

Review Article

Repair of Bowel Perforation: Endoscopic State of the Art

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Abstract

Background: Intestinal damage from various etiologies can result in the potentially dangerous complication of bowel perforation. Emergent treatment of small bowel perforation includes surgical repair with or without small bowel resection. As the number of therapeutic and diagnostic endoscopic procedures increase, more studies may be required to properly evaluate and report incidences of bowel perforation. Given the advantages of interventional procedures, novel endoscopic technologies which may prove beneficial in bowel perforation repair are continuously undergoing development.

Bowel perforation can lead to peritonitis and sepsis - a medical emergency requiring immediate attention. Following diagnosis, hemodynamically stable patients may be treated conservatively whereas unstable patients undergo more intensive surgical procedures. Endoscopic procedures for bowel perforation repair also exist and recent advances in technology are furthering the scope of such closure methods.

Methods and Findings: Endoscopic suturing technologies, while capable, require extensive training and entail prolonged activation processes. Wound vacuum sponge closure via endoscopy provides convergence of wound defects but may not be efficacious in defects larger than 5 cm. Furthermore, this method may be limited by inadequate seal and placement in the intestine. Endoscopic clipping is another modality beneficial for smaller perforations only. T-tag suturing has shown promising results in *ex-vivo* studies but entails blind placement of T-tags for perforation closure. Stents can be inserted endoscopically under fluoroscopic visual guidance. This technique, however, may result in stent migration, perforations and potential occlusions. Sealants can be injected for perforation closure but have not demonstrated clear efficacy. Robotic flexible endoscopy provides several novel features yet may require advanced training and sometimes more than one operator.

As interventional procedures continue to gain popularity, a better understanding of endoscopic modalities is helpful for furthering their development. Regarding bowel perforation, this review aids in an overall understanding of the technologies which exist and are advancing further into more standard modalities for practical medical applications.

Conclusion: There are currently various methods to repair perforation of the gastrointestinal wall and except for urgent exploratory laparotomy when indicated, there is likely no single method that is superior to others. It may be beneficial for the physician to consider all options for repair when evaluating a potential bowel perforation, considering physician preference and individual success or difficulty with a given modality. In more recent years as the focus has narrowed on minimally invasive procedures, future modalities will likely include increased automation and ease of use with the help of robotics, which will hopefully lead to decreased time to diagnosis, faster recovery and reduced morbidity and mortality.

Keywords: Bowel, Endoscopy; Perforation; Stents; Exploratory Laparotomy; Robotics

Introduction

Bowel perforation is the loss of intestinal wall integrity and can occur by several mechanisms including infection, obstruction, inflammation, trauma and iatrogenic causes. Incidences of bowel perforation have been reported ranging from 1-7% in pediatric trauma patients and 0.02-8% in adults, with perforation secondary to diverticular disease accounting for up to 15% of duodenal perforations and ulcerative disease being the most common etiology [1,2]. Additionally, with the increasing use of diagnostic and therapeutic endoscopy comes the resulting increase in the incidence of adverse events, including perforation. The incidence of bowel perforation in adults may be higher than these reported values given the increasing use of diagnostic and therapeutic endoscopic modalities and lack of available data on small bowel perforation.

There is no specific classification for gastrointestinal perforations, but several methods have been used to describe perforations based on etiology, including systemic, inflammatory, medication, neoplastic and instrumentation-induced perforations. Treatment for acute endoscopic perforations was traditionally open surgical repair which is associated with high morbidity (25-36%) and mortality (7-10%), but continual efforts toward less invasive methods may provide better outcomes [3]. In contrast to surgery, benefits of endoscopic closure include no requirement for general anesthesia and decreased leakage of gastrointestinal contents, which carries the potential to reduce both morbidity and mortality.

Clinical Presentation and Diagnosis

The clinical presentation of bowel perforation typically includes abdominal pain and distension, nausea, vomiting, decreased appetite and potentially other symptoms of inflammation and infection, including fever, hypotension and tachycardia- although these may suggest a delayed perforation of over 24 hours. Timely diagnosis and management are necessary as delay can be life-threatening, considering the risk of septic peritonitis and sepsis. Diagnostic evaluation in this setting includes radiologic imaging of the abdomen. A direct sign of perforation on upright abdominal X-ray is pneumoperitoneum, or free abdominal gas, which may be recognized incidentally in asymptomatic perforations. The sensitivity for detection on upright abdominal X-rays ranges from 50 to 70% and is inferior to Computed Tomography (CT) imaging which can better detect small amounts of gas [4]. Ultrasound is typically not helpful in detecting free gas, but can help identify a free fluid or intestinal paresis [5].

Most endoscopically-induced perforations are recognized immediately by direct visualization, or by the target sign in the case of polypectomy: a central white or cauterized elevated portion of the resected specimen representing a partial or full-thickness resection of the muscularis propria [6]. However, diagnosis of perforation is often delayed and one study reported a median time to diagnosis of 12 hours [7]. After confirming a perforation is present, the type and severity must be identified swiftly to initiate treatment if necessary [8].

Management

Management of bowel perforation typically includes consultation with the surgical team and options include non-surgical management in hemodynamically stable patients without peritonitis, or laparoscopic or open laparotomy repair in more severe cases [2,9,10]. More recently, endoscopic closure has also been reported with high success rates, including the use of stents, sealants and clipping. Endoscopic Vacuum Therapy (EVT) is a more novel approach that has been proposed, but has yet to gain widespread acceptance [11,12]. Robotic flexible endoscopy represents another growing field that may be used to repair bowel perforation in the future [13].

Generally, there are multiple goals of treatment - firstly, to restore continuity of the gastrointestinal tract, secondly to prevent bowel contents from contaminating the peritoneum, thus preventing infection and thirdly, to drain any peritoneal fluid that has collected. Small leaks that are diagnosed early are sometimes managed with conservative treatment alone, consisting of nasogastric suction, antibiotics, proton pump inhibitor therapy, fluid replacement and NPO diet [14]. When open surgery can be deferred, endoscopic treatment may provide a means of closure or may serve as a bridge to a more invasive therapy if definitive repair of the perforation is not attainable endoscopically. Indications for invasive abdominal exploration may include abdominal sepsis, bowel ischemia, hemodynamic instability and complete or closed-loop bowel obstruction [15].

Endoscopic Therapies

Technological advancements have allowed for endoscopic suturing techniques and robotic flexible endoscopy including the

Overstitch and the Endomaster Endoluminal Access Surgical Efficacy (EASE) system, previously known as the Master and Slave Transluminal Endoscopic Robot (MASTER) [13,16-22]. The Eagle Claw was the first attempt at endoscopic suturing over a decade ago, that while proven successful in live porcine models, was never approved for use on humans [23]. However, the Eagle Claw's initial design led to the development of the Overstitch, likely the most common endoscopic suturing device [16,24]. Disadvantages of the Overstitch include limited device mobility in addition to proficiency requirements with a convoluted activation process [11,18]. Placement of endoscopic sutures by this method may not result in seal-proof closure, but is often successful in approximating opposing tissue margins to reduce the size of the perforation. Endoscopic suturing with the Overstitch is limited by device configuration and excessive tightening can result in cheese wiring which may further compromise the integrity of the bowel wall [11].

Endoscopic Vacuum Therapy (EVT)

Other approaches to endoscopic closure include EVT and at least one case report describes using a wound vacuum sponge sutured to a nasogastric tube with mild continuous suction applied [12]. However, more traditional EVT techniques include the backpack method, where the sponge drainage system is parallel to the endoscope and the over-tube method, where the sponge is pushed down through the tube and continuous vacuum pressure applied [11]. The application of suction leads to fluid removal for improved healing in tandem with accompanying mechanical forces which allow for defect edges to converge, causing cytoskeletal deformation and initiating signaling mechanisms that stimulate cell proliferation and migration and increased angiogenesis [25]. Drawbacks to this method include limitations to occluding defects greater than 5 cm, given the size of the sponge. Proper placement and sealing of the sponge may be inadequate if loculations are present and if an entero-cutaneous fistula complicates the pressure seal respectively [25-27].

Clipping

Endoscopic clipping is accomplished by deploying either Over-The-Scope Clips (OTSC), which are mounted onto the distal tip of the endoscope and Through-The-Scope Clips (TTSC), which are introduced through the working channel [3,11]. OTSC have an approximation force adequate for indurated tissue. Still, this method requires loading the clips onto a cap mounted at the tip of the endoscope which necessitates either preloading or withdrawal of the endoscope for mounting the clip cap. OTSC caps fit 11, 12 and 14 mm diameter endoscopes and clips are available as a blunt or a traumatic type (A type), atraumatic type with short pointed teeth (T type) and a traumatic type with long pointed teeth (GC type) [11]. Practical use of OTSC is limited to relatively small perforations (less than 2 to 3 cm) where the tissue margins can be suctioned and retracted into the cap. The primary indication for OTSC is the management of iatrogenic perforations. TTSC devices can be successful where stent placement may be challenging or when small perforations may occur intra-procedurally. TTSC can be placed without scope withdrawal; however, weak approximation force and limited wingspan limit use to only small defects [11,28].

T-Tag Suturing

T-tag suturing is yet another endoscopic approach that can be employed to treat bowel perforation. Closure by this method requires a T-tag anchor placed through the gastrointestinal wall with a needle covered by a transparent plastic chamber to protect abdominal organs from needle puncture during deployment. This chamber, which contains a lateral window that allows placement of the gastrointestinal wall inside, is used to transluminally place a T-tag anchor through the entire thickness of the gastrointestinal wall, which remains on the serosal side with the suture material inside the lumen. The endoscope then must be retracted and the end of the suture material remains through the mouth. After reloading, the endoscope is placed on the opposite side of the perforation and another T-tag anchor is deployed. The sutures are then tied with a metallic tie-knot. This process can be repeated as necessary, sometimes requiring up to six T-tags to close a perforation. While this method avoids retrieving the suture through the mouth, it requires the needle to be placed through the gastrointestinal wall blindly, without visualization of the serosa and nearby organs that may be punctured. Animal studies have shown limited success sometimes requiring other modalities to rescue intraoperative complications, but *ex-vivo* histologic evaluation of these lesions revealed complete restoration of the mucosal lining [29,30].

Stenting

Where endoscopic closure may not be successful, stenting offers another closure method. Some stents can be delivered endoscopically via passage through a working endoscopic channel. The procedure typically utilizes fluoroscopic visual guidance

and requires a guidewire for appropriate stent placement. Multiple methods including Over-The-Wire (OTW), Through-The-Scope (TTS) and Over-The-Scope (OTS) techniques can be utilized for stent placement. Depending on the procedure, a particular method may be favored. The OTS technique compresses the stent over the endoscope using a temporary suture, which is then released to deploy stents in hard-to-reach locations of the GI tract [31,32]. There are a variety of stents available including Self-Expandable Plastic Stents (SEPS), Partially Covered Self-Expandable Metal Stents (PCSEMS), fully covered Self-Expandable Metal Stents (fSEMS), fully covered Self-Expanding Plastic Stent (fSEPS) and biodegradable stents which in some cases may be personalized by CT-guided manufacturing [11,33]. However, stent migration requiring readjustment or repeat stent placement is a limitation [11]. For example, the migration rate of commonly used fSEMS and fSEPS ranges between 13 to 46% [34]. Because uncovered stents affix into the tissue, the incidence of migration is lower when compared to that of covered stents. Furthermore, stent-related perforations and stent occlusions are other potential complications that serve as limitations in this technique [31].

Sealants

Biocompatible sealants that function similarly to clips can be administered via endoscopic injection and are yet another option for closure of bowel perforations [35]. Tissue compatible glues include protein derivatives involved in coagulation or adhesion such as cyanoacrylate, which unlike biological glue, is nonabsorbable and may result in a hypersensitivity reaction [11]. However, sealants appear to be relatively ineffective in a retrospective multicenter study on endoscopic therapy for upper GI postsurgical leaks, closure via tissue sealants provided closure in only 2 of 9 leaks (22.2%, n = 9) [36].

Robotics

Robotic flexible endoscopy is another growing field that allows endoscopists to overcome the limitations of traditional flexible endoscopy. For example, robotics offers more degrees of freedom than a conventional endoscope, which may improve Endoscopic Submucosal Dissections (ESDs) and Natural Orifice Transluminal Endoscopic Surgeries (NOTES) [13]. Endoscopic robots are often assumed to be an improved permutation of traditional flexible endoscopes and robotic control of conventional flexible endoscopes has been investigated with relative success. Still, the size and positioning of a shaft manipulation module remain an obstacle to be overcome [37]. The Endomaster EASE improves the MASTER robotic system, which consists of a conventional double-channel endoscope with two attached arms, one with forceps and an electrocautery hook. More recent implementations contain a third instrument channel to insert conventional, non-robotic endoscopic instruments. The other two channels allow interchangeable robotic instruments including a needle holder for suturing, a hook and a grasper. While this device provides nine degrees of freedom, it requires two endoscopists to operate. The surgeon controls the master console, responsible for seven degrees of freedom and the other endoscopist is responsible for orienting and positioning the slave module at the operating table [22,38]. The ISIS-Scope/STRAS system is a robotic, shortened version of the manual Anubiscope, which also has three instrument channels. This system, which has two lateral channels located at the edges of the shaft and guarded by mobile shells that open after the scope is in place, allows for 10 degrees of freedom and utilizes endoscopic instruments with hollow shafts, to which inserts containing electromechanical actuators can be screwed on at the end of the shaft. Like the Endomaster EASE, the ISIS-Scope/STRAS also requires two physicians in tandem to operate [22,38].

Discussion

Gastrointestinal perforation can result from various etiologies, including inflammation, infection, obstruction, malignancy and iatrogenic causes, often caused by ulcerative disease or instrument-induced direct trauma to the bowel wall. Traditional treatment has involved open surgical repair, associated with relatively high morbidity and mortality compared to other modalities. The evolution and implementation of minimally invasive methods are under continual investigation. While open surgery may be unequivocally indicated in some cases, for either exploration or as a means of definitive closure, this comes with significant risk. Non-surgical management, however, carries relatively less risk of complication, morbidity and mortality, but may be inadequate for non-minor perforations. In contrast to open surgery, endoscopy offers reduced risk and obviates the need for general anesthesia but may not always result in definitive treatment. There are currently several technologies available to the endoscopist in which repair of bowel perforation may be attempted and each carries its advantages and limitations with it. For example, some robotics such as the Endomaster EASE and ISIS-Scope/STRAS require two physicians to operate, which may be impractical or unfeasible in some scenarios. Other modalities such as T-Tag suturing have proven successful in animals but have yet to gain wide acceptance for human use. Endoscopic clipping and endoscopic suturing with the Overstitch have gained commercial market share, but require depositing permanent metal implants, although likely insignificant and have a complex

learning curve for the operation that hinders its use respectively. Stenting may also succeed in some cases but may require reorientation due to stent migration.

Biological sealant is often used in conjunction with other modalities as adhesive alone and may not have a high probability of success. The risk of hypersensitivity reaction remains even with closure with sealant alone. Conservative management and EVT may carry minimal risk but are often inadequate for a significant perforation. Despite sometimes not creating permanent repair of a perforation, endoscopic management may provide a bridge to a more definitive procedure such as laparoscopy or laparotomy.

Conclusion

There are currently various methods to repair perforation of the gastrointestinal wall and except for urgent exploratory laparotomy when indicated, there is likely no single method that is superior to others. It may be beneficial for the physician to consider all options for repair when evaluating a potential bowel perforation, taking into account physician preference and individual success or difficulty with a given modality. In more recent years as the focus has narrowed on minimally invasive procedures, future modalities will likely include increased automation and ease of use with the help of robotics, which will hopefully lead to decreased time to diagnosis, faster recovery and reduced morbidity and mortality.

Conflict of Interest

The authors have no conflict of interest to declare.

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