Is modern management of fistula-in-ano acceptable?

Fistula-in-ano has been managed by a number of techniques and there remains no consensus on the most appropriate management for all patients. The mainstay of any treatment balances the need to control sepsis *vs* the risk of potential incontinence post-intervention. Management should focus on the primary source of sepsis.

Cryptoglandular anal sepsis is the proposed aetiology of fistulae-in-ano. Anatomically there are two different types of gland arising from the anal crypts of Morgagni and only one type of gland – the intramuscular gland – is responsible for fistula-in-ano. These intramuscular anal glands account for 20% of all anal glands and they pierce the sphincter muscles of the anus. The remaining 80% of all anal glands are submucosal glands and these lie entirely within the submucosa (Tucker and Hellwig, 1934; Seow-Choen and Ho, 1994).

When a submucosal gland becomes infected, a small abscess forms, which eventually discharges into the anal canal and heals spontaneously without complication. However, when an intramuscular gland becomes infected the internal sphincter muscle prevents spontaneous discharge into the lumen and the tracking infection follows the path of least resistance along the fibres of the longitudinal layer of muscle, which can result in anal fistula formation. There are approximately six to eight of these glands per individual but they occur in only 60% of the population and this has been postulated as the reason for the variation in susceptibility of individuals to anorectal sepsis (Seow-Choen and Ho, 1994). This is the cryptoglandular theory of the pathogenesis of anal fistulae and will be the focus of this article. This theory is further backed up by animal studies confirming that dogs, which do have intramuscular anal glands develop fistulae-in-ano, whereas cats, who do not possess intramuscular glands, do not develop this pathology (McColl, 1967).

Classification of fistulae

The most widely recognized system of classification of anal fistulae is that of Parks et al (1976), dividing anal fistulae into four groups, defined by the route of the primary tract linking internal and external openings and its relation to the anal sphincter muscles:

1. Intersphincteric fistulae
2. Trans-sphincteric fistulae
3. Suprasphincteric fistulae
4. Extrasphincteric (*Figures 1* and *2*).

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Figure 1. The frontal section of the sigmoid colon, rectum and anus section.

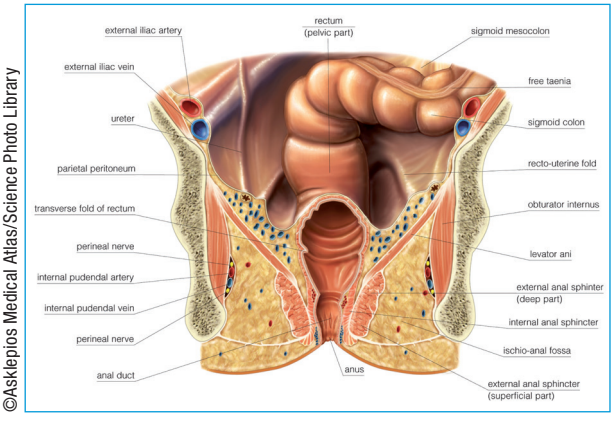
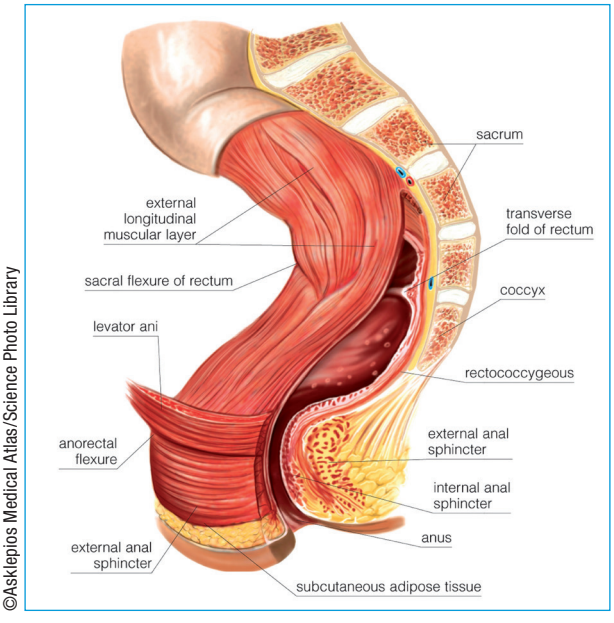


Figure 2. Illustration of the large intestine, rectum and anus.



Despite the complexity and multiple potential tracts resulting from the disease process, the underlying pathology for all Parks' groups of fistula-in-ano is that of one infected intramuscular anal gland. Superficial fistulae were not included in the classification as they were thought to have a different underlying aetiology.

Key principles for the chronological management of anal fistulae are as follows:

1. Drain sepsis
2. Identify anatomy and eradicate fistula tract
3. Address pathology and prevent recurrence
4. Preserve continence.

Sphincter-compromising treatments

Fistulotomy has been used as a treatment for hundreds of years and involves dividing the superficial tissue to 'lay open' the fistulous tract (Goligher et al, 1984). This remains the gold standard treatment for simple low-lying fistulae as there is allegedly minimal risk to continence and recurrence rates are very low (Westerterp et al, 2003; Tyler et al, 2007).

However, the risk of impairment of function resulting in varying degrees of incontinence makes the use of fistulotomy controversial in more complex fistulae. In a study by Phillips and colleagues sepsis control was achieved in 93% of patients undergoing fistulotomy, but 20% of patients suffered deterioration in continence after surgery (Tozer et al, 2013). The authors believe that the functional outcome following such surgery is unacceptable to the colorectal surgeon and debilitating for the patient.

The seton suture is the oldest surgical approach to treatment of fistula-in-ano (McCourtney and Finlay, 1995) and was first described by Hippocrates. A seton suture is a simple non-absorbable thread which is pulled through the fistula tract and ligated to form a ring between the external and internal openings. These sutures can be tied loose, controlling infection, or as a tight cutting seton.

Loose setons maintain patency of the fistula tract, preventing stasis, allowing adequate drainage and reducing the chances of perianal abscess formation. Placement of a loose seton allows for reduction in inflammation, aids definition of the anatomy and acts as a bridge to definitive treatment.

The use of a cutting seton involves the suture being regularly tightened to attempt to divide the sphincter muscle very slowly, allowing scarring to occur with minimal disruption of the muscular ring, in the hope that there will be little impact on continence. However, studies have reported high rates of functional disturbance (Christensen et al, 1986), including one study with an incontinence rate of 25% at 42 months (Hammond et al, 2006).

It seems that for some patients this surgery may just swap the problem of purulent discharge for that of faeculent discharge and the authors question whether this is acceptable in the modern management of this difficult condition. Given the high risks of reduction in continence with these 'older' treatments for fistula-in-ano, there has, in recent years, been a move to investigate newer sphincter-preserving techniques which have been developed in the hope of minimizing sphincter disturbance and improving success rates. This article concentrates on the success of these sphincter-preserving treatments in controlling sepsis based on the cryptoglandular theory of the underlying pathology.

Sphincter-preserving treatments

Ksharasutra or chemical seton

Perhaps the oldest example of these is the Ksharasutra or chemical seton. These are a variation on the seton which has been used extensively in the Indian subcontinent since ancient times but with limited use in the western world. A Ksharasutra is a seton lined with Ayurvedic medicines derived from plant extracts. This has aseptic properties but also possibly causes a caustic effect on the infected intramuscular anal gland.

Several prospective studies have compared Ksharasutra to open fistulotomy (Radhakrishna and Tamby, 1991; Ho et al, 2001; Dutta et al, 2015). The most recent by Dutta et al (2015) showed a recurrence rate of 3.9% *vs* 12.5% respectively, although this was not reported as statistically significant. The largest study to date conducted by Radhakrishna and Tamby (1991) randomized patients to surgical intervention (n=237) or Ksharasutra (n=265). Although healing rates were significantly longer in the Ksharasutra group (8 weeks *vs* 4 weeks) use of the Ksharasutra was associated with a significant reduction in fistula recurrence at 1 year (4% *vs* 11%, P=0.03). In one published study comparing Ksharasutra to normal seton in 60 patients (Srivastava and Sahu, 2010), recurrence rates over a 4-year follow-up period were 3.33% *vs* 13.33% in the Ksharasutra and plain seton groups respectively. This impressive control of sepsis along with a low incidence of incontinence in the Ksharasutra group suggests an additional benefit over plain seton alone.

As the vast majority of these studies have been conducted in the Indian subcontinent it is unclear whether the results can be generalized to western populations. Despite this, chemical setons have the potential to be to be a useful adjunct in the treatment of perianal fistula and more could be done to explore their use in western populations.

Fibrin glue

A more modern sphincter-saving approach is the use of fibrin glue which combines fibrinogen, thrombin and calcium and is injected down the fistula tract through the external opening. Its mode of action is thought to involve stimulation of fibroblasts and pluripotent endothelial cells to encourage growth of collagen and extracellular matrix, thus 'sealing' the fistula tract.

The first report of the use of fibrin glue by Hjortrup et al (1991) was very encouraging, with overall success rates of 74%. However, data from later studies reported

wide-ranging success rates from 14% (Buchanan et al, 2003) up to 74% (Patrlj et al, 2000). The reasons for the wide variation in results include differing trial design such as length of follow up, heterogeneity in patient selection and variations in the fistula anatomy. The absence of impairment of continence makes this an attractive option (Lindsey et al, 2002), although Buchanan et al (2003) reported that in some cases injection of the glue may result in abscess formation leading to the formation of secondary tracts and recurrent fistulae in the long term.

Ligation of intersphincteric fistula tract (LIFT)

Ligation of intersphincteric fistula tract was first described by Rojanasakul et al in 2007. This procedure requires an incision along the anal margin at the site of the fistula where the intersphincteric plane is entered. Without dividing any part of the anal sphincter complex the identified fistula tract is divided and ligated along with the removal of any residual infected glands (Rojanasakul et al, 2007). Using this technique Rojanasakul et al initially reported a 94% success rate with no impact on continence. Despite others not achieving the same results the ligation of intersphincteric fistula tract technique has gained popularity because of its relatively high success rate and preservation of continence. A meta-analysis (Hong et al, 2014) of 24 articles with a total of 1100 patients showed a pooled success rate of 76.5% over a mean 10-month follow-up period with a 0% incontinence rate.

In 2010, Ellis introduced a variation of the ligation of intersphincteric fistula tract technique in which a bioprosthetic graft was placed in the intersphincteric plane to reinforce the closure of the fistula tract (BioLIFT procedure). In this study the BioLIFT was used to repair complex trans-sphincteric fistulae in 31 patients. Clinical healing of the fistula occurred in 94% of patients after a minimum follow up of 12 months.

The only other study to date reporting the BioLIFT technique is that conducted by Tan and Lee (2014). In this study 13 patients underwent a BioLIFT procedure following failure of seton treatment. Over a median follow up of 26 weeks (range 12–51 weeks), 68.8% of fistulas had healed. As yet there is no evidence to suggest that the BioLiFT technique is superior to the ligation of intersphincteric fistula tract method.

Although the evidence for the ligation of intersphincteric fistula tract or BioLIFT procedure is primarily drawn from small case series, and long-term success rates of this technique are yet to be determined, it is seen as a good initial treatment option as it is minimally invasive, associated with low complication rates, is sphincter preserving and if it fails does not preclude other treatment options.

Video-assisted anal fistula treatment (VAAFT)

Video-assisted anal fistula treatment was first developed by Meinero and Mori in 2006. This sphincter-sparing technique is broadly split into diagnostic and treatment phases. The purpose of the diagnostic phase is to correctly locate the internal opening of the fistula tract and identify any secondary tracts or abscess cavities. This is done under direct vision using a fistuloscope inserted through the external opening. Continuous irrigation of the fistula with glycine–mannitol solution aids scope insertion and tract visualization. Having isolated the internal opening the operative phase is commenced. For this purpose, an electrode is inserted along the fistuloscope and the tract cauterized under direct vision. This is followed by closure of the internal opening using a stapler or cutaneous mucosal flap.

Between 2006 and 2011 Meinero and Mori (2011) used this technique on 136 patients. They reported primary healing in 72 patients (73.5%) within 2–3 months of the operation. Of the 62 patients followed up for 1 year 87.1% were reported as having complete healing of their fistula.

This technique has been replicated in several other studies. Seow-En et al (2016) used video-assisted anal fistula treatment in 41 patients, recording a primary healing rate of 70.7% at a median follow up of 34 months. Kochhar et al (2014) reported similar results in 82 patients with a recurrence rate at 6 months of 15.85% while Wałęga et al (2014) observed fistula recurrence in 22% of patients.

While these initial studies show video-assisted anal fistula treatment to be promising and associated with very few complications, they are based on a relatively small cohort of patients. Equally the majority of studies have a relatively short follow-up period and as a result long-term success rates are undetermined. Questions also remain over the preferred method for closure of the internal opening with a suggestion that mucosal flaps are associated with higher failure rates (Seow-En et al, 2016).

Anal fistula plug

The anal fistula plug is manufactured from porcine-derived small intestine mucosa (Surgisis anal fistula plug). It is a strong tissue used as a scaffold for host fibroblasts to promote tissue healing and repair, it is infection resistant and does not induce a foreign body inflammatory reaction. The technique for use involves debridement and curettage of the primary fistula tract, followed by lavage with hydrogen peroxide. The fistula plug is then tied to a probe and passed from the external opening to the internal opening of the fistula. It is then anchored to the mucosa, submucosa and internal sphincter of the anus. A systematic review of 20 studies concluded that this approach resulted in closure of fistulae in 54% of patients, excluding those with fistulae resulting from Crohn's disease (O'Riordan et al, 2012).

Results from randomized controlled trials are awaited to determine the efficacy of this treatment option. The FIAT trial is a large study comparing the Surgisis plug to the surgeon's preference of ligation of intersphincteric fistula tract procedure, advancement flap, fistulotomy or cutting seton for the treatment of trans-sphincteric fistula-in-ano (www.acpgbi.org.uk/members/research/fiat-trial/). Results are expected in 2017.

KEY POINTS

- Principles for the management of anal fistulae include drainage of sepsis, eradication of the tract, treatment of the underlying pathology, prevention of recurrence and preservation of continence.
- The cryptoglandular theory of anal sepsis is the proposed aetiology of fistula-in-ano.
- Historical treatments have not addressed 'preservation of continence' leading to newer more acceptable treatments being developed
- No current treatment has proven to be superior and further studies are required to improve the efficacy and acceptability of modern management of fistula-in-ano.

PERFACT

PERFACT (proximal superficial cauterization, emptying regularly fistula tracts and curettage of the tracts) is a new method for treating highly complex and supralevator fistulae developed by Garg and Garg in 2015. It comprises two steps: superficial cauterization of the anal muscosa at and around the internal opening of the fistula and regular procedures to keep the tracts clean. The aim is to permanently close the internal opening by granulation tissue, allowing the wound and tract to heal by secondary intention.

Garg and Garg (2015) performed this technique on 44 patients with complex fistulae in a prospective study with median follow up of 9 months. They reported a success rate of 79.5% and recurrence rate of 20.5%. A further study was performed using this technique in patients with a supralevator fistula or abscess. Fifteen patients were followed up for a median of 13 months, and Garg (2016) reported an overall healing rate of 80%. Importantly, there was no deterioration in incontinence scores post-procedure. This is obviously a new technique requiring further investigation and comparison to other treatments in order to draw any meaningful conclusions.

Discussion

Successful fistula management is a balance between sepsis control and continence.

For the aetiology of anal sepsis resulting in fistulae-in-ano, the cryptoglandular theory is widely held – with evidence coming from anatomical studies and the pathophysiological reasoning behind it, which fits the pattern of clinical disease experienced. Destruction of this septic focus lying in the intramuscular glands therefore lies at the core of effective treatment and recurrence prevention. However, accurate access to this area around the inter-sphincteric plane hosting the diseased anal gland can be challenging – especially when involving long, complex fistula tracks.

Without the consideration of postoperative continence, it is conceivable that a high success rate of sepsis control might be achieved by fistulotomy alone, even in complex fistulae (Tozer et al, 2013). However, because of the unacceptable levels of incontinence following management of such fistulae, there has been a move to access this area without the purposeful destruction of the sphincteric complex.

The earliest surgical example of this may be the use of the chemical seton, and this has been investigated, demonstrating impressive results for sepsis control compared with simple loose seton alone (Dutta et al, 2015). The superior result likely demonstrates the effect of the caustic nature of the seton lying within the fistula track bringing about the destruction of the diseased anal gland.

Accessing the intersphincteric plane, either by a limited circum-anal incision (ligation of intersphincteric fistula tract technique) or by direct visualization of the tract from the external opening (video-assisted anal fistula treatment), refines the technique of accessing the area of the diseased anal gland and permits excision or ablation of the tissue in that area, while causing minimal disruption to the sphincteric complex. While these innovative methods provide much-needed progress in the surgical management of fistulae-in-ano – with a single randomized control trial for the ligation of intersphincteric fistula tract procedure, and case series reports for the video-assisted anal fistula treatment – further analysis with high quality trials is necessary to provide evidence for their place as mainstream surgical treatments.

An ongoing trial looking at placement of a fistula plug does not appear to have the cryptoglandular theory at the heart of its principles.

It is perhaps difficult to appreciate the therapeutic value of merely occluding a fistula track with various agents (fibrin glue or collagen plug), while leaving the initiating cause unaddressed. Indeed, from the observation by Buchanan et al (2003), there are a proportion of patients in the series with abscess formation after glue insertion. This would occur if the diseased gland continues to suppurate and the pathway to purulent discharge is subsequently sealed (similar to the original abscess before incision and drainage).

The results for the prospective FIAT trial will be available in 2017. If this simple technique demonstrates results similar, or superior to, other modern surgical options, it may be that the cryptoglandular theory on sepsis may have to be questioned as the primary causative factor in the majority of fistula-in-ano. **BJHM**

Conflict of interest: none.

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