The management of cryptoglandular fistula-in-ano

Abstract

Idiopathic cryptoglandular fistula-in-ano is a common pathological condition. Fistula-in-ano has been managed by a number of surgical techniques, and there is still no consensus regarding the management of this condition. Surgical techniques aim to treat and cure the fistula-in-ano with minimal risk of recurrence or complications, and to maintain patient continence.

This article discusses the evidence available to inform the management of idiopathic cryptoglandular fistula-in-ano, and problems that surgeons face because of the lack of high-quality evidence.

Key words: Anal fistula; Anal flap; Fistulotomy; Ligation of the inter-sphincteric fistula; Plug; Seton; Video-assisted anal fistula treatment

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Matthew Sammut[1]

Paul Skaife[1]

Author details can be found at the end of this article

Correspondence to:
Matthew Sammut;
sammutmatthew3384@yahoo.co.uk

Introduction

The management of idiopathic cryptoglandular fistula-in-ano remains controversial, and the search for the ideal surgical procedure to eradicate this continues. The aim is to cure the fistula-in-ano with minimal risk of recurrence and/or complications while preserving anal sphincter function to maintain continence. Regardless of the anatomical type of fistula, the infective or inflammatory process needs to be dealt with and the internal anal opening should be closed without jeopardising the integrity of the anal sphincter complex (Shawki and Wexner, 2011). The range of available surgical modalities indicates that there is no ideal procedure applicable to every patient with fistula-in-ano.

This article discusses the evidence available for the management of cryptoglandular or idiopathic fistula-in-ano. Other causes of anal sepsis and fistula-in-ano include pelvis and/or intra-abdominal sepsis, Mycobacterium infection, Crohn's disease, fungal infection and malignancy; although important, these will not be discussed in this article.

Pathology of idiopathic cryptoglandular fistula-in-ano

A fistula is defined as an abnormal pathological tract between two epithelial surfaces (Seow-Choen, 2003). The male:female ratio for incidence of fistula-in-ano is 6.6:1 (Emile et al, 2018). There are two types of anal glands arising in the crypts of Morgagni:

1. Submucosal glands (80%) are the commonest type. Infection of these glands forms a small abscess which commonly bursts into the anal canal and heals spontaneously.
2. Intramuscular glands (20%) number between six to eight and these pierce the muscular layers of the anal sphincter to varying degrees and depths (Seow-Choen, 2003). Once obstructed, infection ensues and suppuration will follow the path of least resistance. This determines the location of the abscess and the type of fistula-in-ano (Shawki and Wexner, 2011; Alasari and Kim, 2014).

Following incision and drainage of a perianal abscess in the emergency setting, abscess recurrence and/or fistula-in-ano occurs in 14–46% of patients (Hasan, 2016).

Fistula-in-ano can be classified into five main anatomical types (Figure 1, Table 1). Inter-sphincteric and distal trans-sphincteric fistulas are classified as simple or low fistula-in-ano and are the commonest form. Proximal trans-sphincteric (>30% of external anal sphincter involved in the fistula tract), supra-sphincteric fistulas and extra-sphincteric are classified as high or complex fistula-in-ano because of their higher risk of incontinence following surgical management.

Furthermore some authors classify anterior fistula-in-ano in women and fistula-in-ano with multiple tracts as complex fistula-in-ano (Ommer et al, 2017). Horseshoe fistula-in-ano

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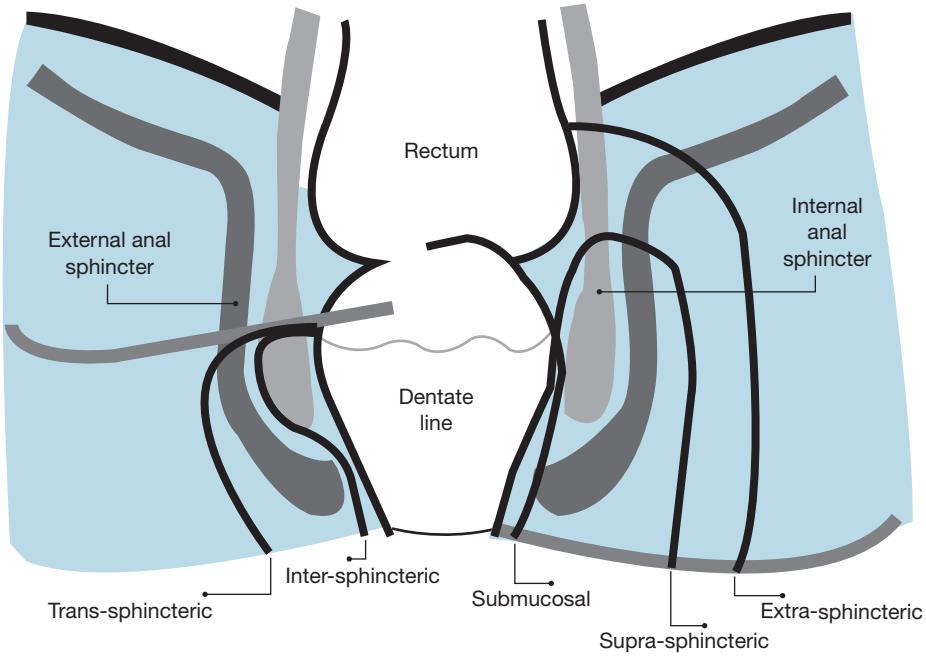

Figure 1. Types of fistula-in-ano.

Table 1. Types of fistula-in-ano

Fistula type	Tract	
Submucosal	Fistula tract passes superficially beneath the submucosa. No involvement of sphincter muscle	
Inter-sphincteric	Fistula tract passes through the internal anal sphincter and continues in the inter-sphincteric space to the perianal skin. Tract does not include the external anal sphincter	
Trans-sphincteric	Fistula tract passes through the internal anal sphincter and external anal sphincter towards the perianal skin	Low type – less than one third of the distal external anal sphincter is involved
		High type – more than one third of the distal external anal sphincter is involved
Supra-sphincteric	Fistula tract crosses the external anal sphincter and internal anal sphincter below the puborectalis muscle	
Extra-sphincteric	Fistula tract is external to the anal sphincter complex (passes through the ischiorectal fossa to the perianal skin)	

is a further type of complex fistula-in-ano which results after a chronic and/or recurring abscess often in the undrained posterior deep ischiorectal spaces. The abscess perforates the external anal sphincter anteriorly and posteriorly to enter deep pre-anal and post-anal spaces with extensive spread in the ischiorectal spaces (Inceoglu and Gencosmanoglu, 2003).

Fistula-in-ano recurs following surgery in 7.5% of patients. Although men have a higher recurrence rate, this is not statistically significant (7.9% vs 4%, P=0.34). Recurrent fistula-in-ano rates are significantly higher in patients who underwent previous fistula-in-ano surgery (P=0.0002) and in those with a complex fistula-in-ano (P=0.0003) (Emile et al, 2018). These results are probably multifactorial in nature because of the complexity of original fistula-in-ano anatomy and alterations to tissues and scarring with subsequent procedures.

Management options

Draining seton

Seton insertion is one of the simplest surgical procedures in managing fistula-in-ano. The seton material varies, with a non-absorbable suture, vessel sloop or surgical drain being

used. This material is guided through the fistula tract and normally tied externally. The correct insertion technique is required to avoid patient symptoms and recurrence. Tight or cutting setons involve the insertion of a seton which is progressively tightened at successive patient encounters. The seton cuts through the anal sphincter and allows scarring to occur. Tight or cutting setons are no longer recommended because of the high risk of incontinence. In view of this, only draining or loose seton procedures are discussed in this article. A loose seton preserves the anal sphincter and works by controlling sepsis while stimulating fibrosis. This allows healing and maturation of the tract, which may allow identification of the tract for other future procedures (Subhas et al, 2012).

Daodu et al (2018) reported that the median time for seton suture removal was 36.6 weeks. In this study, 73.7% of patients were asymptomatic after removal of a draining seton. The chance of complete healing or improvement of symptoms in patients with a draining seton was 61.9%. These results support the use of drain setons as the primary treatment for fistula-in-ano. A complication rate of 12% in patients with trans-sphincteric fistula-in-ano was reported when a draining seton was used, with 19.5% of patients requiring a further seton procedure (Eitan et al, 2009).

Omar et al (2019) examined whether rerouting the fistula-in-ano to preserve the external anal sphincter with draining setons was useful. Although postoperative pain after external anal sphincter-sparing seton was found to be significantly less compared to the conventional seton procedure, there was no significant difference in incontinence rates or recurrence rates between the groups.

Fistulotomy

Fistulotomy involves laying open a fistula-in-ano tract from the internal opening to the external opening with division of the anal sphincter muscles below the fistula. Fistulotomy of a perianal abscess in the emergency setting has a recurrence rate of 0–10%. However, continence may be impaired in up to 40% of patients (Quah et al, 2006). Fistulotomy was reported to significantly decrease maximum anal resting pressure (85.9±20.4–60.2±18.4 mmHg, $P<0.0001$) and length of the high pressure zone (3.92±0.69–3.82±0.77 cm, $P=0.035$), but did not affect voluntary contraction pressure (164.7±85.2–160.3±84.8 mmHg, $P=0.28$). Fistulotomy is useful in low or simple fistula-in-ano since the risk of recurrence and incontinence is low. In the study by Tyler et al (2007) of 137 patients, fistulotomy as a sole procedure was successful in 38 patients; 99 patients (72%) required staged procedures.

Marsupialisation (suturing the wound edges to the edge of the fistula tract with absorbable sutures) following fistulotomy remains controversial. Although the risk of fistula recurrence with marsupialisation was reported to be slightly lower (56 per 1000 vs 45 per 1000; odds ratio=1.26), there was no statistical significant difference reported in a review comparing the surgical techniques (Tj et al, 2010). In a randomised controlled trial of fistulotomy with and without marsupialisation, patients undergoing fistulotomy with marsupialisation healed quicker (4.85±1.39 weeks vs 6.75±1.83 weeks, $P=0.035$) (Jain et al, 2012).

Ligation of the inter-sphincteric fistula track

Ligation of the inter-sphincteric fistula track was initially described by Rojanasakul (2009) and gained popularity because of its success rate, low incontinence rates, low postoperative complication rates (1.83%) and because it is a minimally invasive procedure. In a meta-analysis of 13 different studies, the pooled weighted success rate of the ligation of the inter-sphincteric fistula track procedure was reported to be 69%. There was no significant change in weighted success rate (65%) after a 12-month follow-up period. The overall mean non-healing rate was 19.8% (range=0–49%) (Stellingwerf et al, 2019). These results are echoed in a meta-analysis which included ligation of the inter-sphincteric fistula track procedures performed for trans-sphincteric fistulas. The overall healing rates of the pooled data were 78.9%. The failure rate for the ligation of the inter-sphincteric fistula track procedure in trans-sphincteric fistula-in-ano was 17.9% (Gendia et al, 2018). The mean recurrence rate was 13.3% after a mean 15-week follow-up period (Alasari and Kim, 2014), which increased to 21.2% after 12 months (Stellingwerf et al, 2019). Although only a few studies report incontinence rates, no change in continence has been reported in the literature (Gendia et al, 2018).

Despite variations to the ligation of the inter-sphincteric fistula track procedure being used, a review of 26 studies found no significant difference in overall success rates (Sirany et al, 2015). Romanisyzn and Walega (2019) combined video-assisted anal fistula treatment surgery and ligation of the inter-sphincteric fistula track to perform video-assisted ligation of the inter-sphincteric fistula track. In this study, there was no statistical difference in the primary healing rates (87.5% for ligation of the inter-sphincteric fistula track vs 87.5% for the video-assisted procedure, $P>0.05$) and overall healing rates after long-term follow up (68.7% for ligation of the inter-sphincteric fistula track vs 66.7% for the video-assisted procedure, $P>0.05$). The authors concluded that the additional cost of equipment in the video-assisted procedure was not justified (Romaniszyn and Walega, 2019).

In a randomised controlled trial comparing ligation of the inter-sphincteric fistula track and ano-rectal advancement flaps, ligation of the inter-sphincteric fistula track was quicker to perform ($P<0.001$), and resulted in less postoperative pain ($P=0.17$), higher patient satisfaction rates ($P=0.001$) and earlier return to work ($P=0.01$). There was no difference in recurrence rates between the two procedures (Mushaya et al, 2012). In pooled weighted results, incontinence rates following the ano-rectal advancement flap procedure were significantly higher than those following ligation of the inter-sphincteric fistula track (7.8% vs 1.6%) (Stellingwerf et al, 2019). In a prospective study comparing ligation of the inter-sphincteric fistula track and mucosal advancement flaps, the ligation of the inter-sphincteric fistula track procedure has a better primary healing rate (94.2% vs 91.4% for mucosal advancement flaps), a shorter median healing time (26.6 days vs 38.1 days), lower recurrence rates (21.2% vs 28.1%) and better overall healing rates (74.3% vs 65.7%) (Madbouly et al, 2014).

Rectal advancement flaps

Rectal advancement flaps achieve fistula-in-ano healing without division of the anal sphincters, thus preventing faecal incontinence. The procedure has variations depending on the surgeon performing it and tends to be reserved for complex types of fistula-in-ano. Three main types of flaps have been described: mucosal, partial thickness (fibres of the internal anal sphincter are included), and full thickness rectal advancement flaps (includes the entire internal anal sphincter).

In a prospective randomised controlled trial comparing mucosal and partial thickness rectal advancement flaps in high trans-sphincteric fistula-in-ano, the authors noted a significant decrease in mean resting anal pressures in both patient groups ($P<0.001$) and a significantly lower mean squeeze pressure after partial thickness rectal advancement flaps. The recurrence rate in the partial thickness group was 10% compared to 40% in the mucosal rectal advancement flap group (Khafagy et al, 2010). In a meta-analysis that compared rectal advancement flap surgery to the anal fistula plug procedure, patients who underwent rectal advancement flap surgery showed a significantly higher pooled healing rate ($P=0.01$) and a significantly lower recurrence rate ($P=0.009$) compared to the anal fistula plug procedure for complex fistula-in-ano (Lin et al, 2019).

Balciscueta et al (2017) noted in their meta-analysis that the literature available for rectal advancement flaps was limited, with low levels of evidence and significant study heterogeneity. The total pooled recurrence rate for rectal advancement flaps was 21%. Mucosal flaps had a recurrence rate of 26.7%, partial thickness flaps had a 22.9% recurrence rate, while full thickness flap recurrence rate was 7.4%. The pooled faecal incontinence rate was 13.3%. Full thickness rectal advancement flaps have a 20.4% patient incontinence rate. However, the significant degree of study heterogeneity makes it difficult to draw conclusions.

Video-assisted anal fistula treatment

Video-assisted anal fistula treatment is performed using a kit developed by Piercarlo Meinero and Karl Storz GmbH (Figure 2).

The procedure allows identification, cauterisation and removal of debris within the tracts to allow the fistula-in-ano to heal. Meinero and Mori (2011) reported a primary healing rate of 73.5% (72/98 patients) with the video-assisted anal fistula treatment procedure. The patients did not report any continence problems or postoperative pain following the procedure and no major complications were reported by the authors.

Figure 2. Video-assisted anal fistula treatment endoscope

Kochhar et al (2014) reported that the mean operating time was 45 minutes and 26.8% of patients were pain free in the immediate postoperative period. Anal manometry performed preoperatively and postoperatively showed no statistically significant changes in mean anal resting pressure and mean squeeze pressures with video-assisted anal fistula treatment. The recurrence rate in their cohort was 15.9%. A prospective study reported that following video-assisted anal fistula treatment the fistula-in-ano took a mean 52 days (range=15–98 days) to heal, with a statistical difference in overall success healing rates (73.3% simple trans-sphincteric vs 39.5% complex, P=0.011). It was also noted that women with complex fistula-in-ano had better healing rates with video-assisted anal fistula treatment (77.8% vs 27.6%, P=0.016). There was no reported worsening in continence (Romaniszyn and Walega, 2017).

Jiang et al (2017) reported complete healing without recurrence in 84.6% of patients, and 80.6% of patients who had previous fistula-in-ano surgery achieved primary healing. The authors used the Gastrointestinal Quality of Life Index to assess quality of life and procedure effectiveness, and showed a statistically significant improvement in the Gastrointestinal Quality of Life Index score after video-assisted anal fistula treatment (P<0.001). There was no significant difference in healing in patients who had had seton insertion before video-assisted anal fistula treatment (P=0.803). In a meta-analysis of eight studies that included 786 patients, the success rate was 76% with a complication rate of 16% and no worsening of continence rates (Garg and Singh, 2017).

Anal fistula plug

Anal fistula plugs are composed of bioprosthetic materials and provide a scaffold for the growth of regenerative cells that allow healing of the fistula-in-ano. Although several anal fistula plugs have been developed, the BioDesign Surgisis anal fistula plug (Cook Medical, Bloomington, IN, USA), composed of acellular, lyophilised porcine intestinal submucosa, is one of the most established.

The multicentre randomised controlled Fistula-In-Ano Trial recruited 304 patients with high trans-sphincteric fistulas. The trial compared the Surgisis anal fistula plug (152 patients) to the surgeon's preference of advancement flap, cutting seton, fistulotomy or ligation of the inter-sphincteric fistula track (152 patients). The trial reported no differences in quality of life among participants treated with the anal fistula plug compared with those receiving other treatments after a 12-month follow-up period. Successful fistula healing was achieved in 54% of patients treated with the anal fistula plug compared to 55% treated with an alternative technique. A higher rate of unexpected pain at the 6-week was noted in the anal fistula plug group (Jayne et al, 2019).

A study comparing anal fistula plug and anal mucosal advancement flaps for complex anal fistulas showed that although there was no statistically significant difference in healing rates at 6 months and at 12 months follow up (66.7% vs 75.8%), the anal fistula plug

procedure was significantly shorter (19.3 vs 29.8 minutes (P<0.001)) (Schwandner et al, 2018). Long-term success was assessed in a retrospective study by Ellis et al (2010). Of note, this study included 12 (19%) patients with Crohn's disease and a draining seton for at least 6 weeks was performed in 95.2% of patients. The initial anal fistula plug procedure was successful in 76% of patients after a 12-month follow-up period. Multivariate analysis showed that smoking, previous anal fistula plug failure and a posterior fistula-in-ano were independent predictors of anal fistula plug failure.

Fistula tract laser closure

Diode laser has been used for the treatment of fistula-in-ano. Fistula tract laser closure involves passing a laser fibre through the internal and external fistula opening and gradually withdrawing the fibre as it is activated. The internal opening is closed using a mucosal flap and the external opening is widened to allow draining.

In the study by Wilhelm et al (2017) 117 patients underwent fistula tract laser closure. Although the cohort included 13 (11.1%) patients with Crohn's disease fistula-in-ano, the authors reported the results for cryptoglandular fistula-in-ano separately. The primary success rate of fistula tract laser closure was 64.1%, with a secondary success rate of 88.0%. Interestingly, no difference in success rate was noted between those with cryptoglandular fistula-in-ano and Crohn's perianal fistulas. Only 5.7% patients reported minor soiling and no major incontinence was reported. An overall successful procedure rate of 82% was reported by Ozturk and Gulcu (2014). However, Lauretta et al (2018) reported a primary cure rate of 33.3% in trans-sphincteric fistula-in-ano, increasing to 40% after repeat procedures. The authors note that fistula tract laser closure achieved a significant primary healing rate with fistula tracts shorter than 30 mm (58.3% vs 16.6%; P<0.02).

The main disadvantage of fistula tract laser closure is the cost of the laser fibre. The other main issue is that this is essentially a 'blind' procedure and may miss secondary fistula-in-ano tracts. However, fistula tract laser closure could be a potentially clinical effective procedure (Wilhelm et al, 2017; Lauretta et al, 2018).

Radiofrequency

Radiofrequency uses high frequency alternating current to produce thermal energy that simultaneously cuts and coagulates tissues. In a study by Gupta (2003), 97 patients with low fistula-in-ano were treated using a 4 MHz radiofrequency probe. Compared with conventional fistulotomy, the author reported a statistically significant shorter procedure time (12 minutes vs 27 minutes, P=0.002), faster healing time (37 days vs 54 days, P=0.0017), shorter hospital length of stay (17 hours vs 36 hours, P=0.0014), and earlier return to work (7 days vs 11 days, P=0.029) with no changes in continence (Gupta, 2003). The author reported a 1.7% recurrence rate after a 15-month follow-up period (Gupta, 2004).

In a study comparing radiofrequency and rectal advancement flap surgery in patients with complex fistula-in-ano, there was a statistically significant higher failure rate with radiofrequency. Although patients with Crohn's disease were included, this study is included here because of the lack of recent studies exploring the use of radiofrequency. Following a 12-month follow-up period, the radiofrequency failure rate was 87.4% compared to the rectal advancement flap failure rate of 35.7% (P=0.0004) (Merlini l'Héritier et al, 2019).

The use of radiofrequency has been hypothesised as a potential alternative management option as the anal sphincters are preserved and it is less painful as less tissue trauma occurs compared to conventional diathermy (Gupta, 2003, 2004). However, randomised controlled trials and long-term studies are required to assess the feasibility of radiofrequency.

Proximal superficial cauterisation, regular emptying and curettage of the tracts

Proximal superficial cauterisation, regular emptying and curettage of the tracts was described by Garg for supra-sphincteric fistula-in-ano. It involves superficial cauterisation of the anal mucosa around the internal fistula opening and repeated procedures to keep the fistula-in-ano tract clean. An overall healing rate of 80% and a recurrence rate of 26.7% was reported. No changes in incontinence rates were reported (Garg, 2016). This is a novel technique with promising results, but further long-term studies are needed.

Discussion

It is difficult to formulate a one-size-fits-all management protocol for cryptoglandular fistula-in-ano. Although a number of trials have been performed, some include small patient numbers, so are inadequately powered to detect significant differences between procedures. Blinding in studies is difficult because of the nature of the procedures, resulting in potential study bias. Furthermore, there is a degree of heterogeneity in the classification of fistula-in-ano which makes interpretation of the different management options difficult. Magnetic resonance imaging is becoming increasingly important in classifying fistula-in-ano. In the study by Garg et al (2017), a third of clinically simple fistula-in-ano were upgraded to complex fistula-in-ano following the use of magnetic resonance imaging. Magnetic resonance imaging increases the cost of treatment of fistula-in-ano, but diagnosis of secondary tracts and accurate classification may decrease recurrences. Thus, magnetic resonance imaging may be cost effective in the long term.

With any surgical management of fistula-in-ano, continence needs to be addressed. Preserving the anal rectal ring will prevent major incontinence. Another issue is the use of different incontinence scores to evaluate patients' continence. This may result in difficulties in interpreting results when comparing different surgical procedures. A real estimation of continence requires the use of validated incontinence scores preoperatively and postoperatively (Stellingwerf et al, 2019).

Another degree of study heterogeneity occurs because of the difference in patient follow-up periods. It is generally accepted that the ideal length of follow up for fistula-in-ano treatment is 12 months (Ellis et al, 2010). Different recurrence symptoms, incontinence symptoms and success definitions increase the difficulty in interpretating and comparing results. There are very few well-conducted trials comparing treatments for fistula-in-ano, and in turn assessing recurrence, incontinence and long-term success (Tj et al, 2010). There is also a lack of objective assessment following treatment of fistula-in-ano. Although most studies report success as the patient being asymptomatic (Daodu et al, 2018), objective assessment of fistula healing may require the use of magnetic resonance imaging.

Conclusions

The best and ideal treatment for fistula-in-ano both remain unclear. As shown above, results for the different type of cryptoglandular fistula-in-ano types and surgical options are limited by the lack of good evidence. Drawing conclusions from the available literature remains difficult because of studies heterogeneity. Further high-quality randomised controlled trials are needed to provide strong evidence.

Author details

[1]Colorectal Department, Aintree University Hospital NHS Foundation Trust, Liverpool, UK

Conflicts of interest

The authors declare no conflicts of interest.

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Key points

- Management of idiopathic cryptoglandular fistula-in-ano remains controversial.
- The management of fistula-in-ano aims to control sepsis, delineate fistula anatomy, have a low recurrence and complication rate, and preserve anal sphincter function to maintain patient continence.
- Cutting or tight setons are not recommended – loose or draining setons preserve the anal sphincter, control sepsis and stimulate tract fibrosis and maturation.
- Procedures that can be used include fistulotomy, ligation of the inter-sphincteric fistula track, rectal advancement flaps, video-assisted anal fistula treatment, anal fistula plugs, fistula tract laser closure, radiofrequency and proximal superficial cauterisation, regular emptying and curettage of fistula-in-ano tracts.
- Further studies are needed to evaluate the best treatment for different types of fistula-in-ano.

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