Management Approaches for Enterocutaneous Fistulas

JAMIE HEIMROTH, M.S.,* ERIC CHEN, M.D.,† ERICA SUTTON, M.D.*

From the *Hiram C. Polk, Jr MD Department of Surgery, University of Louisville, Louisville, Kentucky;
†Department of Neurosurgery, University of Nebraska Medical Center,
Omaha, Nebraska

There are very few clinical studies that highlight a definitive and comprehensive guideline for the management of enterocutaneous fistulas. Most accepted guidelines are found in textbooks and are taken from expert advice and case reports. The goal of this review is to highlight advancements relevant to the management of enterocutaneous fistulas from the recent two to three years. Although strong evidence-based guidelines are lacking, the consensus is that a multidisciplinary team working with a clear treatment plan targeting multiple aspects of management can maximize patient outcomes.

ENTEROCUTANEOUS FISTULAS (ECF) ARE characterized by abnormal connections between the intestinal lumen and the skin. Whereas up to 30 per cent of ECFs spontaneously arise from malignancy, radiation, sepsis, or inflammatory bowel disease, more than 75 per cent of ECFs are attributed to postoperative complications such as inadvertent enterotomy and anastomotic disruption.[1–3] ECFs are common complications of abdominal surgery and result in mortality in 15 to 25 per cent of the cases.[1]

Enteroatmospheric fistulas (EAFs) are an increasingly common type of ECF that can result in more serious complications ranging from persistent infection, sepsis, and leakage and often require major surgical intervention.[3–5] EAFs can be divided into two categories, deep and superficial, that are determined by the site of leakage of intestinal contents. Deep EAFs drain directly into the abdominal cavity and may cause peritoneal infection. Superficial EAFs drain onto the skin surface and usually result in the formation of granulation tissue, which impedes wound healing.

ECFs have come to represent a significant financial burden on patients and the overall healthcare system by increasing length of hospital and intensive care unit days (up to 82.1 ± 100.8 days from 16.2 ± 17.3 days; $P < 0.001$), leading to a significant increase in medical expense per patient (up to \$539,309 from \$126,996, $P < 0.001$).[6] The presence of EAF can further increase the cost and length of intensive care unit stay.[1, 7]

A great deal of controversy surrounds every aspect of ECF management from nutritional supplementation to wound management and definitive surgery.[2, 8] The goal of this article is to gather the most recent evidence in ECF management and review those therapies with the greatest potential to improve outcomes and control costs for this complex diagnosis.

Prevention

The best strategy for the treatment of an ECF is prevention. Techniques such as covering the bowel, if possible, with the greater omentum, or burying and covering suture lines within the abdomen, making sure to avoid direct contact between nonabsorbable mesh and bowel epithelium can be used.[4] In addition to surgical techniques, nutritional management can also play a part in the prevention of fistulas. A recent study demonstrated lower rates of fistula formation in patients who were given early enteric feeding, initiated within four days of the celiotomy, compared with those who were given late enteric feeding, initiated after four days.[9] Medication prophylaxis has also been proposed as a mean to prevent ECF, although currently there is little evidence in the literature to support its use. The use of infliximab to treat inflammatory bowel disease, a major risk factor for the development of ECF in patients undergoing abdominal surgery, did not affect the rate of major postoperative complications, such as anastomotic leakage, abscess formation, or ECF formation.[3] Although high-quality studies surrounding prevention of ECF have not been undertaken, the best patient outcomes have been observed for preventive surgical techniques and early nutritional support.

Stabilization of the Patient

Once an ECF has developed, the stabilization of the patient is the first priority. Anemia and electrolyte imbalances are common and should be corrected immediately.[1] Nearly all fistulas have an output that is rich in potassium, making hypokalemia the most common electrolyte disturbance which should be aggressively treated and corrected to avoid arrhythmia and organ damage.[1] Leaks due to upper gastrointestinal ECFs should be replaced with normal saline to replenish lost volume and potassium to avoid cardiac complications and death associated with hypokalemia.

High-output fistulas (greater than 500 mL fluid loss daily) are associated with higher rates of morbidity and mortality, and these patients are especially vulnerable to fluid and electrolyte imbalance and malnutrition.[10] High-output fistulas should be assessed for volume several times per day and the composition of the fluid leakage assessed to better manage electrolyte replacement. ECFs that originate from the duodenum are typically high output and often facilitate a loss of pancreatic secretions that should be addressed with the addition of sodium bicarbonate. With long-standing or high-output ECFs, it may be necessary to give zinc supplementation along with double the recommended daily allowance of vitamins and trace elements and 10 times the recommended daily allowance of vitamin C.[11] Patients should also be given copper, folate, and vitamin B12, if deficient.[10]

Control of infection is critical for stabilizing the patient with ECF. If the patient has developed sepsis from complications of ECF, broad-spectrum antibiotics have been reported to reduce mortality by up to 30 per cent in some cases and should be given without delay.[12] Sepsis treatment consists of 7 to 10 days of antibiotic therapy with early, aggressive broad-spectrum antibiotics within the first hour of the sepsis diagnosis followed by antibiotics de-escalation, switching to a narrower spectrum based on the microbiological results.[13, 14]

Nutritional and Metabolic Control of the ECF

Nutritional goals are multifactorial and a tailored approach works best when managing a patient with ECF. Malnutrition resulting from ECF is a major prognostic factor in patient outcome and should be treated with micronutrient and macronutrient therapies in addition to early enteral nutrition and parenteral nutrition (TPN).[2] One hospital's adherence to a guided ECF management algorithm was shown to result in a high closure rate (87%) and low mortality rate (10%) when management focused on aggressively treating sepsis and stabilizing albumin levels before surgery.[5, 15] Higher rates of spontaneous fistula closure were also observed in patients receiving ≥ 1500 kcal/day of enteric feeding.[16] Patients who experience a catabolic state as a result of ECF require aggressive nutritional support to regain a positive nitrogen balance and promote wound healing. Without optimal nutrition, these patients can experience delayed wound closure, decreased incidence of spontaneous closure, and worse overall outcome.[10]

A 10-year study of pediatric ECF cases showed especially high mortality rates in the presence of hypoalbuminemia, hypokalemia, and high-output fistulas. Pediatric patients that were given high-protein and high-carbohydrate nutrition had significantly greater rates of spontaneous ECF closure and decreased incidence of sepsis and metabolic disturbances.[6, 17]

Although 60 to 70 per cent of patients with ECF ultimately require TPN, it is preferable to provide enteric nutrition (EN) through either a nasogastric tube or a percutaneous endoscopic gastrostomy (PEG) device. Enteric feeding preserves gut mucosa, and immunological and hormonal function of the intestinal tract.[9] Enteric feeding has also shown to not only be safe but superior in promoting anastomotic healing in rat models.[18] In addition, enteric feeding is cheaper than TPN (US$90.60/day for TPN, US$25.00/day for EN; $P < 0.001$), and PEG devices are possible to implement in an outpatient setting.[19]

The use of formulated feeds designed to module the immune response to injury has been studied in the context of critically ill patients. Glutamine, a nitrogen and energy source for lymphocytes and intestinal mucosa is especially of interest because it is depleted during metabolic stress and infection. Alhough data show that glutamine supplementation in serious diseases, such as, ECF resulted in a significant reduction in postoperative complications, there was no significant effect on overall mortality.[20, 21]

Nutritional support is important but must be appropriately implemented. Feeding too quickly may result in refeeding syndrome, which can cause or exacerbate a number of electrolyte and metabolic abnormalities.[16, 22] Patients can experience a sudden shift from fat to carbohydrate nutrition once put on EN or TPN. The increased levels of insulin result in the cellular uptake of phosphate and phosphorylation of glucose. The resulting hypophosphatemia can yield neurological, pulmonary, cardiac, and hematologic complications and should be carefully monitored.[16]

In distal ileal or colonic fistulas, patients may be able to obtain nutrition via mouth or gastric tube. In proximal duodenal fistulas, a PEG or J-tube can be used. Fistulas that originate in between these locations may not allow enough enteral absorption proximal to the fistula and can be managed using fistuloclysis,

which involves radiologically guiding the placement of a feeding tube directly into the fistula.[23]

Fistuloclysis has been shown to be a cost-effective alternative to TPN with the added benefit of gut mucosa stimulation. A previous investigation comparing the nutritional support of 12 patients with jejunocutaneous or ileocutaneous fistulas is currently the only study that has compared the tolerability and efficacy of different nutritional formulas. Patients were given polymeric feed (Fresubin©, 1.0 kcal/mL, 300 mOsm/kg, 15.0% medium-chain triglycerides; Fresenius-Kabi, Warrington, UK), semi-elemental feed (Perative©, 1.3 kcal/mL, 380 mOsm/kg, 42.0% lipid as medium-chain triglyceride; Abbott Nutrition, Maidenhead, UK), and elemental feed (Emsogen©, 0.8–1.3 kcal/mL, 539 mOsm/kg, 83.0% lipid as medium-chain triglyceride; SHS International, Liverpool, UK), respectively, depending on how well the patients could tolerate the formula.[24] The infusion rate through the fistuloclysis was increased by up to 20 mL/h each day until the optimal rate of 90 mL/h was reached.[24] This step-wise method was able to provide the estimated effective nutritional support required in ECF patients.

Pharmaceutical Control of the ECF

Medical therapies such as somatostatin and its analogs, octreotide and lantreotide, are used synergistically with TPN to decrease fistula fluid output. The somatostatin analogs discussed previously have reduced efficacy for decreasing fistulas output as compared with somatostatin.[25] Of the somatostatin analogs, octreotide is the most studied in randomized ECF patients.[26–29] The use of octreotide increases the likelihood and speed of wound closure.[30, 31] However, its use has not been shown to significantly affect mortality.[31]

Wound Management and Surgical Control of the ECF

Fistulas, in general, can produce significant excoriation and maceration as well as pain and discomfort. Management of the surrounding skin and wound area can improve both the outcome and comfort of the patient.[32] Skin damage limits future options of management and control, and can lead to new or recurring fistulas.[33]

Deep EAFs are often more difficult to treat and almost never close spontaneously. The presence of a deep EAF is a significant risk factor for sepsis, peritonitis, and catabolic syndrome and, if possible, should be converted to a superficial EAF. A recent and novel method of stabilizing a deep EAF involves stenting the cutaneous component of a fistula using a 12 mm silastic stoma stud (Kapitex Healthcare Ltd.,

Wetherby, West Yorkshire, UK) to prevent skin closure and recurrent sepsis in patients with recurrent EAF formation after benign colorectal resections.[34] Another method used to stabilize a deep EAF is the Wound Crown technique which isolates fistula drainage. This technique collects the fistula drainage in an ostomy appliance attached to a collapsible fistula isolation device.[35] Both techniques promoted skin and wound healing in hostile abdomens, allowing patients to avoid surgery and further complications.

The aim of fistula wound care is to isolate the fistula from the surrounding tissue and to promote healing of the surrounding tissue while protecting the surrounding skin and granulation tissue from irritation or caustic fluid (Figs. 1–2).

Management becomes especially difficult when the ECF is associated with a hostile abdomen where the viscera may be swollen, the bowel edematous, and the abdominal wall is noncompliant, preventing the closure of the abdomen. The longer the abdomen remains open, the greater is the risk of mortality.[7] One study suggests that surgically closing ECF and abdominal defects in a single-stage setting can result in a durable repair in patients complicated with open abdomen and ECF.[36]

The traditional usage of a drainage catheter in the abdomen was shown to have low efficacy and result in larger fistula.[7] However, the use of Malecot catheters and early mobilization of skin and subcutaneous tissue flaps have shown promise in managing EAF with limited complications.[37]

One solution of isolating the wound is to use the floating stoma technique, where an IV bag is fashioned into a physical barrier that segregates the intestinal effluent and the peritoneum. Consequently, the exposed bowel has a better chance of developing granulation tissue, leading to healing and contracture of the abdominal wound.[38] Another solution used in wound isolation is to use a vacuum-assisted wound closure system (V.A.C.® Abdominal Dressing; Kinetic Concepts Inc., San Antonio, TX).[7] A porous, nonadherent layer envelops the visceral organs and is covered by an airtight membrane placed on vacuum suction. The negative pressure of the vacuum promotes the migration of several tissue healing factors and also aids in wound drainage. Versions of this device can also be created with standard hospital supplies and are less expensive than commercialized solutions.[39]

There are notable discrepancies in the reports of the safety and efficacy of using negative-pressure wound healing.[3, 40–42] Some studies suggest that vacuum-assisted closure is associated with increased incidences of new fistula formation and mortality, but the results appear to be multifactorial and require more extensive analysis.[41, 43] Factors such as multi-organ
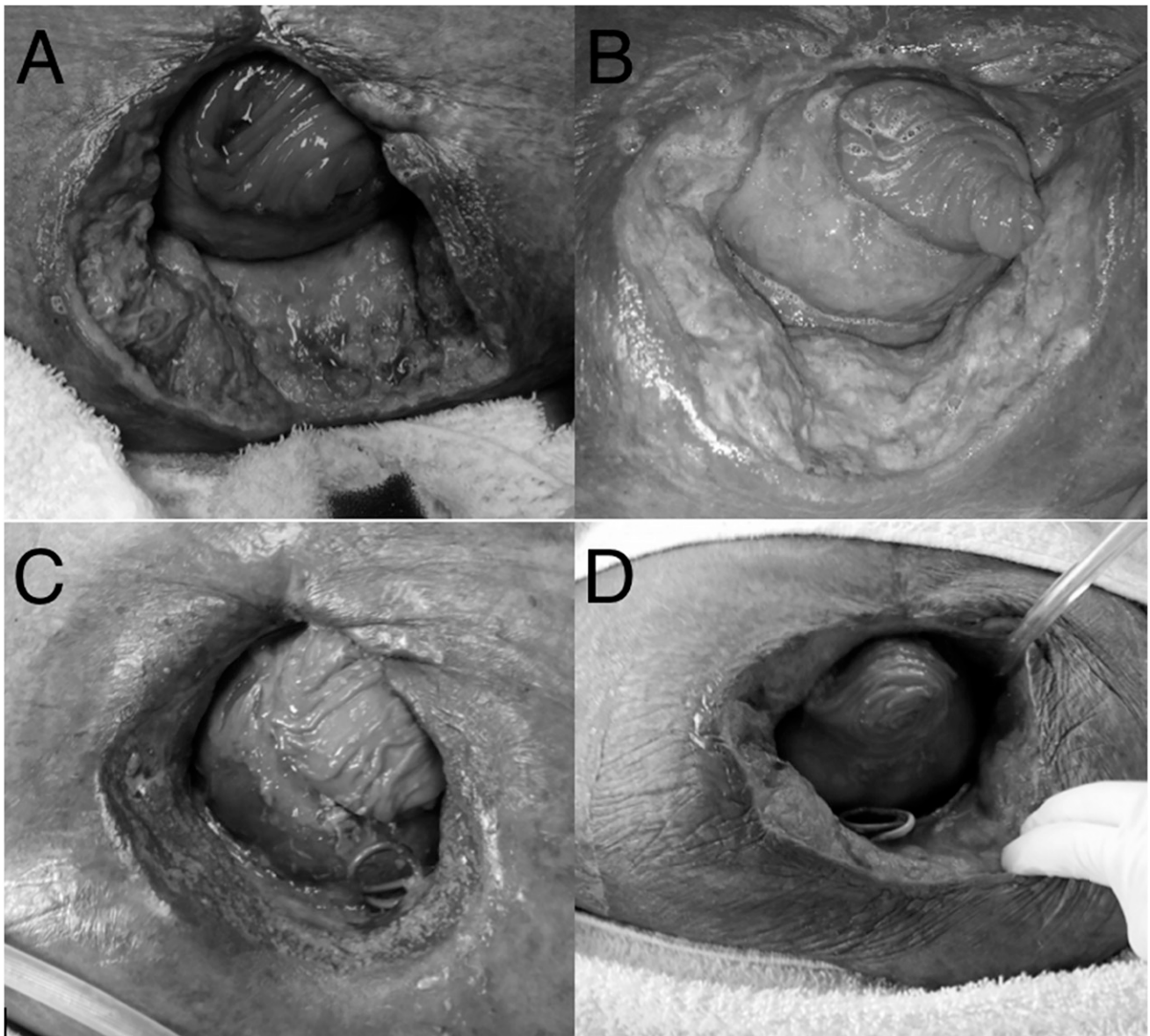
Fig. 1.   Progression of enterocutaneous fistula healing (*A–D*) after the isolation of a fistula from the surrounding tissue.

failure, intestinal anastomoses, and abdominal sepsis may have contributed to the significant increase mortality in those studies.[41] One study has found vacuum-assisted closure to be safe; no increased rate of ECF formation was noted.[40] A review of 151 patients with ECF showed the vacuum-assisted closure rate to be 64.6 per cent with wound healing taking an average of 58 days.[44] Open abdomens treated with both vacuum-assisted closure and mesh-mediated fascial traction, however, showed high closure rates (89%) with few complications during a one-year follow-up study showing asymptomatic incisional hernias as the most common complication.[42, 45]

A novel method of providing for control, accurate measurement, and collection of fistula effluents in the presence of a frozen or hostile abdomen can be made using a standard baby bottle nipple and Foley or Malecot catheter in conjunction with vacuum-assisted closure. The technique can promote granulation tissue formation over the bowel, making the area amenable to subsequent skin grafting.[46]

A retrospective review of 23 years of ECF management found that therapies that emphasized the closure of the abdominal fascia and aggressive control of infection and sepsis significantly improved patient outcome and decreased ECF recurrence (RR 0.47) and mortality (RR 0.38).[4, 47] One method of closing the abdominal fascia is a scheme for mitigating high-output jejunal ECFs using the rectus abdominis muscle, which can be sutured over the ECF opening via

Fig. 2.   Epithelialization of the surrounding tissue after the isolation of the enterocutaneous fistula.

a parachuting technique. The muscle can then be covered with a skin graft and subsequently immobilized using a negative-pressure device. This method provides tension-free closure of the fistula without compromising tissue vascularization or necessitating bowel resection. The method also facilitated the implementation of early mobilization and early enteral nutrition.[48]

Recently, an inexpensive and simple technique was developed for closure of a complex fistulous opening by transfixing the entire thickness of the bowel wall. The central suture across the fistulous opening is then inserted last to confer the smallest amount of stress to the most fragile area. A direct, viable pedicle flap fashioned from adjacent healthy, well-vascularized tissue and held in place by suture, further reinforces the closure. This technique allows for the early closure of the fistula without significant delay or concern of contamination.[49]

Investigation and Decision

With proper nutrition, oxygen, and wound care, 20 to 30 per cent of ECFs will close spontaneously. If a fistula does not close within four to six weeks, it is unlikely to do so spontaneously.[1] Most often, ECF requires surgical repair.

Definitive Surgery and Recovery

Evaluation of ECF for surgical resection begins with radiological studies and the use of other imaging modalities such as MR or CT enterography, ultrasonography, endoscopy, and contrast studies such as fistulograms.[50] Radiological assistance is often required for identifying and treating abscesses and obstructions found in the intestinal tract, which can otherwise negatively alter the course of management and prevent healing.[50]

An exploratory laparotomy is important for determining the intestinal anatomy, presence of adhesions, and planning the location and amount of bowel to resect or repair.

Before proceeding to surgery, a split thickness skin graft is often applied to the tissue bed to reduce the surface area of the wound and advancing wound edges.

It may sometimes take up to three months to a year for the patient to be ready for surgery.[1] The pinch test to determine the amount of separation between the skin graft and fascia is used to determine the next step in treatment. If separation is adequate, a better outcome and less complex surgery are predicted.[1]

The aims of ECF surgery are to enter the abdomen, lyse any visible adhesions, resect the fistulous segments of intestine, establish intestinal continuity, and finally, successfully close the abdominal wall. However, even successful resection or repair of the injured anatomy can lead to recurrence of ECF or short gut syndrome.[33]

Patients with high output, small bowel EAF and a history of open abdomen have a high chance of recurrent ECF/EAF after closure. This can be mitigated by careful preparation of the patient with adequate stabilization, nutrition, and fistula control before surgery. In addition, waiting for a patient to stabilize with nutritional support and electrolyte replacement has proven beneficial.[51]

A fistulogram, exploratory laparotomy, or staining the bowel with methylene blue are options that aid in the visualization of the defect and planning of the surgery. Surgeons have the option of repairing ECFs by either suturing over adjacent tissue or resecting the diseased bowel and anastomosing the ends of the healthy bowel. The end-to-end anastomosis post-resection technique is less prone to recurrent fistula formation (16%) compared with over-sewing the fistula without resection (36%) and is, therefore, the preferred method.[12] Following the anastomosis of the healthy bowel, the omentum should be used to separate the bowel from the abdominal wall.[52]

Some guidelines advise the use of an artificial or biologic mesh prosthetic to mitigate fascial dehiscence when closing the abdomen.[1] However, in multiple studies, absorbable meshes have been associated with higher rates of mortality and recurrent EAFs when compared with delayed primary fascial closure.[53] Yet, a recent study demonstrated a lower rate of incisional hernias with no significant elevation in the rate of ECF formation when intra-abdominal composite meshes were implanted in patients with contaminated or dirty wounds.[54] Furthermore, in traumatic events such as abdominal wall necrosis and abdominal compartment syndrome, the use of biologic meshes may be the only option available for patients with a complex, infected, or hostile abdomen. In this context, biologic meshes have shown promise in managing ECF.[55]

Promising Future Therapies

The use of acellular dermal allograft (ADA) to provide an expedient method of tension-free closure of postoperative patients requiring complex abdominal wall reconstruction has been shown to result in skin closure, wound debridement, and lower rates of wound infection.[56–58] ADAs are not limited to ECF treatment alone and have been used for other abdominal wall reconstructions such as hernia repairs and intestinal transplantations.[59, 60] Unlike other biologic meshes, ADA material is pliable which allows it to conform more easily to defects and reduces the risk of increased intra-abdominal pressure. In addition, one study has mentioned the possibility that repair using ADA may result in less postoperative pain, a thought that was not specifically assessed.[59] Although the study has found good success in the use of ADA in abdominal wall reconstruction, the patients that received ADA were treated more aggressively once their postoperative course became complicated, which may have affected outcomes such as wound closure and length of stay.

Regenerative surgery via endogenous cell activation or through autologous cell transplantation shows promise as a tool for managing ECF. A combination of cell infusions, platelet gel, and V.A.C. therapy to promote healing was successfully used to stabilize a nonhealing ECF that was refractory to all standard procedures and warrants further assessment.[61]

Conclusion

The appearance of enterocutaneous fistulas is frequently associated with complications and a significant risk of mortality. In addition, ECF increases patient discomfort and the financial burden of the healthcare system. The evidence is clear that the best outcomes are observed when preventive strategies are used, followed by an aggressive nutritional support and infection control of patients who develop ECF/EAF. Wound care and closure of the abdomen play an important role in promoting spontaneous ECF closure. Finally, definitive surgery with bowel resection, and anastomosis is required to correct ECFs that do not close spontaneously.

Recent advancements in technology and novel solutions have expanded the arsenal of tools surgeons can use to mitigate complications, yet management of ECF remains controversial owing to the range of ECF subtypes and difficulty in replicating single institution or surgeon results. Therefore, each case is best managed with a clear plan based on the best scientific evidence available and an aggressive, interdisciplinary approach to addressing the patient's metabolic needs while working to close the fistula.

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