

## Management of enterocutaneous fistula: Surgical intervention

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### Key messages:

1. Abdominal enterocutaneous fistula (ECF) in Crohn's disease most often occur postoperative after bowel resection.
2. Prior to operative treatment, maximal medical therapy is warranted.
3. Definitive surgery is generally delayed for several months (>6 months), until both local and systemic conditions have been optimized.
4. Successful surgery requires the resection to the ECF and associated bowel.
5. Owing to the intrinsic bowel pathology and the poor quality of the abdominal wall due to multiple abdominal operations, the ECF recurrence rate remains high.

### Learning objectives:

1. To describe the principles of multidisciplinary management of Crohn's patients with abdominal enterocutaneous fistulas.
2. To understand the timing and techniques of surgical treatment options.

### Abstract:

#### Introduction

Abdominal enterocutaneous fistulas (ECFs) cause significant morbidity and mortality for all patients, including those with inflammatory bowel disease (IBD), and represent a challenging management issue. It is estimated that 75-85% of ECF form after operation as a result of bowel injury, inadvertent enterotomy and/or anastomotic leakage. The remaining 15%-25% form spontaneously secondary to underlying pathology; Crohn's disease (CD) being the commonest cause in the developed world.

1. Approximately 15-20% of IBD patients, mostly those with CD, develop ECF during their lifetime.
2. Crohn's ECF most often occur after surgical resection (anastomotic leak or recurrence) or spontaneously. The St. Marks reported on 277 ECF, whereas 111 were CD-related (68% postoperative, 30% spontaneous and 2% after radiological drainage).
3. Published studies of surgical treatment of EHC are very heterogeneous as results of Crohn's and non-Crohn's ECF are rarely reported separately. The aim of this article is to review the current surgical literature on ECF focusing on Crohn's abdominal ECF.

#### Maximal medical therapy

Prior to embarking on operative treatment, maximal medical therapy is warranted. Infliximab, has been shown to effectively induce closure of perianal fistulas in 55% of patients after 3 doses.<sup>4</sup> In another study including 26 fistula patients 54% needed surgery despite therapy with infliximab. None of the ECF in this study responded to the biologic therapy.<sup>5</sup> However, despite its success, over 50% of patients (abdominal>perineal ECF) will eventually require surgical intervention and resection. Spontaneous healing is unlikely where there is an associated abscess cavity.

#### Assessment of ECF

There is no universally accepted classification for abdominal ECF. Charac-

terization is usually made on the basis of anatomy (site of origin, simple or complex fistula, end or lateral fistula, and presence or absence of distal obstruction) or fistula output (with high output usually defined as more than 500ml per 24h). The exact anatomy of ECF is usually delineated by a combination of clinical observation, biochemical analysis of fistula effluent and radiological investigation (contrast CT and MRI).

Crohn's disease ECFs require a multidisciplinary approach and a team of specialized individuals including the surgeon, gastroenterologist, interventional radiologist, dietician and most importantly a dedicated wound ostomy nurse. Patients may have multiple external openings, bridges of intervening healthy skin, and prior abdominal scars that make proper pouching extremely difficult. Protection of the skin is a vital early step in the management of ECF.

#### Pre-Surgery treatment

A useful acronym to apply to the management of Crohn's ECF patients is "SNAP", representing management of Sepsis and Skin care, Nutritional support, definition of intestinal Anatomy, and development of a surgical Procedure to deal with the fistula.

Initial fistula management should include controlling ECF effluent by pouching and skin protection. Early and aggressive treatment of sepsis is very important, as sepsis caused the majority of death (23/30 patients in the St. Marks experience).<sup>3</sup> Similarly, adequate nutritional support is recognized as a key factor in reducing the mortality. There is ongoing discussion about the best route of nutrition.<sup>1</sup> It has been suggested that parenteral nutrition may decrease small bowel secretions and so not only decrease fistula output but also possibly increase the likelihood of spontaneous closure. However, there have been no randomized trials comparing enteral to parenteral nutrition. It is our policy to use enteral nutrition as early as possible to prevent bacterial translocation and to maintain immune function.

Surgical procedures for intestinal reconstruction should be deferred until both local and systemic conditions have been optimized and should be avoided in the presence of significant (<30 g/l) hypoalbuminemia. Definitive surgery is generally delayed for several months, until physiologic deficits have been restored and intra-abdominal conditions are less hostile. Initial surgery was delayed for 5.8 month and a median of 3 operative procedures were necessary to achieve healing in a study of 95 Crohn's ECFs.<sup>4</sup>

#### Surgical strategies

Successful surgery requires the resection to the ECF and associated bowel. The Cleveland Clinic evaluated various techniques for definitive treatment of ECF. A resection of the diseased bowel was associated with a significant lower recurrence rate (15%; 12 of 83 patients) compared to oversowing (75%; 9/12 patients,  $p < 0.001$ ) in Crohn's ECF. Crohn's disease by itself did not influence recurrence, whereas oversowing and wedge resection were independent predictors of recurrence.<sup>4</sup> After the bowel is reanastomosed, it should be separated, if possible, from the abdominal wall with omental fat.

For complex ECF there is often a significant portion of the abdominal wall that needs to be resected. The Mayo Clinic reported on 11 patients where a human acellular dermal matrix (hADM) was used to reconstruct the de-

fect.6 After a mean follow-up of 1 year  $\pm$ 18 days, 10 of 11 patients remained free of ECF while on a general oral diet. Only 2 of the 11 patients stayed on medical therapy. Although hADM is an expensive material (\$4'100 for a single 12x12cm sheet), these results justify its use because refractory ECF and the associated long-term cost of dealing with the complications in this high-risk population is far greater. Successful reconstructions of the abdominal wall have also been reported using an island pedicled anterolateral thigh flap.7

The healing rate after definitive surgery, delayed for a median of 8 months (1-180), was 82% in a large series of the St. Mark's Hospital, although more than one attempt was required in some patients.3 Successful healing was reported in 35/55 patients (63%) in the only prospective study published, where 35% were Crohn's ECF.8 Owing to the intrinsic bowel pathology and the poor quality of the abdominal wall due to multiple abdominal operations, the ECF recurrence rate remains high.4

#### Combined medical-surgical approach

A small case series of three patients treated with a combined approach of Infliximab 5mg/kg two month prior to surgery and maintenance after resection and reconstruction demonstrated healing in all three cases.9 The use of infliximab (within 12 weeks prior to surgery) was not associated with an increased risk of surgical complications in several studies.10, 11. However, one study demonstrated a higher readmission rate.12 In the absence of abscess a combined surgical-medical approach with TNF- $\alpha$  antagonist (stopped 8-12 weeks prior to major abdominal surgery) seems to be a valuable option for Crohn's patients with ECF.

#### Malignant transformation

Malignant transformation of perianal and ECF is very rare and occurred only in 4 out of 6'058 CD patients (prevalence of 0.004%) after a follow-up of 17 years. The malignancies developed 25 years (IQR 10-38) after CD diagnosis and 10 years (IQR 6-22) after fistula diagnosis.13

#### Future perspectives

In a phase I study four patients with Crohn's ECF have been injected with expanded adipose-derived stem cells. At one year 75% were successful, with complete re-epithelialization of the external opening at week 8.14 These data are promising, but need to be confirmed in controlled trials.

#### References:

- Lloyd DA, Gabe SM, Windsor AC. Nutrition and management of enterocutaneous fistula. *Br J Surg* 2006; 93(9):1045-55.
- Poritz LS, Gagliano GA, McLeod RS, et al. Surgical management of entero and colcutaneous fistulae in Crohn's disease: 17 year's experience. *Int J Colorectal Dis* 2004; 19(5):481-5; discussion 486.
- Hollington P, Mawdsley J, Lim W, et al. An 11-year experience of enterocutaneous fistula. *Br J Surg* 2004; 91(12):1646-51.
- Lynch AC, Delaney CP, Senagore AJ, et al. Clinical outcome and factors predictive of recurrence after enterocutaneous fistula surgery. *Ann Surg* 2004; 240(5):825-31.
- Poritz LS, Rowe WA, Koltun WA. Remicade does not abolish the need for surgery in fistulizing Crohn's disease. *Dis Colon Rectum* 2002; 45(6):771-5.
- Taner T, Cima RR, Larson DW, et al. Surgical treatment of complex enterocutaneous fistulas in IBD patients using human acellular dermal matrix. *Inflamm Bowel Dis* 2009; 15(8):1208-12.
- Chang SH, Hsu TC, Su HC, et al. Treatment of intractable enterocutaneous fistula with an island pedicled anterolateral thigh flap in Crohn's disease--case report. *J Plast Reconstr Aesthet Surg* 2010; 63(6):1055-7.
- Datta V, Engledow A, Chan S, et al. The management of enterocutaneous fistula in a regional unit in the United kingdom: a prospective study. *Dis Colon Rectum* 2010; 53(2):192-9.
- Fries W, La Malfa G, Costantino G, et al. Combined approach with biologics and surgery for enterocutaneous fistulas in Crohn's disease. *Inflamm Bowel Dis* 2011; 17(2):671-3.
- Tay GS, Binion DG, Eastwood D, Otterson MF. Multivariate analysis suggests improved perioperative outcome in Crohn's disease patients receiving immunomodulator therapy after segmental resection and/or strictureplasty. *Surgery* 2003; 134(4):565-72; discussion 572-3.
- Colombel JF, Loftus EV, Jr., Tremaine WJ, et al. Early postoperative complications are not increased in patients with Crohn's disease treated perioperatively with infliximab or immunosuppressive therapy. *Am J Gastroenterol* 2004; 99(5):878-83.
- Appau KA, Fazio VW, Shen B, et al. Use of infliximab within 3 months of ileocolonic resection is associated with adverse postoperative outcomes in Crohn's patients. *J Gastrointest Surg* 2008; 12(10):1738-44.
- Baars JE, Kuipers EJ, Dijkstra G, et al. Malignant transformation of perianal and enterocutaneous fistulas is rare: results of 17 years of follow-up from The Netherlands. *Scand J Gastroenterol* 2011; 46(3):319-25.
- Garcia-Olmo D, Herreros D, Pascual M, et al. Treatment of enterocutaneous fistula in Crohn's Disease with adipose-derived stem cells: a comparison of protocols with and without cell expansion. *Int J Colorectal Dis* 2009; 24(1):27-30.

#### Disclosure of conflicting interests:

No disclosures and no conflict of interest.