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Endoscopic management of fistulas, perforations, and leaks

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ABSTRACT

Although endoscopic management of fistulas, perforations, and leaks is rapidly evolving, management still revolves around the principles of closure, containment, and drainage. Successful endoscopic management is dependent upon several factors, including underlying etiopathogenesis, lesion chronicity, local tissue viability, concurrent illnesses, device availability, and the expertise to deliver the desired endoscopic interventions. Unlike acute perforations, fistulas and leaks typically require a multimodal approach and more than one treatment session to achieve resolution. Although complete resolution remains the goal, endoscopic interventions may enable clinical stabilization of the patient, allow enteral feeding, and facilitate hospital discharge or elective surgery. Herein, we highlight current knowledge and future role of endoscopic interventions in the management of gastrointestinal defects.

Introduction

Gastrointestinal (GI) defects, such as perforations, anastomotic leaks, and fistulas are a source of considerable morbidity and mortality. The goal of this review is to outline the magnitude of this health care problem and highlight the rapidly emerging role of interventional endoscopy and novel endoscopic techniques for the management of these luminal defects.

Magnitude of the Problem

The causes of GI defects are various, including postsurgical complications, inflammatory bowel disease, trauma, foreign bodies, and rare infections. More than half a million patients undergo surgeries involving the GI tract for bariatric indications or to manage neoplastic or inflammatory disorders of the digestive tract each year. Postsurgical fistulas, perforations, and leaks are devastating complications as they prolong hospitalization and result in significant mortality. Postoperative leaks and fistulas can develop after esophagectomy in up to 8% of patients, with a 3-month mortality rate of 18.2% [1]. Leaks and fistulas are more commonly encountered in cervical (13.6%) than in thoracic anastomoses (2.96%) [2]. In patients undergoing bariatric surgery, postoperative leaks and fistulas occur in 1.7%-5.2% of cases of Roux-en-Y gastric bypass and in 1.5%-2.4% of cases after sleeve gastrectomy [3-12]. An anastomotic leak is the strongest independent risk factor for postoperative mortality, with rates of 6%-15%. The rates are as high as 40%-50% with leaks that involve jejunojejunal anastomoses [13-17].

Enterocutaneous fistulas are also associated with high morbidity and mortality, ranging from 5%-30% [18,19]. In the presence of coexisting aggravating factors, such as sepsis, malnutrition, and large abdominal wall defects, the mortality rate can exceed 60% [20]. Similar to defects in the proximal GI tract, colonic anastomotic leaks and fistulas occur in 3%-11% of cases, and the rate of these complications increases the closer the anastomosis is to the anal verge. This results in fecal contamination of surgical wound and peritoneal cavity, leading to mortality rates of 10%-16% [21-24].

Spontaneous fistulas that occur in the absence of GI surgery raise concern for underlying neoplastic or chronic inflammatory disorders, such as Crohn's disease, vasculitis, and rare fungal or mycobacterial infection [25-27]. Approximately 489,000 patients carry the diagnosis of Crohn's disease in the US, with a cumulative risk of fistula ranging from 14%-38% [28–30]. In Crohn's disease, the presence of fistulas leads to a more disabling course and requirement for surgery, advanced immunotherapy (biologics), and removal of the rectum with permanent ostomy in 10%-20% of patients [25,31]. In patients with complex perianal fistulas, 38% require complex surgery, including resection, stoma creation, and proctectomy [32].

Given that GI fistulas, perforations, and leaks are relatively common and are associated with high morbidity and mortality, these conditions are in desperate need of novel management options, including endoscopic interventions. Herein, we present the historical treatment approaches, current endoscopic interventions, and novel endoscopic techniques and devices for the management of these challenging problems.

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Historical Management of GI Defects and Outcomes

Although overarching management principles remain the same, specific strategies to manage fistula, perforation, and leak vary depending on etiopathogenesis and acuity of presentation.

Postsurgical defects, such as perforations and leaks, are generally managed either by rescue surgery when the defect is present within the first 7-10 days or a watch-and-wait strategy followed by secondary surgery if symptoms persist. The watch-and-wait approach includes nothing by mouth, parenteral nutrition, antibiotics, and imaging-directed drainage or diversion of GI contents.

Spontaneous closure rates with conservative and radiological interventions are highly variable [33-42] with reported rates of 37% and 46% in 2 studies [43,44]. Contrary to this, in another recently published study involving 135 patients [45], spontaneous closure was achieved in only 16% of cases. Factors that predispose to delay or absence of spontaneous fistula closure include older age (>65 years), malnutrition, leaks arising from duodenum or ileum, high-output fistula (>500 ml/day), associated malignancy, inflammatory bowel disease, radiation enteritis, immunosuppression, sepsis, diabetes, renal failure, and chemotherapy [56,18,34,46,47]. A complex or multiple fistulizing process is unlikely to heal spontaneously. Defects >1 cm in size where eversion of mucosa or distal occlusion occurs, along with diseased adjacent bowel, abscess or abdominal wall defect, typically turn into indolent fistulas that are resistant to therapy. The anatomic location of GI defects also determines the outcome. Approximately 3%-14% of all enterocutaneous fistulas and leaks are located in the duodenum where the digestive enzyme-rich environment poses a challenge to management [48,49].

Conservative management, along with radiological and standard endoscopic interventions, is successful in only 50% of cases at 35 days follow-up and carries a 4%-9% mortality rate. In patients who fail conservative treatment and undergo surgical intervention, the mortality increases to 15%-30%. Recurrence after surgical repair is also not uncommon and occurs in 13%-33% of patients with added mortality of 9%-30% [50,51]. Given the subpar success rate, high morbidity and mortality, as well as a 10-fold increase in cost of care of these patients (with an overall health care burden of approximately $10 billion each year), there is an urgent need to develop, institute, and optimize novel interdisciplinary approaches, including new endoscopic interventions, to manage fistulas, perforations, and leaks.

The management approach for Crohn's patients with complex fistulas is most challenging. The standard of care includes surgery and medical treatment. A randomized study of infliximab in patients with fistulizing Crohn's disease showed an initial good response, but only 36% of patients had sustained fistula healing at 52 weeks [52]. The surgical options for patients with complex fistulas include long-term seton placement for drainage, fibrin glue injection, or placement of a biodegradable fistula plug to promote healing [36,53]. These options are in addition to concurrent medical management. Despite these interventions, success has been limited for Crohn's perianal fistulas [53]. In patients who do not respond to the above techniques, an advancement flap may be an option but the recurrence rate approximates 50% for Crohn's fistulas [54]. For refractory fistulas, surgery in the form of diverting colostomy or ileostomy and proctectomy is an option. Indeed perianal fistulizing disease is an independent risk factor with respect to the need for intestinal surgery in patients with Crohn's disease [55]. Thus, similar to postsurgical fistulas, there is a critical need for better, safer, and more effective therapies in complicated fistulizing Crohn's disease.

Current and Future State of Endoscopic Management of GI Defects

Endoscopic modalities are increasingly being utilized as primary therapy for perforations and are an integral part of multimodal approaches to manage leaks and fistulas. Postsurgical patients with anastomotic leaks and fistulas typically undergo resuscitation, sepsis control, and interventional radiologic drainage of extra-luminal fluid collections before being referred for an attempt at endoscopic management. Endoscopic examination helps to identify the defect, assess the extent of disruption, determine surrounding tissue viability, and provide therapy, as appropriate. Endoscopic management includes primary closure by tissue apposition and leak containment by diversion or drainage of enteric contents away from the defect site. As endoscopic therapy is an emerging field with respect to the management of defects, such as leaks and fistulas, the scientific evidence for this approach is limited primarily to case reports or case series with few randomized trials. Nevertheless, the limited evidence regarding endoscopic management points to novel paradigms and approaches.

Definitive Therapy Vs Bridging Therapy

Endoscopic management of fistulas and leaks can be categorized into definitive or bridging therapy. In a subset of patients, a single session or a series of endoscopic interventions results in definitive resolution of the fistula or leak. In other patients, endoscopic interventions may not be able to definitively resolve the fistula or leak, but serve as a bridge to definitive surgical repair by diverting noxious enteric contents, creating enteral access for nutrition, and relieving any obstruction precluding healing, thus shifting the status of patients who are high surgical risks to a more optimized surgical state.

Several factors eventually influence the final outcomes, including extent of disruption of luminal continuity, retroperitoneal vs intraperitoneal leak, contained vs free peritoneal leak, low-pressure vs high-pressure gradient across the tract, and chronicity of illness. Therefore, careful assessment of the GI defect at initial endoscopic examination is important, not only in the selection of the type of therapy, but also in setting clear and achievable expectations both from the patient and the referral source. The historical factors outlined above that are known to be associated with delayed or failed fistula closure [56,18,34,46,47] provide the setting where endoscopic intervention might only be useful as bridging therapy until the patient can undergo more definitive surgical treatment.

Centrifugal Vs Centripetal Drainage

The standard approach to drain a leak is to percutaneously place a catheter attached to a negative pressure device. This approach diverts GI secretions centrifugally. Endoscopic drainage has revolutionized the management of pancreatic necrosis by draining retroperitoneal contents into the stomach or duodenum (Table 1). This approach, which we call centripetal endoscopic drainage, has been anecdotally used to manage perirectal, paracolic, and paraesophageal fluid collections that are extraperitoneal or extrapleural in nature, where a computed tomography or ultrasound-guided approach is not feasible. However, it remains unclear if the centripetal approach could work in a contained or uncontained leak in the peritoneal or pleural space. If there is no obvious luminal bulge or if imaging suggests a vascular structure between the collection and the gut lumen, endoscopic ultrasound-guided drainage is an alternate approach. Akin to the management of infected cutaneous wound by vacuum-assisted closure system [57], endoscopic vacuum therapy (EVT) has been applied to treat leaks from the proximal or distal digestive tract. The concept here is that the negative pressure assists wound healing by draining inflammatory exudates and secretions, and by promoting