Entero-Cutaneous and Entero-Atmospheric Fistulas

Subjects: Surgery

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Enteric fistulas are a common problem in gastrointestinal tract surgery and remain associated with significant mortality rates, due to complications such as sepsis, malnutrition, and electrolyte imbalance. The increasingly widespread use of open abdomen techniques for the initial treatment of abdominal sepsis and trauma has led to the observation of so-called entero-atmospheric fistulas. Because of their clinical complexity, the proper management of enteric fistula requires a multidisciplinary team. The main goal of the treatment is the closure of enteric fistula, but also mortality reduction and improvement of patients' quality of life are fundamental. Successful management of patients with enteric fistula requires the establishment of controlled drainage, management of sepsis, prevention of fluid and electrolyte depletion, protection of the skin, and provision of adequate nutrition.

enteric fistula | enterocutaneous fistula | entero-atmospheric fistula | negative pressure wound therapy | open abdomen

1. Introduction

Enteric fistulas (EF) are challenging conditions in abdominal and gastrointestinal surgery and remain associated with significant morbidity and mortality rates, due to complications such as sepsis, malnutrition, and electrolyte imbalance [1][2][3][4][5][6].

EFs are most commonly iatrogenic and usually the result of a surgical misadventure (e.g., anastomotic leakage, injury of the bowel or blood supply) [7]. In addition, fistulas may result from erosion by suction catheters, adjacent abscesses or trauma. Contributing factors may include previous chemo-radiation therapy, intestinal obstruction, inflammatory bowel disease, mesenteric vascular disease, or intra-abdominal sepsis [8][9][10][11].

The abnormal fistulous connection can occur between the gastrointestinal tract and the skin (enterocutaneous fistula, ECF), another portion of the gastrointestinal tract (entero-enteric fistula) or the urogenital tract. The increasingly widespread use of open abdomen (OA) techniques for the initial treatment of abdominal sepsis and trauma has led to the observation of the so-called entero-atmospheric fistulas (EAF) [12][13][14][15].

Because of their clinical complexity, proper management of EF requires a multidisciplinary team. The main goal of the treatment is the closure of the fistula. Mortality reduction and improvement of a patient's quality of life are also fundamental. The treatment must include correction of malnutrition, which can be achieved both through parenteral and enteral nutrition even for a long time, and surgical strategies to obtain abdominal closure [16][17][18].

ECF and EAF show different characteristics and require different approaches. The resolution rate of ECF with conservative management is between 19.9 and 81.4% [19][20]. With the wound care measures used, 90% of spontaneous closures occurred in the first month after the resolution of sepsis. An additional 10% of closures occurred in the second month. No spontaneous closure occurred after 2 months [21]. With vacuum-assisted closure (VAC) and other negative pressure wound therapies (NPWT), there are case reports of fistulae closure during the second and third months [22][23]. Surgery, instead, is needed for 13–80% of the cases and it is influenced by anatomical and physiological features. This heterogeneity determines different treatments and a lack of a standardized protocol [24]. In EAF, the first-choice treatment is conservative, and surgical therapy should be considered only in case of its failure because of the high risk of bowel injury due to the presence of a “frozen abdomen” [15][25][26][27][28][29][30].

2. Etiology of ECF

Surgery remains the most common cause of ECF due to anastomotic leakage or an unrecognized injury of the bowel [31]. About 50% of fistulas are due to non-anastomotic iatrogenic perforations. Another 50% is due to a partial or total anastomotic dehiscence [31][32]. Patients who undergo a challenging adhesion dissection have a greater risk of iatrogenic perforation.

An intestinal infection can determine an abscess formation and create an internal and/or external fistula. These fistulas are quite common in the developing countries. Typhus is the most common cause of post-infective fistulas, followed by salmonellosis, amebiasis, actinomycosis, coccidiomycosis, and HIV.

The post-radiotherapy fistula usually occurs in the first 5 years after radiant therapy, but can also happen 30 years later, more rarely. The physio-pathological mechanism consists of persistent damage caused to the gut’s vessel and connective tissue that can determine ischemia, erosion, and a fistula because of the tenacious adhesions. Ablation with radiofrequency or other methods (e.g., microwave) can directly cause damage to nearby organs. Ablative therapies used in liver or kidney tumors can cause the appearance of intestinal perforation due to direct, thermal or chemical injury, with subsequent formation of abscesses and fistulas or, in severe cases, peritonitis [33][34]. In the literature, 4–8% of patients treated with abdominopelvic radiation therapy can develop serious complications such as fistulas, perforation, or abscesses [35][36]. Radiation dose, radiation field size, and combination with other anticancer treatments are the main risk factors for intestinal perforation during radiotherapy [37].

Bowel perforation is a rare but serious complication of chemotherapy [11]. Several mechanisms may be responsible for gastrointestinal perforation from oncologic treatments. Anticancer drugs induce vascular damage by thrombosis and thromboembolism. In these cases, when intestinal vessels are involved, bowel ischemia with perforation may occur [38]. Perforation of the gastrointestinal tract can also occur after prolonged obstruction [39] or due to treatment responses with tumor lysis, as in cases of lymphomas or gastrointestinal stromal tumors [40]. Finally, bowel perforation can be a result of other complications of oncologic therapies, like pneumatosis or enterocolitis. Various chemotherapeutic agents can cause perforation. In the literature, the drugs with which this complication most commonly occurs are fluorouracil, taxols, cisplatin, interleukin-2, and mitomycin [41][42][43][44]. Among the molecular targeted therapies, bevacizumab is most commonly associated with gastrointestinal perforation, with an incidence of 0.9% [45] and a correlation with late anastomotic leakage [46]. Risk factors for bevacizumab-related perforation are specific tumors (colorectal, prostate, and gynecological cancers), combination with other treatments, such as oxaliplatin and taxanes, the presence of a primary tumor in situ, and a recent history of endoscopy or abdominal radiotherapy [45][47][48][49].

3. EAF and OA

EAFs are a devastating complication of OA treatments and originate when there is a large dehiscence of the abdominal wall or in the case of a “frozen abdomen” [15][30][50][51]. EAFs are associated with severe morbidity rates, reduced patient health-related quality of life, and increased rates of mortality, duration of hospital stay, and hospital costs [52]. The cost of fistula care is significant and typically more than $500,000 [53].

Damage control surgery for abdominal trauma and/or for source control in severe abdominal sepsis and the management of abdominal compartment syndrome are the main clinical conditions in which OA (**Figure 1**) is currently applied [12][17][27][54][55][56][57][58][59][60][61].

Figure 1. Damage control surgery for abdominal trauma. Open abdomen and Bogota bag (Personal observation).

The etiology of an EAF may often be multifactorial and represent a combination of several independent factors including the primary diagnosis and cause for OA treatment, iatrogenic lesions of the intestinal tract during laparostomy/relaparotomy, postoperative anastomotic rupture, dehydration, swelling and ischemia of the intestine, exposure of the bowel to materials used for temporary abdominal closure, adhesions between the bowel and the abdominal wall, wound infections. Delayed abdominal closure, large fluid resuscitation volume (>5 L/day) and the application of polypropylene mesh directly to the viscera increase the risk of this complication [17]. Although the use of NPWT, presence of bowel injury, bowel repairs or anastomoses, and intra-abdominal infection/sepsis were previously considered risk factors for EAF, subsequent studies did not support these associations [58][62].

4. Classification and Evolution

A fistula is often classified according to output, etiology, and source. These factors dictate both treatment and morbidity/mortality rates. ECF can be internal and external fistulas. This helps in identifying the organs involved and providing characteristics of the fistula tract. Internal fistulas have communications between two hollow viscera and if symptomatic should be treated by resection and re-anastomosis. The external fistulas connect hollow viscera to the skin. External fistulas that have favorable outcomes include esophageal, duodenal stump, pancreaticobiliary, and jejunal fistulas with small enteric defects (<1 cm) and long tracts (>2 cm). Gastric, lateral duodenal, ligament of Treitz, and ileal fistulas are less favorable to close spontaneously (**Figure 2**).

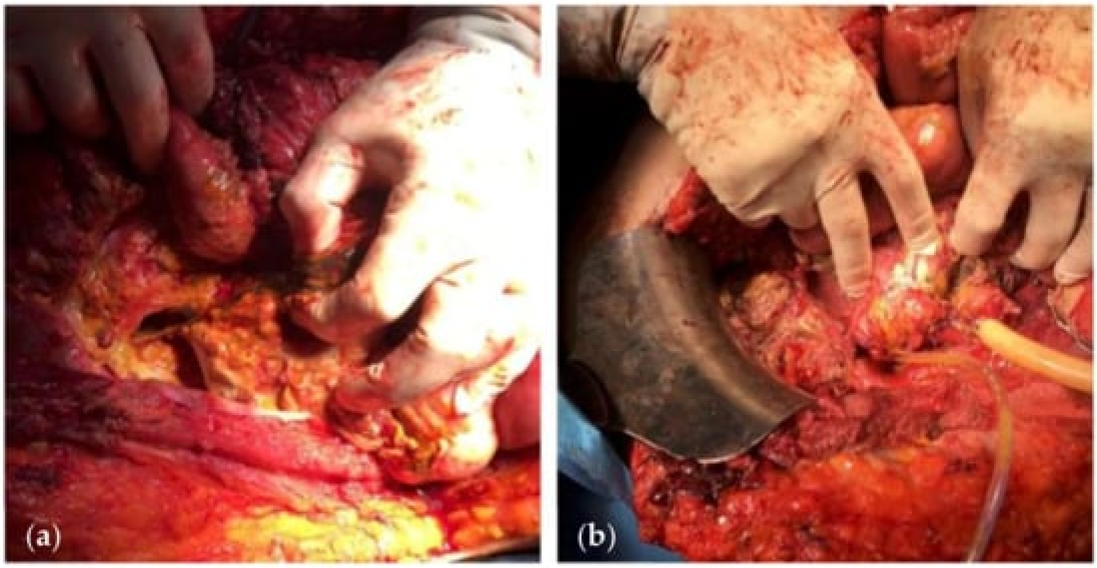

Figure 2. (**a**) Lateral duodenal fistula in a patient subjected to previous subtotal gastrectomy with Roux-en-Y reconstruction for gastrointestinal stromal tumor. (**b**) Reconstruction of the duodenal wall on a Petzer tube. Kehr T-drainage in the biliary tract. (Personal observation).

According to the organ of origin, ECF can be classified into type I (abdominal, esophageal, gastroduodenal), type II (small bowel), type III (large bowel), and type IV (EAF, regardless of origin). Small bowel fistulas (type II) are more common (60 to 70%) than fistulas from other parts of the gastrointestinal tract. EAFs can also be classified as proximal or distal, or, in OA, as superficial or deep.

5. Physiopathology

ECF causes a loss of fluids, electrolytes, and nutrients that can determine or worsen dehydration, electrolyte imbalance, malnutrition, skin, and wound lesions (e.g., abrasions, mycosis, bacterial infections). All these conditions can enhance and make patients more vulnerable to hypovolemia, arrhythmias, immunodeficiency, asthenia, pneumonia, sepsis, liver and renal failure, shock, and death in the most severe cases [63][64].

High-output fistulas are a risk factor for intestinal failure because of a massive reduction of absorption [65]. The increased intestinal losses of fluids and electrolytes, the disruption of the enterohepatic cycle, the restricted oral/enteral nutrition or total fasting (bowel rest) to decrease fistula output, the impaired intestinal peristalsis, and increased metabolic demand related to concomitant sepsis and inflammation are further mechanisms of intestinal failure [66].

6. Outcomes

The mortality rate is currently about 5.3–21.3%, despite a previous much higher rate of 40–65% [20][67][68]. This reduction is probably due to improvements in nutritional support, intensive care, antimicrobial strategies, and surgical invasive and non-invasive techniques (i.e., NPWT). The main causes of death in these patients continue to be electrolyte imbalance, severe malnutrition, and sepsis. This is particularly true for patients affected by high-output fistulas, such as duodenal and jejunal fistulas. The mortality rate still reaches 35% in these cases [69]. Hypoalbuminemia (albumin < 3.5 g per 100 mL) is most commonly associated with fistula formation [70][71].

Over the past few decades, mortality rates for EAF have generally decreased from more than 70% to 40%, as a result of more appropriate advanced intensive care and improved surgical techniques [1][15][17][72][73]. The morbidity rates of EAFs are also high. These are related to the pathophysiological consequences. Changes that occur in EAF include severe fluid and electrolyte losses, acid–base homeostasis imbalance, hypercatabolism (hypoalbuminemia and hypoproteinemia), vitamin and trace element deficiencies, and septic wound complications due to leakage of enteric effluents onto the open abdominal surface.

7. Treatment

There are some defined principles that must be followed for the management of ECF and EAF. A common acronym used to describe ECF care protocol is “SNAP”, which stands for the management of skin and sepsis, nutrition, the definition of fistula anatomy, and proposing a procedure to address the fistula [74][75].

Sepsis control and an adequate nutritional status have to be reached in order to obtain a fistula closure [76][77][78]. Sepsis is responsible for 77% of mortality associated with ECF [3]. A bowel obstruction in a distal intestinal segment does not allow the fistula to heal. Spontaneous closure in patients affected by malignancies or Crohn’s disease is infrequent.

The management of patients with an OA and an EAF is very challenging [18][71]. These patients are usually critically ill and hypercatabolic and deteriorate rapidly if complications occur during their hospitalization in the intensive care unit. Unfortunately, proximal diversion (**Figure 3**) of enteric contents is almost technically impossible to achieve, due to the thick and shortened mesentery, the edematous bowel, the noncompliant abdominal wall, and the rather hostile environment of the OA.

Figure 3. (**a**) A 65-year-old woman undergoing multiple surgical procedures with consequent various fistula formation. (**b**) A jejunostomy was performed with application of NPWT on white foam on the midline laparotomy. (**c**) NPWT on the midline incision 4 weeks after the first surgery. (**d**) Wound at 6 weeks. (Personal observation).

The principles of the non-operative support of the critically ill patient with an EAF are the following:

(a) Recognition and management of sepsis: organ dysfunction or progressive organ failure should be promptly managed;

(b) Source control is crucial for the resolution of sepsis;

(c) Antibiotic regimen based on culture results;

(d) Reducing fistula output: nil per os, a nasogastric tube as well as an attempt to reduce secretions of the gastrointestinal tract by administering proton pump inhibitors and to reduce enteric and pancreatic secretions using somatostatin or octreotide [79];

(e) Nutritional support: In the presence of OA, the patient is in a hypercatabolic state. Hypercatabolism is further worsened by the presence of an EAF. The main parameters on which nutritional support should be based are the following: (a) increased caloric requirements, usually calculated by 30–35 kcal/kg/day; (b) increased protein depriving, calculated by adding 1.5 g protein/kg/day and 2 g protein losses for each liter of fluid collected from the raw surface of the OA; and (c) deficiencies of vitamins and trace elements. Adequate nutritional support based on the patient's nutritional status, a positive nitrogen balance, adequate trace minerals, and vitamin replacement, along with glycemic control, may allow the surgeon to proceed to surgical treatment of the fistula. Additionally, several known parameters, such as weight, prealbumin, albumin, and transferrin, are correlated with postoperative mortality and morbidity and spontaneous fistula closure rates [65][80][81].

Once sepsis and electrolyte imbalance have been treated, defining the fistula anatomy is mandatory. So, a CT scan, a fistulography or a bowel/colonic transit have to be performed. Studying the rectum or colon patency is also useful, especially in those patients who had a colostomy or diverticulitis.

The operating surgeon must define the best surgical approach and technique for closing the fistula. Moreover, it is also important to select the right mesh to use in case of abdominal hernias or if the fascial gap is too wide. The main goal of the surgical approach is to improve the patient's quality of life. Other targets are recreating bowel continuity, minimizing ECF recurrence risk, and avoiding hernias and surgical site infection. Sometimes, different techniques have to be combined to reach all the above-mentioned outcomes. Patients with ECF or EAF have an abdomen that can be defined as "hostile", and access can be challenging for the surgeon (**Figure 4**).

Figure 4. EAFs in hostile abdomen. (Personal observation).

Reconstructive surgery should be postponed for 3–6 months [82]. Spontaneous healing is possible for ECF, but most of them, especially in cases of high output, require surgical treatment. The time interval in which operative intervention is associated with significantly higher mortality has been outlined in the literature.

The new laparotomy should be as far as possible from the previous incisional site, but this is usually not possible (especially for patients who had an urgent laparotomy for trauma). Also, a transverse incision can be an option. It is necessary to excise the involved bowel loop for making a fistula excision. If there are more fistulas, the ideal scenario is when they are all in continuous and closed segments. So, a single en-bloc resection and anastomosis can be performed. All of the bowel and colon must be explored, from the Treitz ligament to the rectum. If there are doubts about the anastomosis, it needs to be revised or a loop ileostomy can be performed.

The surgical treatment of ECF has a successful rate of about 80–90% [68][76][83][84]. It is crucial not to cause other perforations during the dissection. Surgery principles of avoiding a too extensive resection of the mesentery and tension on the anastomosis or performing it on a hypoperfused tract are still valid. The failure rate increases with infectious and noninfectious complications. Additionally, following surgery, ECF recurrence is 14 to 34% [85][86]. Recurrence rates are minimized (18%) when the involved bowel is fully mobilized and resected.

8. NPWT Assisted Closure

As spontaneous EAF closure is rare and depends on fistula localization and output, new treatment options are needed. For the management of OA, NPWT can be considered the standard of care, but the presence of an EAF complicates management remarkably [87][88][89][90][91][92][93][94]. Therefore, the goal is to keep the wound clean and avoid fecal contamination by isolating the EAF.

The first studies on NPWT were focused neither on physio-pathological effects nor on the determination of ideal pressure levels. Morykwas et al. dealt with that with their research on animal models in 1997 [95]. They produced circular wounds of 2.5 cm diameter on the back of a certain number of pigs. Then, they covered them with a polyurethane sponge (sponge pores 400–600 μm). The duplex was used for measuring blood flow in the subcutaneous tissue and the muscles surrounding the lesion. In the meanwhile, growing levels of depression were applied both continuous and intermittent. The granulation process was evaluated considering the dimensional reduction. They compared the results to a control group whose wounds were treated in a conventional way, with swabs and saline solution. The authors observed a better rate of granulation compared to the control group both with continuous and intermittent NPWT (63.3 ± 26.1% and 103 ± 35.3%, respectively). Moreover, these studies demonstrated that NPWT was associated with a significant reduction of bacterial growth compared to the control group after only 4 days of treatment.

NPWT was shown to limit tissue damage in burns on porcine models, measured as an extension of the lesion itself during the first 12 h. The hypothesis was that NPWT could avoid blood flow reduction removing the secretions and the biochemical mediators.

Damage control surgery has spread a lot in recent years and the OA techniques with it [27][58]. This has determined a growing incidence of EAF. This happens because of the trauma that the bowel loops are subjected to during the OA treatment. The introduction of NPWT in the management of EAFs in OA raised many controversies [96]. It was stated that the use of NPWT directly over the intestinal loops might cause the development of new fistulas [97][98]. Higher depression levels were associated with a consistent bowel blood flow reduction with a consequent increase in bowel ischemia and necrosis. This condition can determine a fistula development.

The application of a specially designed non-adherent layer of NPWT system was a breakthrough element that improved the long-term results in the field of OA treatment significantly [6][13][99][100]. It was proven that NPWT facilitates spontaneous EAF closure, especially those characterized by distal location and low-output fistula [2]. The aim of this strategy, which can also involve NPWT, is to transform the fistula into a controlled stoma (**Figure 5**).

Figure 5. NPWT. (Personal observation).

9. Conclusions

In a nutshell, EFs usually affect patients in severe clinical conditions who cannot undergo a surgical operation because of their higher mortality and morbidity risks. These patients require a multimodal approach involving both total parenteral nutrition and NPWT. This association can reduce the fistula output and promote its healing, although with a longer treatment. It was proven that the closure rate of EAF is still not satisfactory, especially in high-output fistula. Thus, the general acceptance for the treatment of dominant EAFs with mucosal protrusion as a stoma is well-accepted worldwide. Patients with OA and EAFs have a high mortality rate. The surgical repair of an EAF has a high failure rate. Primary resection of the affected bowel loop results in the best outcome.

NPWT influences the spontaneous EF closure. This is true, especially for distal and low-output fistula. NPWT creates favorable conditions for the outflow of intestinal contents, enhances the granulation of the wound bed, and decreases local inflammation. Furthermore, NPWT avoids fistula recurrence after surgery.

Although significant progress in the field of NPWT for OA has been observed in recent years, there are still some technical aspects of the treatment that remain questionable with a lack of a firm consensus. Although there are some proposals for an algorithm for NPWT in OA with EAF, there is still an absence of solid recommendations. Thus, it is crucial to collect data and outcomes for creating guidelines regarding NPWT in OA management complicated with EAFs. The inadequacy of prospective studies and/or systematic reviews does not allow a proper comparison of different treatments. A patient-tailored approach is the best option currently.

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