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ABSITE CORNER
Gastrointestinal fistulae

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SUMMARY & GENERAL INFORMATION

Key points: (a) Gastrointestinal fistulae (GIF) continue to be associated with high morbidity and mortality; (b) Approximately 85% to 90% of GIF result from surgical procedures; (c) Spontaneous GIF (10% to 15%) most commonly result from inflammatory bowel disease, malignancy, and infection (i.e., diverticulitis); (d) Fistula classification and natural behavior are discussed; followed by (e) Discussion of diagnostic and treatment principles, as well as special issues encountered in GIF management.

ABSITE CORNER is a section of OPUS 12 Scientist dedicated to brief topic reviews geared toward resident preparation for the American Board of Surgery In-Training Examination. Each quarterly edition of OPUS 12 Scientist will contain one or two condensed overviews, along with a list of selected references. Resident contributions via regular article submission process are welcome, subject to Editorial Board and Section Editor approval.

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INTRODUCTION

Despite significant medical and surgical progress over the last two decades, gastrointestinal fistulae (GIF) continue to be associated with high morbidity and mortality (nearly 40% with postoperative high-output fistulae).

Approximately 85% to 90% of GIF arise following surgical procedures. Gynecologic patients appear to be at an increased risk of GIF (up to 30%), mainly because of the high incidence of malignancy and associated aggressive therapeutic regimens. Urgent/emergent surgical procedures, foreign body close to the suture line, tension on the suture line, complex suturing patterns/techniques, distal bowel obstruction, hematoma or abscess near the anastomosis, tumor, under-resuscitation, and poor nutritional status all contribute to postoperative GIF formation.

Spontaneous fistula development (10% to 15% of cases) is most often attributed to inflammatory bowel disease, malignancy, infection (i.e., diverticulitis), vascular insufficiency/mesenteric ischemia, and radiation exposure.

There are multiple reasons that account for the poor prognosis associated with GIF. These factors include: (a) frequent presence of associated severe systemic disease (malignancy, inflammatory bowel disease, etc.); (b) difficulty in maintaining adequate nutritional status; (c) frequent presence of ongoing systemic inflammatory response and/or sepsis; (d) associated severe fluid and electrolyte disturbances; and (e) often complex and difficult to manage wounds.

DEFINITIONS

A **fistula** is defined as an abnormal communication between two epithelialized surfaces. **Gastrointestinal fistulae** (**GIF**) represent abnormal communications between the gastrointestinal tract and another epithelial-lined surface. The communication may involve the skin, another part of the gastrointestinal tract, or another organ system (biliary, respiratory or genitourinary).

CLASSIFICATION OF GIF

There are two broad classifications of gastrointestinal fistulae, **congenital** and **acquired** (focus of this review). Acquired fistulae include the following subtypes: (a) **intestinal** (gut-to-gut); (b) **extraintestinal** (involves genitourinary, biliary, vascular, respiratory, or other structures); (c) **external** or **cutaneous** (can be further divided into high- or low-output); and (d) **complex** fistulae (both internal and external).

NATURAL BEHAVIOR OF GIF

Approximately 70% to 90% of GIF will close spontaneously if appropriately managed (see subsequent sections). Spontaneous closure is more likely if the following conditions are met: (a) bowel continuity is maintained; (b) there is no associated abscess; (c) the bowel defect is small (less than 1 cm in diameter); (d) the adjacent bowel is healthy and there is no distal obstruction; (e) the fistula tract is not epithelialized or more than 2 cm in length; and (f) there is no associated malignancy. Spontaneous closure rate also depends on the fistula location; while a colonic fistula may take 30 to 40 days to close, an ileal fisula may take 40 to 50 days.

Table 1. The ***FRIENDS*** mnemonic

Factors associated with failures of fistula closure
Foreign body
Radiation
Inflammatory bowel disease or **I**nfection
Epithelialization of the tract
Neoplasm
Distal obstruction
Short tract (< 2 cm)

External fistulae can be further classified into high output (> 500 mL/day in drainage) and low output (< 500 mL/day in drainage) fistulae. In case of pancreatic fistulae, a high-output fistula is defined as one with greater than 200-300 mL of drainage daily. Of note, high-output fistulae are likely to produce serious metabolic, fluid, and electrolyte disturbances. Mortality and morbidity is also increased with high-output fistulae.

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Gastric, lateral duodenal, ligament of Treitz, and ileal fistulae are least likely to spontaneously close. Therefore, these fistulae require the most aggressive medical therapy and are likely to require operative intervention.

Table 2. Causes of acquired gastrointestinal fistulae

Aortic aneurysm and/or graft
Foreign body
Idiopathic
Inflammatory
Crohn's disease/Inflammatory bowel disease
Diverticulitis
Infection, most often atypical
Cholecystitis
Appendicitis
Pancreatitis
Ischemic
Malignancy
Peptic ulcer disease
Radiation
Surgical/Iatrogenic
Traumatic

External fistulae are usually apparent when abnormal fluid/succus discharge appears. These GIF are often associated with abdominal pain and tenderness, ileus, fever and elevated white blood cell count. The enteric character of the discharge is usually diagnostic. If the exact nature of drainage is unclear, the fluid may be sent for laboratory analysis (amylase, lipase, creatinine, bilirubin, etc), and radiographic contrast studies may be used to confirm the diagnosis, or a dye test (such as methylene blue) may be performed for confirmatory purposes.

Table 3. Important considerations when approaching gastrointestinal fistulae

Factor	**Likely to close**	**Unlikely to close**
Anatomy	Oropharyngeal, esophageal, duodenal stump, jejunal	Gastric, lateral duodenal, jejunal, ligament of Treitz
Nutritional status	*Well nourished*	*Malnourished*
Sepsis	Absent	Present
Condition of bowel	*Healthy adjacent tissue, small leak, no abscess, 'dormant' disease*	*Total disruption, distal obstruction, abscess, active disease process*
Other factors	Fistula tract > 2 cm, bowel defect <1 cm	Epithelialized tract, foreign body

Internal fistulae are usually more subtle in presentation than **external fistulae**. Symptoms of internal GIF may include diarrhea, rectal bleeding, systemic inflammation/sepsis, weight loss, and exacerbation of the underlying disease process. Other presentations of internal GIF may include gallstone ileus in cases of **cholecystoduodenal** fistulae and pneumaturia/recurrent urinary tract infections in cases of **enterovesical** fistulae.

DIAGNOSIS OF GIF

When approaching gastrointestinal fistulae, the diagnostic goal is to establish precise anatomic definition and classification of the fistula. Clinical evaluation of any GIF should begin with detailed examination of the patient's medical and surgical history, followed by assessment of the patient's general condition, serum electrolyte levels, and nutritional status (including **albumin** and **prealbumin** levels).

Further diagnostic evaluation may include upper and lower endoscopy, upper and lower intestinal radiography with soluble contrast medium, ultrasonography, computed tomography, and/or MRI scanning (when appropriate). Fistulography with fluoroscopy may be very useful and is usually readily available. When approaching **extraintestinal** fistulae, additional imaging/diagnostic techniques may be needed. In cases of suspected biliary fistula, an MRCP and/or ERCP may be needed. In cases of suspected bladder fistula, cystoscopy, pyelography, and cystography may be helpful.

GIF: MANAGEMENT PRINCIPLES

In general, the management of GIF can be divided into specific phases. These three distinct phases are: (a) fistula **recognition** and patient **stabilization**; (b) fistula **investigation** and **assessment**; and (c) **definitive treatment** of the fistula.

Once the fistula is recognized, the patient has to be **stabilized**. This includes fluid resuscitation, correction of serum electrolytes and normalization of acid-base imbalances. Control and reduction of fistula output also helps in stabilizing electrolyte, fluid, and acid-base status. Control of sepsis is very important because fistula-related mortality is often associated with uncontrolled infection. Protection of skin and continued local wound care are extremely important. Finally, adequate nutritional support is crucial in patient **stabilization**.

Following initial patient **stabilization**, the fistula **investigation** and **assessment** phase begins. Here, the fistulogram is the most important initial procedure. Fistulography may involve traditional fluoroscopic and roentgenographic studies, or may employ modern computed tomographic imaging. Regardless of the imaging modality, the information to be derived includes: (a) the source of the fistula; (b) the nature of the fistulous tract (length, course, relationships); (c) the absence or presence of bowel continuity; (d) the presence versus absence of distal obstruction; (e) the character of bowel adjacent to the fistula (presence of inflammation, stricture, etc); and (f) the presence or absence of an abscess cavity in communication with the fistula.

Once the patient is clinically **stabilized** and the fistula adequately **investigated** and **assessed**, the management enters the **treatment** phase. There are different treatment options available, depending on the type and behavior of the GIF. In cases of clinically stable external high-output fistulae, somatostatin and analogues can be used in conjunction with aggressive nutritional supplementation in order to facilitate spontaneous fistula closure. If there is no significant reduction in fistula output following initiation of somatostatin therapy, the somatostatin administration should be re-evaluated. In fact, clinical evidence suggests that while octreotide significantly decreases fistula output, its use does not

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speed spontaneous closure rates and may be associated with increased morbidity.

Depending on the fistula location and the nature of drainage, definitive surgical intervention involves resection of the fistula and primary bowel anastomosis or diversion of the fecal stream proximal to the fistula. Premature attempts at operative fistula closure increase the risk of peritoneal contamination, intraoperative bleeding and recurrent fistula formation. Therefore, surgical repair should not be undertaken for at least 3 to 12 months, depending on the complexity of the fistula and the patient's general condition. Definitive surgical treatment should not be undertaken if there is an undrained abscess or if the nutritional status is suboptimal (albumin < 3.5 mg/liter). Operations in the setting of inadequate nutritional status have been associated with high incidence of recurrent fistulae. Emergency surgery should be limited to controlling sepsis, draining abscesses, and insertion of feeding tubes.

GIF ASSOCIATED WITH INFLAMMATORY BOWEL DISEASE

Fistulizing inflammatory bowel disease is characterized by transmural inflammation that leads to bowel adherence to adjacent structures, microperforation and abscess formation, with subsequent fistula development. Approximately 20% to 40% of patients with Crohn's disease will develop a fistula. Of those, approximately half are internal fistulae and half are external.

In the setting of inflammatory bowel disease, there were very few non-surgical therapeutic options prior to the introduction of infliximab (anti-TNF monoclonal antibody). During the pre-infliximab era, medical treatment of fistulae was largely limited to antibiotics, often administered over prolonged periods of time. Infliximab has significantly improved the management of fistulizing Crohn's disease. In the setting of infliximab therapy, external fistulae and perianal fistulae tend to have a higher rate of closure when compared to other types of fistulae. However, because the fistulous tract may persist, recurrent fistulae and pelvic abscesses may occur. Of note, prior to initiating infliximab therapy, the patient should undergo testing for the presence of tuberculosis (PPD skin test) because infliximab therapy has been associated with exacerbations of severe miliary tuberculosis.

GIF: SPECIAL CONSIDERATIONS

Maintenance of adequate nutritional status is crucial in the management of GIF, with the overall goals including positive nitrogen balance, provision of adequate trace mineral and vitamin replacement, and significant caloric (35-45 calories/kg/24 hours) and protein (1.5 to 1.75 grams/kg/24 hours) requirements. The trend in nutritional support for patients with GIF is away from total parenteral nutrition (TPN) whenever possible. It is well established that enteral nutrition is associated with: (a) decreased nosocomial (especially fungal) infection rate; (b) improved immunologic, hormonal, and barrier functions of the gut; and (c) fistula closure rates similar to those achieved with TPN alone.

Refeeding of the distal bowel segment is still a controversial issue. This concept relies on the fact that without the fistula, all of the biliary, pancreatic, and gastric secretions would be naturally propelled distally through the bowel. In the absence of distal obstruction, refeeding of all or part of the fistula output into the distal bowel, along with enteral feeding into the distal bowel, have been shown to be beneficial, especially in neonatal and pediatric patients with multiple enterostomies. In fact, it is thought that distal bowel refeeding may increase the absorptive function and integrity of the distal segment, help facilitate subsequent operative intervention, improve weight gain, and reduce the requirement for total parenteral nutrition.

Application of negative pressure wound therapy (NPWT) offers new options for patients with fistulae in terms of advanced wound and fistula management. Increasing evidence from various clinical studies supports the role of NPWT in reducing local chronic wound edema, enhancing granulation tissue formation, effectively containing the effluent, protecting the surrounding skin, and promoting healing. Specialized NPWT sponges and other protective equipment (non-adherent dressings, specialized stoma devices, etc) may be required in order to protect any exposed normal bowel and/or skin adjacent to the fistula site.

Figure 1. Example of a duodenal-biliary fistula. Image authored (2000) by Nevit Dilmen, reproduced under GNU Free Documentation License.

GIF: PROGNOSTIC CONSIDERATIONS

The outcome associated with GIF has changed significantly over the last two decades. This is largely due to the evolution of modern intensive care and the ability to provide adequate nutritional support. With conservative medical management that includes adequate enteral or parenteral nutrition, spontaneous closure of fistula occurs in about 25% of patients within 30-40 days. Nevertheless, the mortality (up to 40%) and morbidity rate associated with GIF remain uncomfortably high. Perhaps the most important factor correlating with higher mortality in this patient population is the volume of fistula output. In fact, it has to be emphasized that the closure rates and mortality quoted above are associated with the so-called 'favorable' group of patients who

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have low-output fistulae, and have no underlying systemic disease or fistula-associated abscess formation.

CONCLUSIONS

Despite significant advances over the last two decades, gastrointestinal fistulae continue to present a significant challenge to surgical practitioners. Patients with GIF have the best chance for recovery if an orderly and systematic approach to their care is undertaken. This approach consists of patient stabilization, fistula investigation and assessment, and definitive treatment. While some fistulae close spontaneously with medical management alone, significant proportion of GIF require surgical intervention. Surgery is best performed following adequate patient stabilization and nutritional repletion, which often requires a delay of 3 to 12 months. Prognosis depends on the amount of fistula output, the control of associated infection, and maintenance of adequate nutritional status.

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