the internal anal sphincter, intersphincteric space, levator ani muscle, ischio-rectal and ischio-anal fossa. Parks type 4: this is a long extrasphincteric fistula with internal opening at the rectum and not at the dentate line, which crosses the supralevator space, lavator-ani muscle, ischiorectal and ischio-anal fossa terminating at the buttock skin.

The improvement in MRI techniques, allowed recently the identification of a new anatomical pathway of spread of infection in a recently recognized anatomical space called “outer-sphincteric space”, between the external anal sphincter and its fascia. The inflammatory collection progresses along this space, in a parallel route to the inter-sphincteric space, without the ability to extent in the supralevator space, to be drained into the intra-anal canal and may probably forms a trans-sphincteric fistulous tract [7]. The surgical anatomy of the anorectal canal and the main types of cryptoglandular anal fistulas are shown in the figure of the text.

Simple and complex anal fistulas

The modified Parks classification and MRI imaging may differentiate two distinct groups of fistulas; simple fistulas, treated by surgery and fistulotomy, this is a safe and easy surgical operation, with excellent postoperative outcomes and extremely low rate of recurrences. Thus, in modified Parks classification system superficial fistulas, type 1 and 2 are considered simple; those transphincteric ones (type 2) should contain less than 30% of external anal sphincter named as low transphincteric fistulas (the term low intersphincteric fistula is also in use). All other fistulas are characterized as complex with a higher index of recurrence and increased possibility for incontinence [8]. An accurate clinical classification of fistula, determines the surgical therapy options.

Recurrences after surgery of anal fistula

Most fistula recurrences appear a few months and up to a year after surgery. In the literature numerous risk factors for recurrence have been identified and those can be categorized into preoperative, intraoperative or postoperative factors [9]. In a recent meta-analysis [10], the most important risk factors for recurrence were the presence of a high trans-sphincteric fistula, missing an internal opening non-found during surgery and horseshoe fistulas (high-quality evidence). Other risk factors such as prior surgery, seton placement and multiple fistula tracts were estimated. Recurrence rates range according to the type of fistula from 2.5% in simple fistulas up to 57% in more complex fistulas. Advances in MRI imaging, allow the identification of factors affecting of healing after surgery and in combination with clinical parameters the risk of recurrence may be calculated; recently a new scoring system to predict recurrences was performed 3 months after surgery, based in 4 MRI variables and 2 clinical variables: In MRI the healing or not of the internal opening, of the inter-sphincteric fistulous tract, of external tract in ischiorectal fossa and the presence/lack of a new abscess in inter-sphincteric space postoperatively, are considered risk factors for recurrence. In fact on clinical examination, the passage or not of flatus from any external opening and the discharge or not of liquid excretions intra-anally or via an external opening are important factors to estimate the risk of recurrence [11].

Clinical signs of anal fistula and clinical examination of the anal canal

A recent past history of the patient is important and compatible with a drained anal abscess and sometimes a history of previous anal surgery for anal fistula reveals a recurrence. The patient often reports chronic or attenuated anal symptoms. Clinical examination is performed in lithotomy position and if bed equipment is not available then the left lateral decubitus position with bent lower limbs to the abdomen is preferred, thus the the anal canal is well exposed to the external macroscopic examination. An anal or perianal opening draining pus, mucus, bloody content or feaces is consistent with the external orifice of the anal fistula. Probing the fistula with an appropriate in diameter probe may determine: a) the approximate length of the fistulous tract and the route in the extra-sphincter space (ischioanal/ischiorectal fossa) or inter-sphincter space and b) the existence of an abscess cavity. Thus in the external macroscopic examination the first clinical data are obtained regarding the type of fistula; simple (type 1 or 2) or complex despite the clinical examination of anal canal is incomplete. The next step, at least in complex fistulas is to obtain preoperative MRI imaging. Complete probing of the fistulous tract at this phase should be avoided for two reasons; firstly the attempt to find the internal segment of fistulous tract, forcing the probe in anal sphincteric system creates a patient’s discomfort/pain and secondly there is the risk to create a false route with a new iatrogenic and traumatic transphincteric fistulous tract.

The next step is the examination of the anal canal and proctoscopy under general anesthesia; a very important step for the diagnosis and classification of anal fistula before the final decision making for surgical management of the fistula. Complete probing of the fistula is easier under general anesthesia and different liquids (hydrogen peroxide, methylene blue etc.) injected from the external opening/segment of the fistula may reveal the internal opening. The prediction of the direction and internal opening of the anal fistula may be achieved, applying the Salmon and Goodsall rule based on the position of the external opening; an anterior external opening, located anteriorly of the transvers anal line, during probing follows a straight radial route terminating at the anterior anal dentate line: these fistulas are considered complex fistulas mainly in women as they are low or high thickness regarding the content and participation of anal sphincter system presenting a long fistulous tract and increased recurrence rate after surgery(anterior anal fistulas). They are easily probed and more difficult to manage during surgery. An external opening located posteriorly of the transvers

anal line, during probing follows a curved route terminating at the posterior dentate line, obviously at the 6th o'clock of the anal canal, this is valid most times at least in crypto-glandular etiology fistulas (posterior anal fistulas). An anterior external opening anteriorly to the transvers anal line may follow rarely curved direction passing in posterior perineum and terminating in posterior dentate anal line, thus the diagnosis of a long horse shoe fistulous tract is feasible and sometimes multiple openings at the peri-anal skin may exist across the route of the fistulous tract. The assessment and identification of fistula characteristics under general anesthesia with careful examination of anal canal remain irreplaceable for the further surgical management [12]. Other techniques of fistula identification before or during surgery despite they are easy and cheap, as endo-anal US and fistulography tend to be abandoned and replaced from preoperative MRI.

The role of MRI in assessment of anal fistulas

MRI is considered the most important radiologic examination providing accurate information in the anatomy of the anal canal, sphincter system and the relationship of the anal fistula with pelvic floor and levator ani muscle. Secondary tracts and abscesses cavities may be detected. MRI should be performed under precise protocols for anal fistulas, in order to obtain the optimum imaging data necessary in surgical management of the fistula [13].

Therapeutic surgical options treatment for simple and complex anal fistulas:

To date there are no guidelines for the best surgical therapy of anal fistulas. The goal of surgery is to remove the fistulous tract, to eradicate any local sepsis/abscess cavity and in more complex fistulas to avoid any severe damage of external sphincter resulting postoperative incontinence. Surgical therapy is still empiric based in anatomy and physiology of the anal canal and anatomic study of fistula characteristics in examination under anesthesia of the anal canal (main surgical methods in use and their results are shown in the table of the text)

a) Fistulotomy: Type I and II fistulas (intersphincteric and low transphincteric) are simple fistulas, easily treated by fistulotomy or fistulectomy with success in healing rates more than 95% [14] and without the risk of incontinence. This entity may be not unique during surgery as may be a component of a more complex fistula. If surgery is address to more complex segments of fistula, leaving intact the affected/infected inter-sphincter space, high rates of non-healing and recurrences may be observed [15]. This space is important from Park's era as it is the initial site of spread infection and fistula formation in other anal and perianal anatomic spaces creating more complex idiopatic/crypto-glandular fistulas. This space is considered a closed anatomic space and continuous drainage (Garg's cardinal principles) assure high success rates in surgical therapy of complex fistulas [16]. Fistulotomy in simple fistulas, despite it is an easy surgical procedure with acceptable low recurrence rates may produce minor continence disturbances in higher rates up to 40% [17]. There are old reports, where fisulotomy with immediate reconstruction of sphincter system gives excellent results in healing, but fistulas must be simple with low transphincteric component. This cutting sphincter option therapy with reconstructive surgery has been abandoned last 30 years, as there are in use other sphincter saving procedures

b) Drainage setons: They are more common in use than cutting setons as the last present high fecal incontinence rates in literature ranging from 12-26% [18]. They contribute to control of perianal sepsis and may decrease the length of a long fistulous tract, preserving intact the external sphincter. This is a temporary measure and further surgery for a complex fistula in future is under consideration. According to the local evolution of sepsis they may stay for several weeks, months, even more for years [19].

c) Advancement flaps: this is an old surgical technique using endorectal or dermal flaps. There are many surgical modified surgical procedures and partial thickness flaps are the most common in use. They are used for high complex fistulas. Other techniques before surgery as drainage seton to decrease local sepsis or ligation of internal fistula tract may be used [20]. Failure rates in literature vary from 15-60% [21] based in case series studies. Functional outcomes regarding the continence should not be ignored; in a recent meta-analysis the majority of patients present postoperatively some continence dysfunction [22]. The success healing by the time seems to be decreased [23]. There are not in literature, at least the last 15years, new publications with a large number of patients. Popularity for the method seems to be in low levels.

d) Plugs in fistula: A technique firstly described in 2004, there was initial enthusiasm as the procedure was less invasive, easily performed and few postoperative complications as local abscess and more rarely incontinence. Most reports are small case series. Studies with follow-up period, report a healing rate between 24-50% [24]. It seems that is not first choice procedure for anal fistulas but may be performed as alternative procedure in high complex fistulas and recurrences as it is easy and less invasive surgical procedure [25].

e) Glue sealants: they present low healing rates ranging from 30-60% in the literature after the placement of sealant the first months, decreasing by the time at 14% one year after the glue injection [26]. Despite the low success rate, due to simplicity may be performed in complex fistulas leaving more aggressive surgery for later [27] and probably with more local surgical difficulties if sealants shouldn't be used.

f) Ligation of the internal fistula tract (LIFT): This option treatment is relatively new with a first case series report in 1993 by Robin Phillips [28] as sphincter sparing procedure. This technique became very popular in surgeons last two decades as it is atraumatic, easy, with high healing rate and no significant changes in continence and anal manometry. The procedure may be performed in low transphincteric fistulas, avoiding fistulectomy and minor continence problems in some patients [29]. In complex high fistulas success rates are in high levels > 80% alone performed or combined with other surgical procedures [30]. The method may be performed in intersphincteric fistulas with healing rate at 68% [31]. In a systematic review healing rates are over 70% [32]. The technique is safe, effective, easy as surgical procedure, of low cost and high success rates more than 60% and may be used in many different types of fistulas (simple or complex) alone or with other simultaneously performed techniques as advancement flap or plug in fistula.

g) Laser closure therapy: present in literature a healing rate of 40-60% [33] or more. It is less-invasive technique with a significant percentage of minor anal symptoms postoperatively. Outcomes are better when the fistula's length is short [34].

h) Photodynamic therapy: In complex fistulas, success rates up to 80% are reported [35].

i) Video assisted anal fistula treatment (VAAFT): with success rates more than 70% and no major complications as it is a sphincter sparing technique [36].

Considerations in anal fistula surgery; the best option therapy is the best study of the fistula.

According to the recent and old reports in literature, there is not a surgical panacea therapy for anal fistulas. A plethora of new and old procedures are available and all these techniques reveal the eventual fail of surgery, a recurrence, a new operation and so on some times. The propensity last years is the use of sphincter sparing procedures. Most times patients with chronic anal fistula mention minimal anal symptoms, repeated at times, influencing the quality of life in a

middle age patient, asking an intervention to disappear the annoying local condition. This easy local problem is the most challenging surgical condition, even more in most experienced surgical hands of an anal surgeon, as in surgeon's mind is the best option therapy with complete healing and without postoperative anal continence problems and recurrences. Even more simple fistulas rise in surgeon's mind severe questions before and during surgery and they should be answered, in order to choose the best therapy; Is it the clinical examination accurate and safe? No, as may be undetected secondary tracts, multiple tracts and active local septic cavities influencing the surgical outcomes, increasing the complexity of fistula. The fistula is simple finally, or it is a part of a more complex fistula? We reply in these questions by MRI data; the intersphincteric space as it is the initial infected space in all cryptongladular infections should be estimated well for the further surgical management by the mean to be laid open or not. Even now, more questions are raised regarding the anal continence and the participation of anal sphincter in fistula formation; Finger examination may estimate the external anal sphincter function, but is not accurate and at least in those presenting continence problems, manometry should be a solution for further surgical management, avoiding sphincter cutting procedures. On the other hand simple low transphincteric fistulas containing less than 30% of external anal sphincter are considered simple. The content 30% or less of external anal sphincter may be determined during surgical exanination and probing of the fistula, this is a subjective determination and an approximate determination that could be helped by the preoperative MRI, and this last estimation remain still at approximate; anatomy of the anal canal may be recognized well by the anal surgeons and in MRI, but the function of anorectal canal is unique based in collaboration of the internal, external and lavatory ani sphincter, without concrete starting and ending points for internal, external sphincter and its continuation-joint upwards to levator ani. To date for simple fistulas, fistulotomy is the best surgical procedure, with high rates of healing more than 90% and low complication rates, but more than 5-10% of patients' up to 40% present postoperatively minor continence problems and may be temporary or persistent. This outcome of surgery should be explained to the patient and if is not ready to suffer minor continence problems for an interventional procedure with optimal results, alternative less invasive procedures should be performed. This category of simple fistulas seems to be a very common category of anal fistulas from Park's era with an approximate prevalence of 40-50% of cases reported, despite these simple fistulas are not so simple many times [37]. Therapy with cutting sphincter procedures (fistulotomy) or other sphincter sparing techniques provides excellent surgical results due to simplicity of the fistula.

In complex fistulas success surgical rates for all procedures described vary from 40-80% or any more in some reports, and outcomes depend from the complexity of fistula: Most common complex fistulas are high transphincteric and suprasphincteric accounting an approximate percentage of 50% of anal fistulas. More complex fistulas as supralevator and translevator (the latter is secondary, not of cryptoglandular etiology) seems to be very rare accounting no more than 5% of cases, presenting difficult further management. The complexity is studied by preoperative MRI, a compulsory examination before surgery. MRI examination may predict factors of fail preoperatively and may assess the healing process 2-3 months after surgery detecting factors of fistulas recurrences. As more recurrences appear within the first year after surgery, later recurrences 2-3 years after surgery may exist, revealing the obscure pathogenesis of crypto-glandular theory in the formation of a new abscess/fistula. Complex fistulas should be characterized as crypto-glandular, otherwise, if they are secondary to other anorectal conditions, surgical outcomes are poor and further management more difficult. Repeat surgical procedures for the treatment of a complex fistula may be performed and the failure of applied technique doesn't exclude the use of the same technique for a second time. The patient with complex fistula should be informed for the high rate of recurrences, as at least one patient to 4-6 cases with complex fistulas seems to be candidate for a new operation. Fortunately numerous sphincter sparing techniques offer safety in the therapy of complex fistulas. Long fistulous tracts, with long extrasphincteric route originating from severe intrapelvic inflammatory conditions (secondary and not cryptoglandular fistulas) are observed to rare, and the therapy of these complex fistulas is mainly preventive, treated the underlying disease before the inflammatory intrapelvic process drained in perineum. The supralevator fistulas are also to rare and thus severe operations as diverting colostomy to decrease perianal sepsis seems to be very rare. The final surgical option therapy for complex fistulas remain still empiric, by the mean that is depended by the opinion of anal surgeon and the available equipment for the appliance of a modern sphincter-sparing technique. The surgical results are depended on the complexity of the fistula rather than the surgical procedure performed. To date the only cutting sphincter procedure acceptable is fistulotomy, safe and without continence problems when is performed in simple linear intersphincteric fistulas that account a significant percentage of all anal fistulas. All other cases of fistulas should be treated by a sphincter saving procedure; New surgical techniques as TROPIS [15], PERFACT [38] and TFSIA [39] play an important role in the treatment of high complex fistulas. New innovative techniques (Fistula Laser therapy, VAAFT, photodynamic therapy) despite the cost present significant contribution in therapy of complex fistulas. Recently in a study based in a large number of patients, a new system of classification of anal fistula including risk factors for recurrence, enlarged etiology, recurrences and recommendations for the suitable surgical method should be performed, is available [40]. It seems that it's the time for guidelines for the treatment of anal fistulas.

Table 1: Anal fistulas surgery, therapeutic options and healing rates

Anal fistulas	Therapy	Healing rates
Simple intersphincteric	Fistulotomy	>95%
Simple low transphincteric	Fistulotomy/other sphincter saving procedures	>90%
Complex fistulas:	Sphincter saving procedures	40-80%
	Advancement flap	40-85%
	Plugs in fistula	25-50%
	Glue sealants	30-60%
	Ligation of the internal fistula's tract (LIFT)	60-85%
	Laser therapy	40-60%
	Photodynamic therapy	up 80%
	Video assisted anal fistula therapy (VAAFT)	up 70%

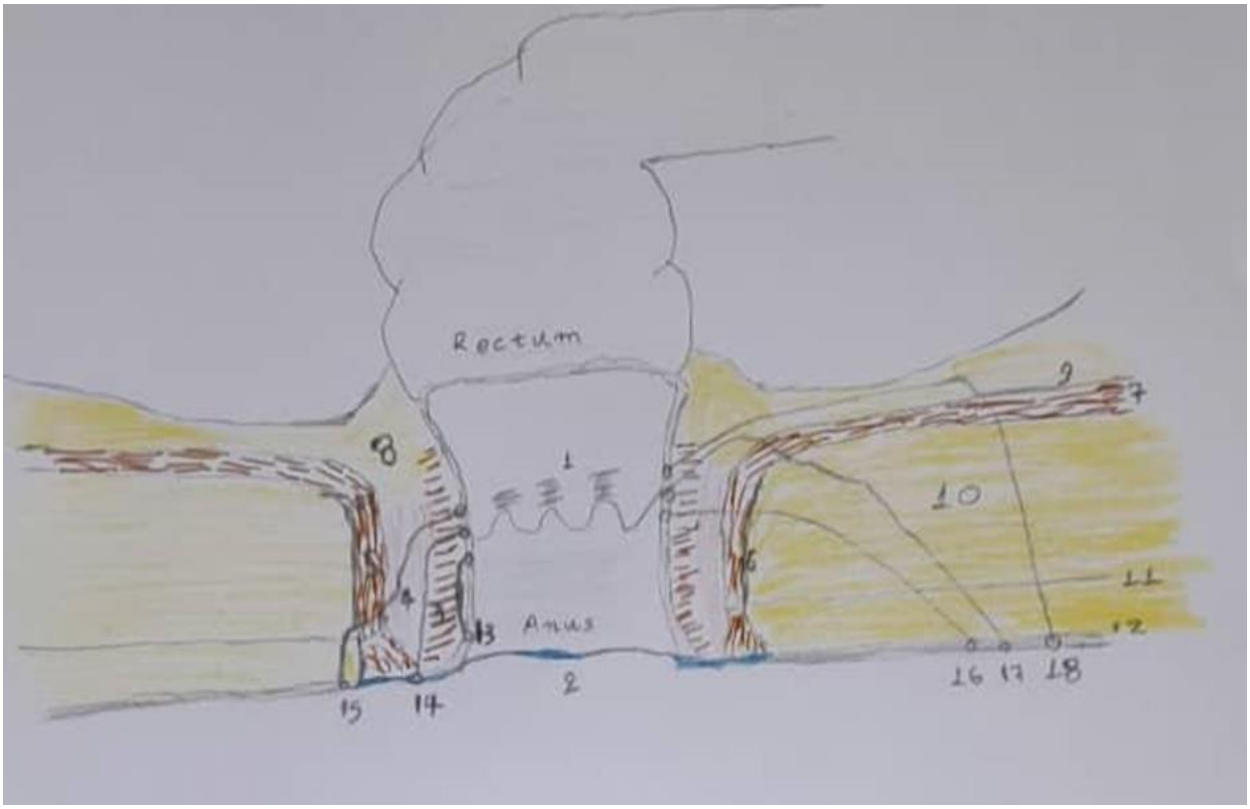

Figure with the main surgical anatomy of anorectal canal and fistulas in coronal plane

1. The dentate line of Hilton with stalks of Morgani; in anal crypts is located the internal opening of a fistula.
2. The anal verge: An external opening of a fistula next to anal verge reveals a simple fistula (13,14,15)
3. The internal anal sphincter
4. The intersphincteric space: a crucial space for the start and spread of infection
5. The external anal sphincter
6. The fascia of the external anal sphincter
7. The levator ani muscle
8. The suprasphincteric space
9. The supralevator space
10. The ischiorectal fossa
11. The transverse septum of perineum
12. The ischioanal fossa
13. Simple superficial (or submucosal) anal fistula: short length, do not compromise the sphincter system. Fistulotomy is an easy operation
14. Simple linear intersphincteric fistula: It is the most common simple fistula. Fitulotomy is the recommended operation
15.Simple low transphincteric fistula: less than 30% of external sphincter participate in fistula formation. Sphincter saving surgical procedures are recommended avoiding fistulectomy and postoperative anal continence problems
16.Transphincteric fistula: The most common complex fistula
17. Suprasphincteric complex fistula
18. Supralevator complex fistula: a rare entity

16+17+18: Complex fistulas should be treated by sphincter saving procedures. Ischiorectal or ischioanal fossa is affected. An external opening of the fistula apart from the anal verge with a long fistulous track(>1.5-2cm) reveals a complex anal fistula

Conclusion

Simple anal fistulas are easily treated conditions by fisulotomy or other sphincter sparing techniques with high healing rates, low recurrences rates and complications. Complex fistulas, present finally excellent surgical results, despite higher recurrences and reoperations as numerous sphincter saving procedures may be performed. Examination of anorectal canal under anesthesia and preoperative MRI are important to assess the simplicity or complexity of the fistula. Fistulas with severe complexity, necessitating aggressive surgical operations are rarely encountered in literature. Crypto-glandular anal fistulas are the most common but secondary etiologies should be detected as management therapy may be more complex and surgical outcomes poor. The crypto-glandular etiology of anal fistula is old and well known from the past, presenting still an unknown and obscure pathogenesis that should be studied in future.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' contributions

All authors fulfil the 4 criteria of authorship according to ICMJE. All authors read and approved the final manuscript.

Ethics approval

Not applicable

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