REVIEW

Sealing the hole: endoscopic management of acute gastrointestinal perforations

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Received 30 October 2018

Revised 3 February 2019

Accepted 16 February 2019

Published Online First

12 March 2019

ABSTRACT

Acute perforations are one of the recognised complications of both diagnostic and therapeutic gastrointestinal (GI) endoscopy. The incidence rate varies according to the type of procedure and the anatomical location within the GI tract. For decades, surgical treatment has been the standard of care, but endoscopic closure has become a more popular approach, due to feasibility and the reduction of the burden of surgery. Various devices are available now such as through-the-scope clips, over-the-scope clips, endoscopic suturing devices, stents, bands and omental patch. All have been tested in studies done on humans or animal models, with a reasonable overall technical and clinical success rate, proving efficiency and feasibility of endoscopic closure. The choice of which device to use depends on the site and the size of the perforation. It also depends on availability of the device and the endoscopist's experience. A number of factors that could predict success of endoscopic closure or favour surgical treatment have been suggested in different studies. After successful endoscopic closure, patients are usually kept nil by mouth and receive antibiotics for a duration that varied between different studies.

INTRODUCTION

In the last decade, there has been a significant increase in the demand for endoscopic procedures. This is primarily due to the endorsement of screening and surveillance programmes for various gastrointestinal (GI) diseases and the development of new procedures. Perforation is one of the most feared complications of GI endoscopy.¹

The mechanism of injury can be mechanical trauma, precipitated by inflammation, tumours, and anatomical abnormalities, direct bowel resection by snare polypectomy, or thermal

injury by hot snaring or argon plasma coagulation.²

Surgical repair has been the standard of care but recent developments in endoscopic accessory devices, such as clips, made it possible for endoscopic closure.

General principles of managing GI perforations

Acute perforations are recognised within 24 hours of the index procedure and can be visualised during the procedure or suspected by sudden loss of luminal distension. Another helpful endoscopic sign is the 'target sign' showing full-thickness muscle tissue surrounded by submucosa.³

After endoscopy, signs and symptoms suggestive of perforation, such as abdominal or chest pain, abdominal distension, fever and shortness of breath should be investigated with a contrast-enhanced CT.⁴

Once perforation is detected, the most important first step is to remain calm and have a clear plan of action. This requires preparation before endoscopic procedures, especially high-risk ones. Alerting assistants and nursing staff immediately is crucial and it is better done in a way that does not cause significant distress to the patient and panic in the endoscopy room. Having an agreed signal that alerts staff to the issue without distressing the patient is sensible. Photo documentation is important.

Switching to carbon dioxide insufflation is recommended to prevent compartment syndrome, caused by air pressure.⁵⁻⁷ Should it develop, needle decompression should be performed immediately, along with generous suctioning, to avoid or minimise any spillage into the peritoneal cavity.

All cases of iatrogenic perforation should be hospitalised and kept nil by

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To cite: Gabr A. *Frontline Gastroenterology* 2020;11:55–61.

mouth and started on intravenous broad spectrum antibiotics and intravenous proton pump inhibitors (PPIs); however, intravenous PPIs are not necessary in colonic perforations.² NG or preferably nasojejunal tubes can be used to divert luminal content, minimise contamination and provide enteral route of feeding.⁸

The decision to close the defect endoscopically will depend on a number of factors: (1) localisation and size of the perforation, (2) stool contamination, (3) availability of instruments to close the defect, (4) the endoscopist's expertise and skills^{1 3 5 7 9} and (5) the cardiovascular stability of the patient.^{10 11}

It is important to emphasise that endoscopic closure should be attempted as soon as the perforation is detected, as a delay could cause a collection or abscess to form, in which case endoscopic closure must not be attempted prior to drainage of the collection.

OESOPHAGEAL PERFORATIONS

The incidence of perforation in diagnostic gastroscopy is around 0.03% with a mortality rate of 17% and a morbidity rate of 40%.^{2 4} When interventional procedures are included, this ratio ranges between 0.5% and 5% in endoscopic mucosal resection (EMR)^{2 5} 4% and 4.8% in endoscopic submucosal dissection (ESD).^{12 13} In retrospective series on EMR mostly for Barrett's oesophagus, the reported perforation rate was between 0% and 3%.^{14 15} Oesophageal dilation for peptic stricture has been reported to have a perforation rate close to 0.65%,¹⁶ whereas pneumatic dilatation of achalasia carries a risk between 0.4% and 14%.^{17 18} Lower oesophagus is the most common site for perforation during diagnostic procedures.¹²

Endoscopic repair has been reported in the literature with the use of through-the-scope (TTS) clip.^{19–21} Using a double channel scope facilitates passing a grasping forceps to hold the edges while deploying the clips from the other channel. An over-the-scope clip (OTSC, Ovesco, Tübingen, Germany) was developed for closure of large defects and treating upper GI bleeding ulcers. The OTSC system has been successfully used in closing perforations throughout the GI tract, up to 18 mm in diameter.²² The European Society of gastrointestinal endoscopy (ESGE) recommends using the OTSC for oesophageal perforations up to 2 cm in diameter while a (TTS) clip is sufficient for perforation <1 cm in diameter.⁴

Oesophageal stents have emerged as a treatment of perforations, ruptures and leakage in the oesophagus. Several types exist as follows: fully covered self-expandable metal stents (FCSEMS), partially covered self-expandable metal stent (PCSEMS), self-expandable plastic stent. Stenting is a treatment option for large perforations, that is, >2 cm in diameter. A systematic review by van Boeckel *et al* on using stents for benign rupture or anastomotic leakage of the oesophagus concluded the effectiveness and safety of placing stents for 6–8 weeks as a treatment option.²³

The systematic review did not show any superiority of any type of stent. Limitations of stents include migration, which seems to be least with the PCSEMS, though tissue overgrowth is common with the latter, which can make it difficult to remove. Though migration can be minimised by fixing the stent with clips or endoscopic suturing device, it tends to be a problem with the size of stents available for common use with strictures. A broader stent is usually needed, but is not routinely available in endoscopy units. Other problems with stents including difficulty applying in the upper oesophagus due to foreign body sensation.

Other devices have been used with success, though there are limited experience of their use in the UK, such as endoscopic suturing device (OverStitch; Apollo Endosurgery, Austin, TX, USA) and endoscopic vacuum-assisted closure which uses negative pressure to absorb secretions and promote wound healing by granulation tissue formation. Eso-SPONGE (Eso-SPONGE-B.Braun) represents an innovative therapy concept for the treatment of this problem in the upper GI tract, which can contribute significantly to the reduction of morbidity and mortality of the patients. A series of pilot studies and retrospective analysis of different working groups have demonstrated particular advantages of the Eso-SPONGE, such as continuous drainage, infection control, mechanical reduction and cleaning of the wound cavity and promotion of granulation tissue.^{24 25} Figure 1 summarises the proposed management algorithm for oesophageal perforations.

GASTRIC PERFORATIONS

The incidence of perforation in diagnostic gastroscopy is around 0.03%. The mortality rate of perforation is of 17% and a morbidity rate is 40%.^{26 27} With therapeutic gastroscopy, this ratio ranges between 0.5% and 5% for gastric EMR²⁸ and 4% and 4.8% for gastric ESD in a Japanese cohort.^{10 29} The rate of incidence varies according to regions of the stomach.

As in the oesophagus, general measures of treatment include nil by mouth, starting antibiotics and PPIs. Inserting a NG tube under endoscopy has been recommended by ESGE.⁴ Small perforations less than 1 cm can be easily treated with endoscopic clips (TTS), taking advantage of the ample space available within the stomach.^{10 30 31} For larger defects up to 2 cm using the OTSC system seems to be a reasonable option, if available, with a reasonable rate of success as shown by many studies.^{32–35}

Another technique for large defects (>2 cm) is the combination of TTS and endoloops, where TTS are placed around the margin of the defect and then closed like a purse string with the endoloop.³⁶ This technique is helpful when OTSC is unavailable. Alternatively, if the omentum is visible through the defect, an omental patch technique could be used, by grasping a piece of the omentum and using it to close the defect, before applying the clips. Omental patch technique is

Figure 2 Proposed management algorithm for gastric perforations: choice of device used will depend primarily on the size of the perforation. OTSC, over-the-scope clip; TTS, through-the-scope.

role in the stomach apart from perforations resulting from dilating pyloric stenosis or gastroenteric anastomosis. All patients should have a contrast-enhanced CT, and a significant extravasation would indicate failure of endoscopic treatment and need for surgery. **Figure 2** is the proposed management algorithm for gastric perforations.

Duodenal/endoscopic retrograde cholangiopancreatography perforations

Endoscopic retrograde cholangiopancreatography (ERCP) has a perforation rate of 0.35%–3% and carries a mortality rate of 16%–18%.^{39 40} Endoscopic ultrasound has a perforation rate of 0.03% and a low mortality rate <0.01%.⁴¹ Most cases are related to sphincterotomy and guidewire insertion causing a perforation that can be detected immediately, with free retroperitoneal gas on fluoroscopy. Predisposing factors are abnormal anatomy such as strictures or Billroth II gastrectomy. Stapfer *et al* classified ERCP-related perforation to four types: duodenal perforation (type I), periampullary perforation (type II), perforation of the bile ducts (type III) and retroperitoneal air (type IV).^{42 43}

While types II, III and IV can be managed conservatively, surgery has been traditionally the main treatment for type I.³⁹ However, endoscopic clips (TTS and OTSC) have been used with success to close type I duodenal perforations.²² Additionally, stenting with FCSEMS should be considered for biliary, periampullary and retroperitoneal perforations to divert fluid

Figure 1 Proposed management algorithm for oesophageal perforations: unfavourable features will preclude endoscopic closure. IV, intravenous; OTSC, over-the-scope clip; PPI, proton pump inhibitor; TTS, through-the-scope.

particularly helpful for very large defects.^{10 31} Other devices were tried in gastric perforations. Bands were successfully applied to close perforation less than 1 cm in two studies on humans, and up to 1.7 cm on animal models.^{37 38} The endoscopic suturing device has been used with success, mainly in Natural orifice trans gastric endoscopic surgery settings. Stents have limited

Figure 3 A retroperitoneal perforation detected on ERCP. ERCP, endoscopic retrograde cholangiopancreatography.

away from the leaking site and could be done at the end of the procedure. Therefore, it is important that the ERCPist check the final X-ray at the end of the procedure, for retroperitoneal gas, in order to place the stent promptly, when needed. **Figure 3** shows an example of retroperitoneal gas detected at ERCP. If placing the stent is successful, then patients can be discharged next day with no need for a follow-up CT abdomen. The treatment of choice for a duodenal

Figure 4 Proposed management algorithm for duodenal perforations: note the importance of timing in deciding best treatment option. ERCP, endoscopic retrograde cholangiopancreatography; PIS, peritoneal irritation signs; SIRS, systemic inflammatory response syndrome.

perforation will depend on site, timing of detection and the presence or absence of peritoneal irritation signs, systemic inflammatory response syndrome or significant leakage of the luminal contents to the peritoneum as shown on imaging, as presence of any will dictate surgery regardless of the timing or site of injury.⁴

If feasible, endoscopic closure should be attempted for all duodenal perforations detected during endoscopy, and if the patient develops any adverse signs as mentioned above, then surgery to be considered. CT follow-up is recommended in most cases. **Figure 4** is the proposed management algorithm for duodenal/ERCP perforations.

COLORECTAL PERFORATIONS

Since its introduction in the late 1960s, colonoscopy has been a safe and effective method of visualising the colon. The incidence rate of perforation is 0.03%–0.9% for diagnostic colonoscopy and up to 4% for therapeutic colonoscopy.^{44 45} The rate could even go higher with advanced EMR and ESD. Mortality rate is 7% after colonic perforation.⁴⁶ Predisposing factors include colonic wall weakness as a result of chronic inflammation (inflammatory bowel disease), decreased mobility (adhesions, diverticula, radiation) and operator inexperience (excessive looping, air insufflation).⁴⁷ Common sites of perforation include the sigmoid colon (53%), followed by the cecum (24%).⁴⁸

Antibiotics and fluids should be started without delay, once perforation is detected, and the patient should be monitored for signs of peritoneal irritation and the need for decompression, in case pneumoperitoneum develops. As with other types of GI perforations, endoscopic closure has been possible with the advent of the closure devices. Several studies confirmed the success of endoscopic clipping with the TTS clip. While others reported the success of the OTSC in closing colonic perforations. Endosuturing was shown to be more effective than clips, offering a cheaper alternative to rescue surgery for colonic perforations, in a recent study by Kantsevov *et al.* However, the study was a single centre, retrospective and included only 21 colonic perforations.⁴⁹ In animal models it can close perforations up to 2.5 cm with high technical success rate. As with gastric perforations, bands were also tried in the colon as a rescue therapy after failed clipping.

If perforation happens during ESD, some authors recommend closing it after completing the procedure, in order to have a complete specimen and not to miss pathology.

Most patients require a contrast-enhanced CT examination after closure, and surgeons to be informed of every case of colonic perforations; however, a small perforation in otherwise stable patient may not require a CT examination. It is reported that endoscopic repair has higher rate of failure, necessitating surgery, in perforation induced by diagnostic colonoscopy, than those induced by therapeutic colonoscopy,

Figure 5 Proposed management algorithm for colonic perforations. In ESD setting, it is agreed to complete the procedure before closing the defect, in order to obtain a complete specimen. ESD, endoscopic submucosal dissection; OTSC, over-the-scope clip; TTS, through-the-scope.

as the mechanism of injury tends to be blunt trauma with high shearing force, resulting in more significant injury.⁴⁵

Figure 5 is the proposed management algorithm for colorectal perforations.

Management post-endoscopic closure

The duration of nil by mouth is one of the most disputed areas in the topic with different approaches. Generally, the school of thoughts can be divided into two main groups: authors who rely on arbitrary numbers and those who rely on clinical parameters. We recommend that decision has to be guided by the site (eg peritoneal vs retroperitoneal) and the size of the perforation, the timing of the perforation closure, whether it is completely or incompletely sealed at endoscopy and the presence or absence of sepsis or collections.

For oesophageal perforations, some authors recommend fasting for 2 days only, then to start liquid diet

on day 3.³⁸ Others require a negative water-soluble contrast swallow before commencing oral intake.² A third, more strict view is to offer patients total parenteral nutrition feeding with an nasogastric (NG) tube to empty the stomach and wait for resolution of C-reactive protein and white blood cell count on bloods, air and fluid on CT then to start feeding 7–14 days later.²⁰

For gastric perforations, Lee *et al* suggested return of inflammatory markers to normal with absence of peritonitis or mediastinitis as a prerequisite for starting oral diet.⁵⁰ While Minami *et al* and He *et al* used a 48-hour window before starting liquid diet.^{10 38}

Han *et al*, as did Imagawa *et al*, allowed oral intake when clinical symptoms resolved, appetite and bowel function returned, and laboratory test values were normalised.^{37 51} Bai *et al* asked their patients to fast for at least 3 days until abdominal pain disappeared.⁵² Tsunada *et al* suggested re-scoping in 48 hours to check closure in addition to clinical improvement before starting oral feeding.³¹

ESGE recommends NG placement and nil by mouth for both oesophageal and gastric perforations.⁴ Interestingly, Jeon *et al* concluded that NG placement did not make difference to the outcome of gastric perforations induced by ESD and closed endoscopically in their study.⁵³

For duodenal and ERCP perforations, it seems there is a general agreement that a period of fasting for a few days is the expectation, till clinical and radiological improvement is confirmed.^{2 4} However, this rule does not apply for small retroperitoneal perforation that was sealed with a (FCSEM) stent, as patients can be discharged on the same or the following day.

For colorectal perforations, some authors advocate fasting for 1 day,^{3 49} others recommend 2 days.⁹ As in upper GI perforations, some authors advocate using parameters of clinical improvement, with absence of pain and fever, and return of bowel sounds combined with laboratory improvement, in addition to absence or decrease in air on repeat imaging.²

DNAER:DO NOT ATTEMPT ENDOSCOPIC REPAIR!

Several factors have been suggested as predictors of unsuccessful or difficult endoscopic closure and the need for surgical intervention as the ultimate method of perforation closure.

Obvious ones are the presence of ongoing sepsis or clinical deterioration, particularly with fluid collection outside the GI tract, such as retroperitoneal or mediastinal collection. Also, resectable tumour in a surgical candidate favours surgical treatment.

Also a delayed detection (>24 hours) post index procedure is considered a strong predictor of failure of endoscopic closure by many authors. This is due to inflammation and necrosis at the edges of the perforation, which render sealing it with an endoscopic device rather difficult.²² Additionally, it predisposes to sepsis

Table 1 Predictors of need for early surgery

Study	Predictors of need for early surgery (DNAER)
Cho <i>et al</i> 2012 (colon) ⁵⁴	Large perforation (OR, 9.25; 95% CI 1.85 to 46.20). Leucocytosis (OR 6.58; 95% CI 1.86 to 23.29). Fever (OR 5.05; 95% CI 1.05 to 24.28). Severe abdominal pain (OR 4.30; 95% CI 1.17 to 15.83). Large amount of peritoneal free air (OR 4.05; 95% CI 1.40–11.71)
Hagel <i>et al</i> 2012 (Oesophagus) ¹³	Large perforation length (13.4±8.8 mm, p<0.02), widths (5±4.5 mm) and area (97.6±149 mm ²). Necrotic or soft inflammatory margins Significantly more OTSC (2.3±0.5, p=0.018) were tried Unfavourable anatomical site of the perforation
Jovanovic <i>et al</i> 2012 (colon) ⁹	Large defects located in angulated areas Stool contamination is present
Hotta <i>et al</i> 2012 (colon) ⁵⁵	Diffuse peritonitis Failure of endoscopic closure
Fushihiro <i>et al</i> 2006 (colon) ³⁰	>1 cm Significant leakage/poor bowel preparation Inexperienced endoscopist Clinical deterioration
Yang <i>et al</i> 2010 (colon) ⁵⁶	Peritoneal irritation Failure of endoscopic clipping Age >65 years Perforations above the rectum

DNAER, do not attempt endoscopic repair.

and collection formation which renders endoscopic closure harmful.

It is important to recognise when endoscopic closure is unlikely to work, and an early surgical involvement would be needed. [Table 1](#) summarises the factors identified in different studies.

CONCLUSION

Acute GI perforations are rare but relevant endoscopic emergencies. The low incidence of perforations is causing it to be a challenging clinical problem, due to lack of experience among many endoscopists. This is aggravated by the absence of well-randomised trials in the future due to obvious ethical reasons. At the moment, increasing awareness and promoting hands on training on animal models are probably the short answers to the problem.

Correction notice This article has been corrected since it published Online First. Figure 1 has been replaced.

Contributors I am the sole author of this work.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interest None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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