Managing non-IBD fistulising disease

Kapil Sahnan ^{1,2}, Samuel Adegbola,^{1,2} Nusrat Iqbal,^{1,2} Charlene Twum-Barima,^{1,2} Lillian Reza,^{1,2} Phillip Lung,² Janindra Warusavitarne,^{1,2} Ailsa Hart,^{2,3} Phil Tozer^{1,2}

¹Department of Surgery and Cancer, Imperial College London, London, UK

²Robin Phillip's Fistula Research Unit, St Mark's Hospital and Academic Institute, Harrow, UK

³IBD Unit, St Mark's Hospital, Harrow, UK

Correspondence to

Mr Kapil Sahnan, Department of Surgery, Imperial College London Department of Surgery and Cancer, London SW7 5NH, UK; ks303@doctors.org.uk

Received 31 March 2020

Revised 3 June 2020

Accepted 7 June 2020

Published Online First

28 July 2020

INTRODUCTION

As well as inflammatory bowel disease, there are a number of other conditions which either predispose to or cause perianal disease. For the most part, these are relatively simple and can be managed by a local specialist but there are cases where more nuanced approach is needed and where tertiary referral maybe more appropriate. In particular, rarer forms of perianal disease such as complex cryptoglandular fistula, rectovaginal fistula (RVF) and those associated with ileoanal pouches are associated with high levels of morbidity, risk and treatment failure. Experience in patient selection, multiple reparative techniques and identifying rare causes are crucial, and where evidence is lacking, this experience is the surgeon's only weapon.

The Association of Coloproctology of Great Britain and Ireland have recently released an updated position statement on anal fistula, once again recognising its complexity and often a lack of high-level evidence for treatment.¹ A greater proportion of men suffer from anorectal abscess than women and these occur at a mean age of 40 in both sexes.^{2–4} Known risk factors associated with developing an abscess include inflammatory bowel disease (IBD), smoking and HIV.⁵ The most commonly reported symptoms are pain and discharge, causing social embarrassment and loss of quality of life (QoL).^{6–9}

It is thought that approximately 90% of abscesses occur due to cryptoglandular suppurative, with infection of the intersphincteric anal glands which lubricate the passage of stool.^{10–11} The remaining ~10% of cases are caused by Crohn's disease (CD), abdominal infections tracking caudally (eg, diverticulitis), penetrative causes (eg, animal bones or by anal digitation),¹² perforated cancers (eg, rectal

or anal) or post radiotherapy, penetrating ulcers,¹³ tuberculosis (TB),¹⁴ actinomycosis¹⁵ or from a complication of local surgical procedures (eg, haemorrhoidectomy, episiotomy) or medical treatment (with nicorandil, which causes perianal or peristomal ulceration and fistulation).

This article will discuss complex and refractory cases related to cryptoglandular disease and discuss other types of non-IBD fistulising disease including rectovaginal and pouch-related anal fistula.

COMPLEX CRYPTOGLANDULAR SEPSIS

Abscess and fistula can coexist, and recurrent abscesses can lead to more than one tract. Some surgeons consider an abscess to be an 'acute fistula', and a fistula to be a 'chronic abscess'.¹⁶ This can be understood through sepsis in the intersphincteric space and a distinction between pathogenesis and persistence.⁸ Approximately a fifth of all patients with an abscess go on to develop a fistula. The majority of fistulas are diagnosed within the first year following abscess drainage and this is most pronounced in patients with CD. The other factors associated with a fistula from a preceding abscess are being of female gender, age 41–60 years and the location of the initial abscess being either ischioanal or intersphincteric.²

Fistulas are described as 'simple' or 'complex'. Simple fistulas may be intersphincteric or trans-sphincteric and traverse the anal sphincter low in the anal canal. Complex fistulas may traverse the sphincters high in the anal canal or have associated secondary extensions. Possible reasons for persistence or fistula being refractory to treatment are anatomical considerations and unrecognised underlying pathology.

The cryptoglandular theory also explains more complex abscess and

© Author(s) (or their employer(s)) 2021. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Sahnan K, Adegbola S, Iqbal N, et al. *Frontline Gastroenterology* 2021;12:524–534.

Figure 1 Types of horseshoe fistula.

fistulas. If the sepsis passes through the external sphincter, an ischioanal abscess will be formed. If this abscess occurs or stretches on both sides of the anus, a 'horseshoe' will form. Horseshoe abscesses or fistulas can occur in any perianal plane and at any level, from low intersphincteric to ischioanal and pararectal horseshoes (figures 1 and 2). Multiple extensions are not confined to perianal CD and failure to appreciate and treat secondary extensions in any fistula is a known cause of recurrence.¹⁷ Of note, supralelevator extensions can be attributed to infection descending from the abdomen/pelvis, ascending from perianal sepsis or an iatrogenic injury—whereby a false passage has been created with a fistula probe in theatre.

Abscess drainage is usually performed without the benefit of imaging and determining the anatomical location of an abscess is therefore dependent on the operating surgeon. However, an observational

Figure 2 Complex supralelevator horseshoe in a patient with a refractory cryptoglandular fistula.

Figure 3 Findings at examination under anaesthesia may not always be easy to interpret; in both cases, the internal and external openings are in the same location, but the cavity is high in the supralelevator space in the left image and in the ischioanal fossa in the image on the right. Drainage of these cavities should take place in different locations so differentiating between them is crucial.

study from the UK revealed that 85% of incision and drainage operations were performed by junior surgical trainees.¹⁸ Examination under anaesthesia (EUA) alone is not without its challenges and in certain circumstances the results can be difficult or impossible to interpret as figure 3 demonstrates.

In the acute setting, patients proceed to an EUA and incision and drainage of the abscess. Internal openings are probably associated with a high proportion of acute abscesses¹⁹ but not all abscesses with an internal opening end up developing a fistula.^{20 21} There is evidence to suggest treating fistulas at abscess drainage yields a reduced recurrence rate^{19 22} but we advocate a more conservative approach with primary abscesses since most 'acute fistulas' like this will heal without recurrence and fistulotomy, especially in the acute setting where the anatomy is hard to define, carries a risk of continence impairment. Even seton placement carries this risk, although deferred into the future.

MRI is the gold standard in fistula imaging and MRI-guided surgery has been shown to further reduce recurrence by up to 75% in patients with recurrent fistula-in-ano,²³ and to guide surgery.²⁴ It has been shown to be superior to EUA²⁵ and endoanal ultrasound,²⁶ and is the most accurate method for classification of the primary tract and any secondary extensions.²⁷ If it is possible to assess the primary fistula in the clinic setting and the tract can be palpated superficially all the way between the openings, with no induration suggesting complexity, then imaging may not be required. In refractory cases, it is essential to understand fistula morphology and the sphincter complex especially as previous surgery is likely to have resulted in further tissue destruction and anatomical distortion. MRI scans are used to inform clinicians about fistula complexity: number of tracts, presence of

sepsis and relation to the anal sphincter, as well as the patients' response to treatment interventions.²⁸

Refractory cases should always prompt the clinician to consider underlying conditions, including CD. Perianal sepsis can occur at least 6 months prior to luminal disease²⁹ and be the presenting complaint in 10%–25% of CD diagnoses.^{30–31} Clinical examination±EUA findings concerning for CD include proctitis, strictures, ulcers, fissures or complex/recurrent abscess drainage or fistulas. Such patients should be referred to a gastroenterologist and be offered a faecal calprotectin assay±endoscopic evaluation. CD-like phenomena also need to be considered such as inherited deficiencies which occur in paediatric populations, such as interleukin (IL)-10 or IL-10 receptor deficiency (IL-10R) which lead to immune dysregulation and enterocolitis.³² Other causes such as trauma, perianal infections including TB and sexually transmitted infections and radiation may underly complex or refractory fistulas. Recent work by our group has looked to explore the metabonomic profile of refractory fistula (CD and cryptoglandular), with the hope to identify metabolites with lead to persistence/recurrence of tracts and further shed light as to why some tracts are so difficult to manage.³³

There are some data to support the presence of a variety of other mechanisms driving persistence including epithelisation^{34–36} of the tract, bacterial components such as peptidoglycan,³⁷ epithelial to mesenchymal transition and molecular factors—anti-microbial defensins, IL-1b, IL-8,³⁸ IL-12p40 (33%) and tumour necrosis factor alpha (TNFα).³⁹ Studies exploring the pathogenesis of anal fistulas will further aid understanding and identification of potential therapeutic targets.⁸

Other cutaneous conditions, such as hidradenitis suppurativa (HS), an inflammatory follicular disease that commonly affects the apocrine glands and presents in the intertriginous areas of skin should be considered. When the perineal region is affected, it creates perineal abscesses of the skin that differ in aetiology, natural history and treatment to perianal abscesses but can be confused with them. It can coexist with CD and fistulas and is associated with smoking.⁴⁰ Perianal HS is more common in men than women, in whom axillary manifestations are more common.⁴¹ Perineal HS follows the distribution of the apocrine glands in the perineal skin and pathology may be exhibited as high as the dentate line, that is, within the lower anal canal. An alternative diagnosis is likely if imaging or EUA demonstrates sepsis above this point.⁴²

The severity, extent, chronicity and anatomic location of HS lesions determine which treatment—or combination of modalities—is most appropriate for each case. The available pharmaceutical options are topical or oral antibiotics, hormonal therapies, biological agents, immunomodulators, corticosteroids and retinoids. In general, patients with Hurley stage II and

III disease may benefit most from surgical treatments. Current surgical options include incision and drainage, lay open/deroofting and radical wide excision with or without reconstruction. Even in patients with mild and moderate HS where medical treatment is most frequently used, limited surgery may also be beneficial to control the disease and avoid wide surgical excision in the future. Surgical intervention halts progression of the disease and mitigates scarring and subsequent disability.

MANAGEMENT

Surgery is still the mainstay of treatment for cryptoglandular anal fistula. Despite the development of several sphincter preserving procedures, fistulotomy remains the best option in terms of cure, with success rates in the region of 80%–100%.^{43–45} Broadly speaking, most simple fistulas can be laid open with only a risk of minor incontinence (flatus incontinence and/or minor marking of the underwear—which may itself be bad enough); however, the concern with complex fistulas is that a significant proportion of the anal sphincter may be divided leading to a poor functional outcome.

Although some (including our group) have reported their experience with high fistulotomy,⁴⁶ where a significant proportion of the sphincter complex is sacrificed, there is no clear consensus as to what constitutes a 'high' fistula. Furthermore, it is noteworthy that even for simple fistulas, fistulotomy may cause functional disturbance in some patients, which they find unacceptable—it is only by the patient that significance and acceptability can be assessed.^{47–48}

Thus, to minimise the functional dilemma in fistula surgery with curative intent, several 'sphincter-preserving' techniques have been described, each addressing specific factors that contribute towards fistula pathogenesis. Many of these have their rationale in disconnecting the fistula tract from the bowel lumen (thus preventing the source of recurrent microbial contamination) such as anorectal advancement flaps. Ligation of the intersphincteric fistula tract (LIFT) not only disrupts the connection to the bowel lumen, but also excises what is presumed to be an intersphincteric focus of sepsis.⁴⁹

Other techniques rely on ablation of the luminal wall of the fistula. Cauterisation of the internal surface of the tract in either video-assisted fistula treatment⁵⁰ or fistula tract laser closure destroys the epithelial lining that contributes towards chronicity and is also often used in conjunction with closure of the internal opening.⁵¹ Anal fistula plugs fill the tract and will additionally provide a scaffold for tissue regeneration, whereas fibrin glue sealants encourage wound healing mechanisms by stimulating the growth of fibroblasts.¹⁷

Despite sound theoretical bases, these procedures have had promising but variable success rates in the published literature and overall trend poorly over time. No single technique has been universally accepted

Figure 4 Complex fistulas—intersphincteric (red) and trans-sphincteric (blue) tracts in a patient with complex cryptoglandular disease.

as the gold standard surgical approach as none can offer the success of fistulotomy without the risk of functional deficit; therefore, selection of sphincter preserving procedures largely relies on expertise of the surgeon, fistula morphology and in some cases patient preference. However, advancement flaps and the LIFT procedure probably carry the greatest weight of supportive evidence and remain the workhorses of the fistula surgeon's stable.

For complex fistulas with multiple tracks, secondary extensions or focal collections or abscesses, one should aim to 'rationalise' the fistula complex prior to attempts

at repair. A staged approach is often required, where drainage of sepsis and treatment of blind ending extensions are carried out first, in order to simplify fistula anatomy before treating the primary tract. In these cases, patient expectations should be managed appropriately, and the myth of a single, curative procedure should be debunked. It is of course feasible that patients may have more than one complex which needs addressing (figure 4). Patients in whom a curative procedure is not possible, for example, in complex recurrent cases, or those who are unwilling to accept the functional risks, further treatment is aimed at palliating symptoms and minimising the risk of recurring abscesses, usually achieved through placement of a long-term drainage seton. Figure 5 shows a simplified schematic to describe the process one might undertake when confronted with abscess or fistula, including more complex disease.

While the decision-making process regarding fistula management is heavily influenced by the factors described above, involvement of patients in this process is crucial in order to ensure that clinician and patient goals align. The impact of fistula symptoms on QoL can be wide ranging but poorly acknowledged in the clinical setting, and infrequently studied in literature. The studies that have been conducted highlight lower QoL in patients with fistula than in the general population and demonstrate an improvement following successful fistulotomy.^{52–54} Despite this, few studies of fistula treatments recognise the value of QoL as an outcome, and work is underway to develop disease-specific instruments to be able to facilitate QoL measurement in clinical practice and uptake into trials assessing treatment efficacy.

Figure 5 Stepwise management from abscess to fistula. I&D, incision and drainage; SPP, sphincter preserving procedure.

POUCH FISTULA

The ileoanal pouch is most commonly created to restore gastrointestinal continuity following proctocolectomy for refractory ulcerative colitis (UC) and familial adenomatous polyposis syndrome. CD is thought to be a contraindication to pouch creation due to the risk of ileal CD resulting in pelvic sepsis, pouch fistula and strictures.⁵⁵

Fistulas associated with the ileoanal pouch pose a unique challenge as fistula persistence may disrupt pouch function, while attempts at surgical repair may threaten continence, with either leading to eventual pouch failure. The incidence of pouch fistula was reported as 4.7% in the 2017 Ileoanal Pouch Registry which included 5352 pouch operations performed over four decades.⁵⁶ The overall rate of pouch failure is 10% in 10 years⁵⁷ but in the presence of a fistula this can be as high as 29%.⁵⁸

AETIOLOGY AND CLASSIFICATION

Pouch fistulas have been classified according to time of onset from pouch creation as either 'early' or 'late' fistulas, an early fistula being one that develops within 12 months of pouch creation, or 3 months following closure of a defunctioning ileostomy.⁵⁹ Early fistulas are thought to result from an anastomotic leak while late fistulas, a delayed presentation of CD. However, a classification based on timing is limited as a fistula may develop from chronic pelvic sepsis many years from pouch creation as a result of a subclinical anastomotic leak. Pouch fistulas can be described by anatomical position. A pouch fistula at the perineum may arise from the pouch anal anastomosis, pouch body or any other anastomotic line involved in pouch creation. We recently published a new classification of pouch fistulas which describes four distinct aetiological groups based on clinical presentation and morphology.⁶⁰ The principles of management are thought to differ according to aetiological origin. Figure 6 shows a representation of the four aetiological groups: group 1 anastomotic dehiscence-related fistula, group 2 IBD, with further subclassifications into CD (group 2a) and non-CD (group 2b) fistula, group 3 cryptoglandular and group 4 malignant fistula.

Figure 6 Representation of the four aetiological groups. IBD, inflammatory bowel disease.

Group 1 anastomotic dehiscence-related fistula

The internal opening in these fistulas arise at the point of anastomotic dehiscence which may be at the pouch anal anastomosis, the seams of the two limbs of a J-pouch or at the apex of the efferent limb of the J-pouch. There may be associated peri-pouch or presacral sepsis. These fistulas may present soon after pouch creation or closure of a defunctioning ileostomy but may develop many years from pouch creation as a result of chronic pelvic sepsis from a previously unrecognised, subclinical anastomotic leak.⁶¹ Pouch vaginal fistulas may result from an iatrogenic injury involving the vaginal wall during proctectomy, or through unwittingly incorporating the vagina in the stapled construction of the ileoanal anastomosis.⁶²

Group 2 IBD related

These fistulas are subcategorised into Crohn's and non-Crohn's IBD-related fistulas. CD-related fistulas must have either discontinuous small bowel disease or histology pathognomonic for CD, such as transmural lymphoid aggregates or mural granulomas.⁶³ Non-CD IBD-related fistula should have evidence of pouchitis or cuffitis in the absence of features definite for CD or an anastomotic leak.

Group 3 cryptoglandular disease-related fistula

These fistulas will arise from the dentate line in the absence of luminal features of IBD or an anastomotic leak.

Group 4 malignancy related

Any new fistula in a previously healthy pouch should raise suspicion of a primary malignancy at the cuff presenting with fistulating disease, especially in the presence of familial adenomatous polyposis or previous dysplasia or cancer in UC. MRI with fistula protocol, pouchoscopy, EUA and biopsy should be used early and evaluated with a high clinical suspicion.

DIAGNOSIS AND SURGICAL MANAGEMENT

Pouch fistulas should be classified as above and a new fistula should prompt EUA±biopsy, flexible pouchoscopy and small bowel imaging.^{63 64} This combination of investigations will define the aetiology and therefore guide treatment. Figure 7 demonstrates an MRI of a pouch anal fistula.

Fistula arising from an anastomotic leak that has been recognised early in its evolution may benefit from defunctioning ileostomy, drainage of pelvic sepsis, insertion of seton and in select cases the use of Endo-sponge.⁶⁵ Delayed surgical repair with pouch advancement or reconstruction, dependent on adequate distance between the anastomotic opening of the fistula and the dentate line, may be possible in select cases.⁶⁶ Various interventions have been reported in the repair of pouch vaginal fistulas, most with less than a 50% success rate, such as ileal pouch advancement

Figure 7 Pouch fistula (green: pouch, red: fistula, blue: internal opening of fistula coming into pouch anastomosis).

flap, transvaginal repair, transanal repair with/without tissue interposition, pouch reconstruction and fistula plug.^{66 67} There is no established gold standard in the surgical management of these fistulas due to the existence of only small reported case series and lack of homogeneity in the aetiology of these fistulas precluding meta-analysis and meaningful assessment of outcomes.

MEDICAL MANAGEMENT OF IBD-RELATED FISTULA

There are no randomised, prospective clinical trials specifically investigating the role of biologics in pouch fistula arising from an inflammatory cause. A systematic review of the efficacy of anti-TNF α therapy in refractory pouchitis and CD-like complications of the pouch such as prepouch ileitis, strictures and fistulas found that 64% with CD-like complications achieved clinical remission after an induction regimen and 57% maintained long-term clinical remission.⁶⁸ In a small case series of 12 patients with pouch vaginal fistula thought to be related to IBD, just over 50% maintained gastrointestinal continuity with long-term anti-TNF α therapy.⁶⁹ The role of anti-TNF α therapy in the management of group 2 IBD-related fistula is difficult to ascertain but a trial of steroids and anti-TNF α therapy is advised in fistulas thought to be arising from an inflammatory cause such as pouchitis, cuffitis or CD.⁶³ Prospective clinical trials are necessary to establish evidence of efficacy. Importantly, fistulas derived from malignancy or anastomotic leak and treated with immunomodulators or biological agents are likely to deteriorate.

Pouch failure is significantly more common in fistulising CD especially in the presence of a pouch vaginal

Figure 8 Anovaginal fistula tract (anus—blue, fistula—red, vagina—green).

fistula and pelvic sepsis.^{63 70} The use of uniform criteria for the diagnosis of fistulas arising from various aetiology will introduce consistency in reporting across institutions and enable standardisation and evidence-based management of these fistulas.

RECTOVAGINAL FISTULA

An RVF is an abnormal connection between (usually the posterior wall of) the vagina and (usually the anterior wall of) the rectum or anus (figure 8). It can be congenital or acquired. Clinically, it presents with the uncontrolled passage of flatus, discharge or stool, rendering to patients recurrent urinary tract infections, vaginitis and a psychosocial burden. It is a rare condition, accounting for less than 5% of all anorectal fistulas.⁷¹ However, the true prevalence and incidence are unknown. The majority of RVFs are secondary to obstetric trauma and CD. Pelvic cancer, radiotherapy, iatrogenic injury, infection (eg, from Bartholin's cyst and perianal sepsis), foreign body, violent acts and reassignment surgery in the neovagina are other known causes.

RVFs are debilitating and devastating, profoundly affecting QoL. Often women live with embarrassment and in secrecy. It is notoriously difficult to manage, and the rare nature of the condition poses many challenges to the surgeon. There are high failure rates of surgical repair. Patients may be exposed to multiple procedures and many require a stoma to help with closure of the tract. Dyspareunia, stenosis and psychological impairment may all ensue, both preoperatively and postoperatively.⁷²

AETIOLOGY

Obstetric

The majority of RVF cases are from obstetric trauma, accounting for up to 88% of all cases.⁷³ In south Asia and sub-Saharan Africa, RVFs are almost endemic, with an estimated incidence of 5000 to 10000 per year.⁷⁴ In

this part of the world, RVFs result from limited access to obstetric facilities and prolonged obstructed labour, causing necrosis on the RVF septum⁷⁵ secondarily from compression.⁷⁶ Other risk factors include perineal lacerations (third or fourth degree tear), shoulder dystocia, instrumental delivery, episiotomy and a breakdown of primary wound repair.^{75 77} Goldabar *et al* reported a study of 24 000 vaginal deliveries of which 1.7% suffered a fourth degree tear and 0.5% developed an RVF.⁷⁸ Following an episiotomy, 0.1% will develop an RVF and 0.05% who undergo a median episiotomy will develop an RVF.⁷⁹ These numbers are likely to be higher in developing nations. A study from the University of Minnesota showed an incidence of coexistent faecal incontinence to be 48%.⁸⁰

Crohn's disease

RVF is a devastating complication of CD and carries an increased risk of proctectomy.⁸¹ It has been reported that up to 50% of patients with CD will develop an anal fistula within 20 years of diagnosis, 9% of which are RVFs.⁸² RVFs are more commonly associated with colonic (23%) than small bowel (3.5%) CD. Surgery is the principle treatment, with adjunctive medical therapy.

Sands *et al* assessed short-term closure of RVF in 25 women with CD on infliximab. This resulted in symptomatic closure in 61% and 45% at 10 weeks and 14 weeks, respectively, with maintenance treatment required for prolonged closure.⁸³ It is unclear which RVF will respond to infliximab or prevent fistula recurrence; however, if luminal disease becomes quiescent as a result of treatment and the fistula and unacceptable symptoms persist, then surgery is warranted. Before consideration of definitive treatment, any sepsis should be drained and a stoma should be considered if stools are loose and frequent. Patients with less hostile luminal and perianal disease and intact sphincter should be offered an endorectal advancement flap. This technique is contraindicated in patients with stenosis and ulceration. Other techniques include rectal sleeve advancement flap, episiotomy, transperineal repair, transvaginal repair and abdominal approaches.

Iatrogenic injury

Iatrogenic injury from pelvic operations causing an RVF is rare. These have been seen with the use of the misfiring of stapled devices (double stapled technique) during low anterior resections. The incidence of RVF as a complication of low anterior resections is variable, ranging from 0.9% to 9.9%.⁸⁴ A study analysed data from 1493 female patients following low anterior resection for colorectal cancer and found 24 patients developed an RVF, giving an incidence of 1.61%.⁸⁴ Risk factors included unsatisfactory anastomosis and short distance between the tumour and the anal verge. Other causes include: postoperative leaks resulting in a pelvic abscess, perineal or vaginal mesh and following other operations in the pelvis, such as a hysterectomy,

rectocele repair, haemorrhoidectomy and proctocolectomy with ileoanal pouch anastomosis.⁸⁵

Infection

RVF may also arise from infection in the anorectal region, the majority of which are cryptoglandular in origin. It can also be caused by TB, HIV, Bartholin's cyst abscess and lymphogranuloma venereum.

Cancer/radiotherapy

Rectal, uterine, cervical or vaginal malignancies, which have significant local spread or have been treated with radiotherapy may lead to RVF. Malignancy can arise within a chronic pre-existing fistula or may mimic a fistula in a patient with CD.⁸⁶ Radiotherapy for cervical cancer is associated with RVF developing in 8% of cases 6–24 months following radiotherapy.⁸⁷ The incidence of RVF following radiotherapy has been shown to be proportionate with high doses of radiotherapy and previous hysterectomy, due to the absent protective barrier from the uterus.^{88 89} Local repairs following radiotherapy are likely to fail due to tissue loss, endarteritis obliterans in the repaired tissue and difficult planes. In this setting, definitive repair requires the interposition of healthy, well-vascularised tissue from outside the radiotherapy field, for example, with a Soave-type procedure in high fistulas and with an interposition such as with omentum in lower fistulas. For cancers with extensive spread, radical procedures are indicated such as pelvic exenteration.

PRINCIPLES OF TREATMENT

Several factors contribute to outcomes following RVF repair. These include aetiology, surrounding tissue health (ie, inflammation, stenosis, proctitis, infection, scarring), comorbidities, height of internal opening and previous failed repairs. Colorectal surgeons advocate closing the internal opening, eliminating inflow into the tract. This means closing the rectal side of the fistula tract. Procedures such as rectal advancement flap follow this principle. It is important that repairs do not include diseased tissue such as proctitis in CD or irradiated tissue from radiotherapy, as these repairs are bound to fail. Gynaecologists and urogynaecologists advocate closing the vaginal side of the fistula, as tissue is well vascularised, pliable and non-diseased ready to be used for repair. One study reported a 100% healing rate in 39 patients treated with the transvaginal approach.⁹⁰ A further study treated 13 patients with the transvaginal approach with a diverting stoma. They reported 12 out of 13 patients healing after 50-month follow-up.⁹¹

Any repair carries a risk not only of failure but of worsening of symptoms associated with enlarging of the fistula. Therefore, a small fistula with only modest symptoms may be best left untreated. It will be abhorrent to some women despite few symptoms, but others

may prefer to live the status quo than risk symptom which more fundamentally impair QoL.

If repair is anticipated, thorough assessment of the fistula is imperative to guide surgical decision-making. This includes the height of the internal opening, tissue intussusception or perineal descent and integrity of the sphincters.⁹²

Timing is also important. Following inflammation or obstetric injury, it is important to allow the underlying tissue to heal, which can take up to 6–9 months. For small less symptomatic RVF, a period of watchful waiting is advised.⁸⁵ One author reported 50% closure in small RVF, following obstetric trauma and recommended watchful waiting of 6 months.⁹³ However, interval follow-up is necessary.

In order to optimise the best outcomes, it is imperative to manage any underlying pathology, ensuring sepsis is resolved, any foreign body is removed and medical treatment is optimised where appropriate. During this time, faecal diversion may be indicated or a draining seton placed, although the latter is unnecessary in short tracts and may even enlarge fistulas, as well as being very uncomfortable and impairing sexual function. Defunctioning allows for any associated inflammation or stenosis to be resolved, allowing pliable tissue to be amenable for repair but evidence to support this practice is limited and the idea will be rejected by many women.

Counselling and addressing the patient's expectations are important. Patients should be informed that they may require multiple interventions to eventually close the fistula and in some instances the tract may never close and may enlarge.

COMMON TECHNIQUES

Abdominal procedures are ideal with a high fistula or one arising from an anastomosis. Healthy colon can be delivered through the denuded rectal tube and anastomosed at the dentate line in a Soave-type coloanal pull though. An adequate space between the anastomosis/internal opening and the dentate line (at least 1 cm, preferably 2 cm) is required.

For lower fistulas, if the sphincter complex is damaged, a direct repair in the rectovaginal septal space can be performed with an overlapping sphincter repair as part of the repair. This is sometimes done in conjunction with a levatorplasty.⁸⁰ If the sphincter complex is intact and there is adequate internal intussusception, an advancement flap may be performed. Where there is not sufficient mobility in the tissues to facilitate a flap, local repair in the rectovaginal septal space bolstered by a flap of healthy interposition tissue can be performed. Gracilis is bulky but mobilisation and the resultant scar are morbid. Martius flaps, derived from the labial fat pad, can lead to asymmetry, numbness or pain in the labia and are suitable only in lower fistulae as the flap is small. Gluteal perforator flaps have good vasculature without causing any

notable functional deformities.⁹⁴ Omentum is versatile and can be mobilised to come all the way down to the perineal skin but is not always retrievable. Our centre demonstrated good results in seven patients who underwent a combined laparoscopic and perineal omental interposition and perineal repair. No recurrence was detected in their last follow-up.⁹⁵

Other techniques in fistulotomy and repair, LIFT procedure and vaginal flaps but the algorithm above is one example, used in our unit, to demonstrate an approach tailored to the fistula and the patient.

DEFUNCTIONING OSTOMY

Little is known about the indication and outcomes of a diverting stoma for the management of RVF. This question is not well explored in the literature. Ostomy formation is often done in conjunction with a repair, to reduce symptoms or as part of an ablative operation such as a proctectomy. We advocate the use of a defunctioning stoma in any abdominal repair or local repair in the rectovaginal septal plane, or in a recurrent fistula repair. There is insufficient evidence to support the use of a stoma to increase healing rates after local repair but no trial has ever effectively and directly asked this question and many fistula surgeons take the view that a stoma will be beneficial in the context of complex surgery or recurrent fistula.

The difficulty is that many women do not want a stoma and that if the repairs fail, the question of what to do with the stoma is a difficult one. This conundrum emphasises the importance of operating only when symptoms demand it. Careful, detailed and honest discussion between surgeon and patient is, as always, crucial in the setting of RVF. Proctectomy is sometimes necessary to improve QoL, particularly where proctitis, stricture, incontinence or severe symptoms blight a woman's personal, professional, social and sexual life and identity in the presence of a refractory or recurrent RV fistula.

CONCLUSION

Complex anal fistula remains challenging to treat and even simple fistulas carry treatment options which demand compromise of the patients, who must choose between the higher chance of a cure or protection of their continence. Sphincter preserving procedures are not currently as efficacious as we would like and demand a relatively simple morphology, which it is sometimes possible to engineer when not initially present. Pouch fistulas should be treated according to their anatomy and aetiology, with special attention paid to the potential for malignancy or underlying IBD when presenting newly. RVF may not need surgery at all and when they do the operation should be tailored to the fistula and the patient. Stomas are an inevitable part of the process for many but not all women. Careful counselling and honest evaluation of outcomes are crucial in managing complex fistulas

and an underlying IBD diagnosis should be sought in complex and refractory cases.

Contributors All authors contributed equally in the creation of this manuscript. All authors were involved in the design of this review. The manuscript was written by KS, SA, NI, CT-B, LR and PT. All authors reviewed and critically appraised the manuscript before submission.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

ORCID iD

Kapil Sahnan <http://orcid.org/0000-0003-3885-5752>

REFERENCES

- Williams G, Williams A, Tozer P, *et al.* The treatment of anal fistula: second ACPGBI Position Statement - 2018. *Colorectal Dis* 2018;20 Suppl 3:5–31.
- Sahnan K, Askari A, Adegbola SO, *et al.* Natural history of anorectal sepsis. *Br J Surg* 2017;104:1857–65.
- Sainio P. Fistula-In-Ano in a defined population. incidence and epidemiological aspects. *Ann Chir Gynaecol* 1984;73:219–24.
- Read DR, Abcarian H. A prospective survey of 474 patients with anorectal abscess. *Dis Colon Rectum* 1979;22:566–8.
- Wei P-L, Keller JJ, Kuo L-J, *et al.* Increased risk of diabetes following perianal abscess: a population-based follow-up study. *Int J Colorectal Dis* 2013;28:235–40.
- Simpson JA, Banerjee A, Scholefield JH. Management of anal fistula. *BMJ* 2012;345:e6705.
- Whiteford M. Perianal Abscess/Fistula disease. *Clin Colon Rectal Surg* 2007;20:102–9.
- Sugrue J, Nordenstam J, Abcarian H, *et al.* Pathogenesis and persistence of cryptoglandular anal fistula: a systematic review. *Tech Coloproctol* 2017;21:425–32.
- Bleier JIS, Moloo H. Current management of cryptoglandular fistula-in-ano. *World J Gastroenterol* 2011;17:3286–91.
- Eisenhammer S. The internal anal sphincter and the anorectal abscess. *Surg Gynecol Obstet* 1956;103:501–6.
- Parks AG, Gordon PH, Hardcastle JD. A classification of fistula-in-ano. *Br. J. Surg.* 1976;63:1–12.
- Sahnan K, Adegbola SO, Tozer PJ, *et al.* Perianal abscess. *BMJ* 2017;j475.
- Marzo M, Felice C, Pugliese D, *et al.* Management of perianal fistulas in Crohn's disease: an up-to-date review. *World J Gastroenterol* 2015;21:1394–403.
- Gupta PJ. Ano-perianal tuberculosis--solving a clinical dilemma. *Afr Health Sci* 2005;5:345–7.
- Fry GA, Martin WJ, Dearing WH, *et al.* Primary actinomycosis of the rectum with multiple perianal and perineal fistulae. *Mayo Clin Proc* 1965;40:296–9.
- Sahnan K, Askari A, Adegbola SO, *et al.* Persistent fistula after anorectal abscess drainage: local experience of 11 years. *Dis Colon Rectum* 2019;62:327–32.
- Limura E, Giordano P. Modern management of anal fistula. *World J Gastroenterol* 2015;21:12–20.
- Pearce L, Newton K, Smith SR, *et al.* Multicentre observational study of outcomes after drainage of acute perianal abscess. *Br J Surg* 2016;103:1063–8.
- Oliver I, Lacueva F, Pérez Vicente F, *et al.* Randomized clinical trial comparing simple drainage of anorectal abscess with and without fistula track treatment. *Int J Colorectal Dis* 2003;18:107–10.
- Tang CL, Chew SP, Seow-Choen F. Prospective randomized trial of drainage alone vs. drainage and fistulotomy for acute perianal abscesses with proven internal opening. *Dis Colon Rectum* 1996;39:1415–7.
- Ho YH, Tan M, Chui CH, *et al.* Randomized controlled trial of primary fistulotomy with drainage alone for perianal abscesses. *Dis Colon Rectum* 1997;40:1435–8.
- Malik AI, Nelson RL, Tou S. Incision and drainage of perianal abscess with or without treatment of anal fistula. *Cochrane Database Syst Rev* 2010;CD006827.
- Buchanan G, Halligan S, Williams A, *et al.* Effect of MRI on clinical outcome of recurrent fistula-in-ano. *The Lancet* 2002;360:1661–2.
- Beets-Tan RG, Beets GL, van der Hoop AG, *et al.* Preoperative MR imaging of anal fistulas: does it really help the surgeon? *Radiology* 2001;218:75–84.
- Phillips RK, Seow-Choen. Insights gained from the management of problematical anal fistulae at St. Mark's Hospital, 1984–88. *Br J Surg* 1991;78:539–41.
- Siddiqui MRS, Ashrafian H, Tozer P, *et al.* A diagnostic accuracy meta-analysis of endoanal ultrasound and MRI for perianal fistula assessment. *Dis Colon Rectum* 2012;55:576–85.
- Sahni VA, Ahmad R, Burling D. Which method is best for imaging of perianal fistula? *Abdom Imaging* 2008;33:26–30.
- Sahnan K, Adegbola SO, Tozer PJ, *et al.* Improving the understanding of perianal Crohn fistula through 3D modeling. *Ann Surg* 9000 https://journals.lww.com/annalsurgery/Fulltext/publishahead/Improving_the_Understanding_of_Perianal_Crohn.95788.aspx
- Eglinton TW, Barclay ML, Gearry RB, *et al.* The spectrum of perianal Crohn's disease in a population-based cohort. *Dis Colon Rectum* 2012;55:773–7.
- Castaño-Milla C, Chaparro M, Saro C, *et al.* Effectiveness of adalimumab in perianal fistulas in crohn's disease patients naive to anti-TNF therapy. *J Clin Gastroenterol* 2015;49:34–40.
- Hellers G, Bergstrand O, Ewerth S, *et al.* Occurrence and outcome after primary treatment of anal fistulae in Crohn's disease. *Gut* 1980;21:525–7.
- Engelhardt KR, Shah N, Faizura-Yeop I, *et al.* Clinical outcome in IL-10- and IL-10 receptor-deficient patients with or without hematopoietic stem cell transplantation. *J Allergy Clin Immunol* 2013;131:825–30.
- Adegbola S, Sarafian M, Sahnan K, *et al.* Metabonomic profiling distinguishes Crohn's perianal fistulas and idiopathic idiopathic (cryptoglandular) perianal fistulas: possible clues to underlying pathogenesis? *J Crohn's Colitis* 2020;14:S174.
- Lunniss PJ, Barker PG, Sultan AH, *et al.* Magnetic resonance imaging of fistula-in-ano. *Dis Colon Rectum* 1994;37:708–18.
- van Koperen PJ, Wind J, Bemelman WA, *et al.* Long-Term functional outcome and risk factors for recurrence after surgical treatment for low and high perianal fistulas of cryptoglandular origin. *Dis Colon Rectum* 2008;51:1475–81.
- Mitalas LE, Dwarkasing RS, Verhaaren R, *et al.* Is the outcome of transanal advancement flap repair affected by the complexity of high transsphincteric fistulas? *Dis Colon Rectum* 2011;54:857–62.
- van Onkelen RS, Mitalas LE, Gosselink MP, *et al.* Assessment of microbiota and peptidoglycan in perianal fistulas. *Diagn Microbiol Infect Dis* 2013;75:50–4.
- Kiehne K, Fincke A, Brunke G, *et al.* Antimicrobial peptides in chronic anal fistula epithelium. *Scand J Gastroenterol* 2007;42:1063–9.
- van Onkelen RS, Gosselink MP, van Meurs M, *et al.* Pro-Inflammatory cytokines in cryptoglandular anal fistulas. *Tech Coloproctol* 2016;20:619–25.

- 40 Rosi YL, Lowe L, Kang S. Treatment of hidradenitis suppurativa with infliximab in a patient with Crohn's disease. *J Dermatolog Treat* 2005;16:58–62.
- 41 Anderson MJ, Dockerty MB. Perianal hidradenitis suppurativa; a clinical and pathologic study. *Dis Colon Rectum* 1958;1:23–31.
- 42 Asgerisson T, Nunoo R, Luchtefeld M. Hidradenitis suppurativa and pruritus ani. *Clin Colon Rectal Surg* 2011;24:071–80.
- 43 Tozer P, Sala S, Cianci V, et al. Fistulotomy in the tertiary setting can achieve high rates of fistula cure with an acceptable risk of deterioration in continence. *J Gastrointest Surg* 2013;17:1960–5.
- 44 Garg P. Is fistulotomy still the gold standard in present era and is it highly underutilized?: an audit of 675 operated cases. *Int J Surg* 2018;56:26–30.
- 45 Göttingen KWA, Janssen PTJ, Heemskerk J, et al. Long-Term outcome of low perianal fistulas treated by fistulotomy: a multicenter study. *Int J Colorectal Dis* 2015;30:213–9.
- 46 Atkin GK, Martins J, Tozer P, et al. For many high anal fistulas, lay open is still a good option. *Tech Coloproctol* 2011;15:143–50.
- 47 Dudukgian H, Abcarian H. Why do we have so much trouble treating anal fistula? *World J Gastroenterol* 2011;17:3292–6.
- 48 Garcia-Aguilar J, Belmonte C, Wong WD, et al. Anal fistula surgery: factors associated with recurrence and incontinence. *Dis Colon Rectum* 1996;39:723–9.
- 49 Rojanasakul A, Pattanaarun J, Sahakitrungruang C, et al. Total anal sphincter saving technique for fistula-in-ano; the ligation of intersphincteric fistula tract. *J Med Assoc Thai* 2007;90:581–6.
- 50 Meinero P, Mori L. Video-Assisted anal fistula treatment (VAAFT): a novel sphincter-saving procedure for treating complex anal fistulas. *Tech Coloproctol* 2011;15:417–22.
- 51 Wilhelm A. A new technique for sphincter-preserving anal fistula repair using a novel radial emitting laser probe. *Tech Coloproctol* 2011;15:445–9.
- 52 Visscher AP, Schuur D, Roos R, et al. Long-Term follow-up after surgery for simple and complex cryptoglandular fistulas: fecal incontinence and impact on quality of life. *Dis Colon Rectum* 2015;58:533–9.
- 53 Owen HA, Buchanan GN, Schizas A, et al. Quality of life with anal fistula. *Annals* 2016;98:334–8.
- 54 Owen HA, Buchanan GN, Schizas A, et al. Quality of life following fistulotomy - short term follow-up. *Colorectal Dis* 2017;19:563–9.
- 55 Chang S, Shen B, Remzi F. When not to pouch: important considerations for patient selection for ileal pouch-anal anastomosis. *Gastroenterol Hepatol* 2017;13:466–75.
- 56 Worley GHT, Fearnhead NS, Brown SR, et al. Review of current practice and outcomes following ileoanal pouch surgery: lessons learned from the ileoanal pouch registry and the 2017 ileoanal pouch report. *Colorectal Dis* 2018;20:913–22.
- 57 Worley GHT, Patsouras D, Sahnian K, et al. Ileal pouch excision: a contemporary observational cohort. *Dis Colon Rectum* 2019;62:454–62.
- 58 Nisar PJ, Kiran RP, Shen B, et al. Factors associated with ileoanal pouch failure in patients developing early or late pouch-related fistula. *Dis Colon Rectum* 2011;54:446–53.
- 59 Shen B, Remzi FH, Lavery IC, et al. A proposed classification of ileal pouch disorders and associated complications after restorative proctocolectomy. *Clin Gastroenterol Hepatol* 2008;6:145–58.
- 60 Reza LM, Lung PFC, Lightner AL, et al. Perianal fistula and the ileoanal pouch - different aetiologies require distinct evaluation. *Colorectal Dis*. In Press 2020. doi:10.1111/codi.15074. [Epub ahead of print: 17 Apr 2020].
- 61 Freeha K, Bo S. Complications related to J-Pouch surgery. *Gastroenterol Hepatol* 2018;14:571–6.
- 62 Lolohea S, Lynch AC, Robertson GB, et al. Ileal pouch-anal anastomosis-vaginal fistula: a review. *Dis Colon Rectum* 2005;48:1802–10.
- 63 Lightner AL, Pemberton JH, Loftus EJ. Crohn's disease of the ileoanal pouch. *Inflamm Bowel Dis* 2016;22:1502–8.
- 64 Ng K-S, Gonsalves SJ, Sagar PM. Ileal-anal pouches: a review of its history, indications, and complications. *World J Gastroenterol* 2019;25:4320–42.
- 65 Rottoli M, Di Simone MP, Vallicelli C, et al. Endoluminal vacuum-assisted therapy as treatment for anastomotic leak after ileal pouch-anal anastomosis: a pilot study. *Tech Coloproctol* 2018;22:223–9.
- 66 Sapci I, Akeel N, DeLeon MF, et al. What is the best surgical treatment of pouch-vaginal fistulas? *Dis Colon Rectum* 2019;62:595–9.
- 67 Maslekar S, Sagar PM, Harji D, et al. The challenge of pouch-vaginal fistulas: a systematic review. *Tech Coloproctol* 2012;16:405–14.
- 68 Huguet M, Pereira B, Goutte M, et al. Anti-TNF therapy in refractory pouchitis and crohn's disease-related complications of the pouch after ileal pouch-anal anastomosis following colectomy for ulcerative colitis: A systematic review and meta-analysis. *United Eur Gastroenterol J* 2016;4:A638–9.
- 69 Sivathondan PC, Bloemendaal A, Travis S, et al. Management of pouch-vaginal fistulas - experience from our institution. *Colorectal Dis* 2020;22:439–444.
- 70 Braveman JM, Schoetz DJ, Marcello PW, et al. The fate of the ileal pouch in patients developing Crohn's disease. *Dis Colon Rectum* 2004;47:1613–9.
- 71 Taskesen F, Arikanoglu Z, Bostanci S, et al. Rectovaginal fistulas: five year's experience. *Clin Ter* 2014;165:129–32.
- 72 El-Gazzaz G, Hull T, Mignanelli E, et al. Analysis of Function and Predictors of Failure in Women Undergoing Repair of Crohn's Related Rectovaginal Fistula. *J Gastrointest Surg* 2010;14:824–9.
- 73 Saclarides TJ. Rectovaginal fistula. *Surg Clin North Am* 2002;82:1261–72.
- 74 Champagne BJ, McGee MF. Rectovaginal fistula. *Surg Clin North Am* 2010;90:69–82.
- 75 Kniery KR. Operative considerations for rectovaginal fistulas. *World J Gastrointest Surg* 2015;7:133.
- 76 Rivadeneira D, Ruffo B, Amrani S, et al. Rectovaginal fistulas: current surgical management. *Clin Colon Rectal Surg* 2007;20:096–101.
- 77 Brown HW, Wang L, Bunker CH, et al. Lower reproductive tract fistula repairs in inpatient US women, 1979–2006. *Int Urogynecol J* 2012;23:403–10.
- 78 Goldaber KG, Wendel PJ, McIntire DD, et al. Postpartum perineal morbidity after fourth-degree perineal repair. *Am J Obstet Gynecol* 1993;168:489–93.
- 79 Homsy R, Daikoku NH, Littlejohn J, et al. Episiotomy: risks of dehiscence and rectovaginal fistula. *Obstet Gynecol Surv* 1994;49:803–8.
- 80 Tsang CB, Madoff RD, Wong WD, et al. Anal sphincter integrity and function influences outcome in rectovaginal fistula repair. *Dis Colon Rectum* 1998;41:1141–6.
- 81 Valente MA. Contemporary surgical management of rectovaginal fistula in Crohn's disease. *World J Gastrointest Pathophysiol* 2014;5:487.
- 82 Ruffolo C, Penninckx F, Van Assche G, et al. Outcome of surgery for rectovaginal fistula due to Crohn's disease. *Br J Surg* 2009;96:1190–5.
- 83 Sands BE, Blank MA, Patel K, et al. Long-Term treatment of rectovaginal fistulas in Crohn's disease: response to infliximab in the accent II study. *Clin Gastroenterol Hepatol* 2004;2:912–20.
- 84 Zheng H, Guo T, Wu Y, et al. Rectovaginal fistula after low anterior resection in Chinese patients with colorectal cancer. *Oncotarget* 2017;8:73123–32.

- 85 Das B, Snyder M. Rectovaginal fistulae. *Clin Colon Rectal Surg* 2016;29:50–6.
- 86 VanBuren WM, Lightner AL, Kim ST, *et al.* Imaging and surgical management of anorectal vaginal fistulas. *RadioGraphics* 2018;38:1385–401.
- 87 Narayanan P, Nobbenhuis M, Reynolds KM, *et al.* Fistulas in malignant gynecologic disease: etiology, imaging, and management. *RadioGraphics* 2009;29:1073–83.
- 88 Perez CA, Breaux S, Bedwinek JM, *et al.* Radiation therapy alone in the treatment of carcinoma of the uterine cervix. II. Analysis of complications. *Cancer* 1984;54:235–46.
- 89 Boronow RC. Repair of the radiation-induced vaginal fistula utilizing the Martius technique. *World J Surg* 1986;10:237–48.
- 90 Rahman MS, Al-Suleiman SA, EL-Yahia AR, *et al.* Surgical treatment of rectovaginal fistula of obstetric origin: a review of 15 years' experience in a teaching hospital. *J Obstet Gynaecol* 2003;23:607–10.
- 91 Bauer JJ, Sher ME, Jaffin H, *et al.* Transvaginal approach for repair of Recto vaginal fistulae complicating Crohn's disease. *Ann Surg* 1991;213:151–8.
- 92 Tozer PJ, Balmforth D, Kayani B, *et al.* Surgical management of rectovaginal fistula in a tertiary referral centre: many techniques are needed. *Colorectal Dis* 2013;15:871–7.
- 93 Mattingly RF. Anal incontinence and rectovaginal fistulas gynecology. *TeLinde's Oper Gynecol* 1977.
- 94 Lee SK, Lee YS, Song SY, *et al.* Double-Sided folded internal pudendal artery perforator flap for the repair of a recurrent rectovaginal fistula. *Arch Plast Surg* 2018;45:90–2.
- 95 de Bruijn H, Maeda Y, Murphy J, *et al.* Combined laparoscopic and perineal approach to omental interposition repair of complex rectovaginal fistula. *Dis Colon Rectum* 2018;61:140–3.