ANTHONY DE BUCK VAN OVERSTRAETEN MD, MSC

Dr. Anthony de Buck MD, MSc, is a colorectal surgeon practicing at Mount Sinai Hospital in Toronto and serving as an Associate Professor at the University of Toronto. With a strong background in surgical and colorectal training, Dr. de Buck has made significant contributions to the field of colorectal surgery and clinical outcome research in inflammatory bowel disease (IBD). Dr. de Buck earned his medical degree at the University of Leuven. To further enhance his knowledge and skills, Dr. de Buck pursued a colorectal fellowship at the University of Toronto in 2013. Additionally, he obtained a Master's Degree in Clinical Epidemiology from the University of Toronto, equipping him with advanced research skills to investigate clinical outcomes in IBD.

Dr. de Buck's scientific work is primarily focused on clinical outcome research in IBD, with a specific emphasis on functional and quality of life outcomes in patients with this chronic condition. His dedication to improving patient outcomes has led him to conduct numerous studies and secure several peer-reviewed grants to support his research endeavors. As a leading researcher, he is actively involved in multi-institutional studies, including randomized controlled trials (RCTs), that aim to advance our understanding of IBD and its impact on patients' lives. In addition to his research pursuits, Dr. de Buck is deeply committed to educating the next generation of medical professionals. As an Associate Professor at the University of Toronto, he plays an important role in teaching and mentoring students, residents, and fellows, imparting his knowledge and expertise to shape the future of colorectal surgery and IBD research.

Affiliations:
Department of Surgery, Sinai Health System, University of Toronto, Toronto, Ontario

SURGICAL APPROACHES TO PERIANAL CROHN'S DISEASE

Introduction
Virtually one-third of patients with Crohn's disease (CD) develop anal symptoms.[1,2] In addition to the typical skin tags and chronic fissures, 50% of these patients develop perianal abscesses and fistulas, which are among the most challenging CD phenotypes to treat. They can significantly affect patients' quality of life (QOL) and result in a significant amount of lost days at school or work, as they often occur in a young, active population.[3,4]

Pharmacologic Therapy
Pharmacologic therapy is the cornerstone of the treatment of anal CD, although none of the currently available treatments have demonstrated high success rates. The surgeon also plays an important role in the management of anal CD. In fact, anal CD requires the highest level of interaction between multiple disciplines, including the gastroenterologist, the surgeon and the radiologist. Close collaboration and transition of care between these disciplines, along with allied healthcare specialists, has a beneficial impact on patient outcome by providing integrated care and optimal patient follow-up.

Surgical Measures
Remission of anal CD is extremely challenging to achieve. Therefore, the initial treatment goal is to control

sepsis, which should be accomplished prior to initiating immunomodulatory therapy. Abscesses require drainage performed by a surgeon. The presence of an abscess can be assessed by clinical examination or pelvic imaging (MRI, CT or ultrasound). An understanding of the perineal anatomy is essential to adequately diagnose perineal abscesses, as well as to identify the optimal and safest form of drainage that avoids any sphincteric harm or results in the fistula becoming even more complex. The Park's classification is typically used by the surgeon to understand and describe the fistula anatomy. This classification is interesting because it describes the relationship of the fistula to the anal sphincter, which plays a role in selecting the most favourable surgical treatment for fistula repair. The surgeon's objective should be to obtain adequate evacuation of the abscess by creating the shortest possible fistula tract and avoiding damage to the anal sphincter. Ischiorectal abscesses (the most frequently-occurring abscesses) require percutaneous drainage by an incision through the skin at the culminating point of the abscess. The skin incision should be large enough to allow for optimal wound care. Supra-levator abscesses that result from a fistula tract in the inter-sphincteric plane should be drained intra-anally to avoid the creation of a supra-sphincteric fistula.

The risk for an abscess recurrence following drainage is reduced by the placement of a seton drain, which is a thread that is positioned within the fistula tract, looping from the external to the internal opening. This drain keeps the external opening patent for better drainage of infected content of the fistula, thereby reducing the risk of abscess recurrence. This procedure is typically well-accepted by patients. While it can remain indefinitely, patients often ask surgeons to remove it at some point during the disease course.

Once the acute sepsis is controlled and the question of treating the fistula arises, surgeons can play a role in fistula treatment using several available surgical techniques. Each surgical technique aims at closing the internal opening of the fistula, which is at the high-pressure zone. Successful closure of this internal opening typically results in the healing of the entire fistula. This is, however, more challenging than it sounds! Therefore, it is important for patients to have reasonable expectations when it comes to success rates of fistula treatment. They need to understand that, frequently, symptom control is the highest achievable goal.

Despite the availability of high-quality imaging, the surgeon typically begins with an examination under anesthesia (EUA) to explore the fistula and obtain a

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Reference

1. STELARA/STELARA I.V. Product Monograph. Janssen Canada Inc., September 9, 2021.

good mapping of the fistula, and to identify possible secondary tracts, horseshoe fistulas or extensions above the pelvic floor. In addition, the surgeon will assess the quality of the tissues and the degree of inflammation, rule out the presence of anal stricture. Anal stricture is a significant predictive factor for surgical failure. If a seton is not already in place, one will often be placed at this time to prepare for surgical repair. The seton remains in the fistula tract to better control for sepsis, minimizing the risk for recurrent abscess formation. There is no strict evidence guiding the timing of seton removal, however, in the PISA trial setons were removed at 6 weeks after initiating anti-TNF treatment to increase the odds for closure under medical therapy.[5] In fact, the timing for seton removal remains at the surgeon's discretion, trying to find a balance between adequate sepsis control and keeping the opportunity for non-operative healing.

The surgical techniques used for closure of CD fistulas were initially described for the treatment of cryptoglandular fistulas. Only a minority of patients included in the literature are CD patients; therefore, the clinical evidence is quite limited. However, the success rate is lower in CD patients vs that of patients with cryptoglandular fistulas. It is also important to note that only select patients are eligible for surgical repair of their CD-related fistulas. In fact, patients with very complex fistulas (i.e., supra-sphincteric fistulas and those with multiple internal openings), rectal stricture and active proctitis are poor candidates for anal fistula repair. More recently, the PISA-II trial compared radiological healing in CD patients with a peri-anal fistula between short-term anti-TNF treatment and surgical closure with anti-TNF treatment alone.[5] At a follow up of 18 months, radiological healing was significantly more common in the surgical group compared to the anti-TNF alone group (32% vs 9%, p = 0.005), further validating surgical repair of fistulas in Crohn's disease patients. It is however important to consider closure at the time of adequate sepsis control and disease control.

Fistulotomy

Simple, superficial fistulas can be successfully treated by fistulotomy. This procedure results in a high success rate, even in CD patients; however, it partially compromises the continence of the anus by dividing part of the sphincter. This technique should be used with great caution especially in CD patients as the risk for recurrence leading to potential subsequent surgeries is high; furthermore, the typical stool consistency of CD patients requires good sphincter function.[6] Therefore, this technique should be reserved only for carefully selected patients at low risk for incontinence. Sphincter sparing techniques are therefore preferred in patients with CD. Several surgical techniques aim to close the internal opening without disrupting the sphincter integrity.

Rectal advancement flap (RAF)

The first sphincter-preserving technique is the rectal advancement flap (RAF). This technique aims at mobilizing a v-shaped mucosal flap to cover the internal opening. It has been reported multiple times in the literature, including a systematic review reporting an overall outcome of approximately 60%.[7] Data specific to CD patients is scarce; however, poor long-term outcomes have frequently been reported. The difficulty in CD patients is the presence of rectal fibrosis restraining the ability of the flap to be mobilized sufficiently. Moreover, the presence of proctitis is a contraindication for this approach. A recent retrospective series has reported a lower success rate for RAF than for ligation of intersphincteric fistula tract (LIFT) in CD patients.[8]

Ligation of intersphincteric fistula tract (LIFT)

As an alternative to RAF, surgeons can use the LIFT technique. This technique aims at dissecting the intersphincteric plane through a semi-circular perianal incision at the level of the fistula.[9] Once the intersphincteric plane is opened, the portion of the fistula in that plane is isolated, ligated and transected, which results in a closed internal opening, without damaging the sphincters. The external opening of the fistula is left open and should heal secondarily once the internal opening has healed. In this case, once more only limited data report on the healing rate in CD patients, with an early healing rate of 65% and a late healing rate of virtually 50%.[10,11] The healing rate is lower than for cryptoglandular fistulas and reflects the challenge of treating CD- related perianal fistulas.

Anal fistula plug

The anal fistula plug is a bio-absorbable xenograft plug composed of porcine intestinal submucosa, which is introduced in the fistula, obturating the internal opening while providing a matrix for tissue regeneration in the fistula tract.[12] Its easy to use, not requiring challenging surgical dissection, has generated significant interest. Unfortunately, several clinical studies have demonstrated its lack of benefit, including one randomized trial that did not show any benefit vs placebo.[13,14] The plug should therefore not be used in the treatment of fistulas related CD.

Video-assisted anal fistula treatment (VAAFT) and fistula laser closure (FiLaC)

Video-assisted anal fistula treatment (VAAFT) and the fistula laser closure techniques aim at introducing a scope or a probe in the fistula tract to cauterize the tract in order to de-epithelialize it, thereby initiating healing.[15,16] However, closure of the internal opening is still a required step for healing. Therefore, these approaches should be considered as add-ons to the previously described techniques. VAAFT

has the theoretical benefit of providing improved visualization of the side tracts of the main fistula for a better understanding of the anatomy; however, the significance of this on the healing rate is unknown.

Mesenchymal stem cells (MSCs)

The newest development in the treatment of CD-associated perianal fistulas is the use of mesenchymal stem cells. This was first described in a case report in 2003 reporting on the healing of a recto-vaginal fistula which healed completely following injection with MSCs.[17] Since then, multiple Phase 1 and Phase 2 studies have been conducted, leading to the publication of a Phase 3 randomized clinical trial (RCT) reporting on fistula healing in 212 patients.[18] Perianal fistulas healed in 50% of patients treated with allogeneic MSCs derived from adipose tissue, while 34% of the patients in the placebo group demonstrated fistula healing, which was statistically significant. Following this study, MSCs were recognized as a viable form of treatment in Europe; however, the high cost of this procedure has been a significant barrier to its clinical use. A second randomized trial completed recruitment of more than 500 patients in February 2023 and the results are expected in Fall of 2023.

Fecal diversion

Patients with symptomatic peri-anal disease despite optimized sepsis control and medical therapy are likely going to benefit significantly from fecal diversion, usually using a loop ileostomy. This will result in better symptom control and reduced discharge and sepsis. However, the challenge is to decide when it is reasonable to close a patient's stoma. There is a high risk for disease recurrence. It is therefore important to inform patients about this significant risk while selecting patients strictly.

It is important to consider the use of a diverting stoma in patients with anal CD. Stomas allow for better control of fistula-related symptoms by minimizing active inflammation, sepsis, incontinence, and pain. Proceeding to a stoma is typically a major decision for patients; however, the majority of these patients experience a significant improvement in QOL with a well-functioning stoma.[19] Selection of the optimal stoma site, and avoiding skin folds and other creases that might increase the risk of leakage are very important. Furthermore, when using an ileostomy, sufficient prolapse is essential for proper functioning. Often, a loop stoma will be considered, which is theoretically reversible and provides some peace of mind to patients who are not yet ready to accept a permanent stoma. It is important, however, to disclose to the patient that closure of their stoma is very likely to lead to recurring symptoms. Clinicians can, however, consider fistula repair under the protection of a stoma as a measure to enhance healing which, in the case of successful repair, will allow for closure of the stoma.

Conclusion

Although the surgical management of perianal CD is challenging, surgeons have multiple options at their disposal for the treatment of a select cohort of patients. Close collaboration between the gastroenterologist and the radiologist are essential for optimal treatment. In the majority of cases, patients undergo a combination of surgery and pharmacologic treatment.

Correspondence:

Dr. Anthony de Buck van Overstraeten
Email: anthony.debuck@utoronto.ca

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