Tech Coloproctol (2008) 12:315–322
DOI 10.1007/s10151-008-0442-6

ORIGINAL ARTICLE

Our experience with endoscopic repair of large colonoscopic perforations and review of the literature

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Received: 8 July 2008 / Accepted: 21 September 2008

Abstract Background Colonic perforation is the most severe complication of lower gastrointestinal endoscopy. Recently successful closure with endoscopic clips has been reported. However large (>10 mm) perforations and perforations occurring during diagnostic colonoscopy are considered a contraindication to endoscopic closure. **Methods** We retrospectively reviewed our own experience with endoscopic closure of colonoscopic perforations. The size of the perforations was determined by comparison with the maximal opening of the clipping device. In addition we reviewed all cases of colonoscopic perforation published in the English language literature. **Results** From January 2006 we performed closure of three large colonoscopic perforations in three patients. One perforation occurred after en-bloc endoscopic mucosal resection of two polyps in the descending colon. The other two perforations occurred during diagnostic colonoscopy. All three cases were promptly diagnosed and successfully repaired with TriClips. Patients were kept on intravenous antibiotics and a clear liquid diet until bowel movement and were discharged between the 2nd and the 8th day after the procedure. A review of the literature, including our series, revealed 75 reported cases of colonoscopic perforations repaired with endoclips. Of these, four perforations were larger then 10 mm and four occurred during diagnostic colonoscopy. Of the perforations occurring during therapeutic colonoscopy, clip closure was carried out in 55–96% of the immediate perforations and was successful in 69–93% of cases. **Conclusions** Nonsurgical management of colonoscopic perforations with endoclips is a highly feasible option. From our initial experience large perforations and perforations occurring during diagnostic colonoscopy are not a contraindication to endoscopic repair, but due to the small number of patients these data must be interpreted with caution.

Key words Colonic perforation · Endoclip repair · Endoscopic clipping

Introduction

Colonic perforation is the most threatening complication after diagnostic and therapeutic lower gastrointestinal endoscopy. Its reported incidence varies from 0.01% to 3% [1–4]. The management of this complication remains controversial [5]. Early recognition of the perforation site is mandatory [6]. Surgical treatment is traditionally advocated if signs and symptoms of abdominal sepsis are present [7, 8]. Prompt endoscopic repair has been described for small (<10 mm) parietal defects in clinically stable patients without peritonism [9–13]. More recently we and others have described successful repair of large colonoscopic perforations using endoscopic clips

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[14, 15]. We report our experience with endoscopic repair of large colonoscopic perforations including two new cases and a review of the literature.

Methods

Since January 2006 we have performed three endoscopic repairs of colonoscopic perforations. One perforation occurred after endoscopic mucosal resection and has been previously reported [15] while the other two occurred during diagnostic colonoscopy. Colonoscopies were performed as outpatient procedures after preparation with 3 l polyethylene glycol electrolyte solution 12 h before the examination and under deep sedation using intravenous propofol. Standard informed consent for colonoscopy was obtained prior to the procedure. In all three cases repair of the perforation was achieved using the TriClip device (Cook Endoscopy, Winston-Salem, NC) as shown in Fig. 1. The size of the perforations was determined by comparison with the maximal opening of the clipping device (12 mm). After a perforation was diagnosed no insufflation was used and after completion of the repair, haemostasis was carefully checked. All patients received intravenous cefuroxime (1 g every 12 h) and metronidazole (500 mg 8 h).

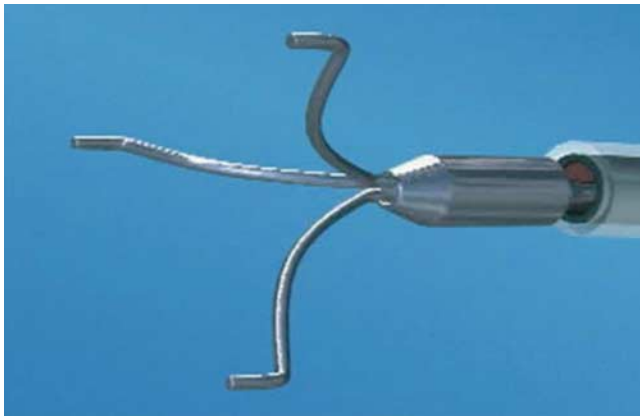

Fig. 1 TriClip endoscopic clip applier

Case 1

A 78-year-old woman, without a previous history of abdominal surgery or diverticular disease, underwent colonoscopy for recurrent abdominal pain. Bowel cleansing was excellent. After inspection of a normal rectosigmoid junction, a iatrogenic perforation of 30×10 mm. was suddenly not evident (Fig. 2a). The first clip was deployed at the border of the gap obtaining a complete approximation of the edges that facilitated the application of further clips (Fig. 2b). A total of three clips were used to close the perforation (Fig. 2c), the whole procedure taking less then 8 min. When sedation wore off the patient had slight rebound tenderness in the left iliac fossa. The patient was started on intravenous broad-spectrum antibiotics and kept on clear liquids. Upright plain abdominal radiography performed 5 h after the endoscopic repair did not show any free air and showed the clips in the left iliac fossa. Rebound tenderness gradually improved and disappeared by the 2nd day after the procedure. The white blood cell (WBC) count was normal (i.e. ≤10.000/mm^3). The patient resumed a regular diet on the 3rd day after she started having bowel movements and antibiotics were stopped. A plain abdominal radiograph obtained on the 5th day showed no residual clips. She was uneventfully discharged on the 8th day and at the time of this report had been asymptomatic for 24 months. The patient refused repeat colonoscopy; therefore a virtual colonoscopy was performed at 11 months, which showed a normal rectosigmoid junction, redundant sigmoid with no diverticula and absence of clips.

Case 2

A 75-year-old woman underwent colonoscopy 1 year after removal of a sigmoid adenoma. Bowel preparation was fair. There were scattered diverticula of the left

Fig. 2 a A 30×10-mm perforation at the rectosigmoid junction. The true lumen is in the upper left corner. Blood is visible at the edge of the gap. There is no muscular or adipose tissue. **b** Complete closure of the perforation after placement of the first clip. **c** Completion of endoscopic repair; three clips were placed

colon, and a diverticulum located in the sigmoid was inadvertently entered and perforated. The perforation was 12 mm in size with bleeding edges (Fig. 3a). The hole was closed with a clip and bleeding stopped (Fig. 3b). Two further clips were placed to secure the closure (Fig. 3c). The procedure took 13 min. Upright plain abdominal radiography performed 1 h after the procedure showed no free air and clips in the left lower quadrant. The patient was completely asymptomatic and her white blood cell count was normal. She was kept on clear liquids until passing a large amount of stool on the first day after the procedure. Antibiotics were stopped, she was started on a regular diet and was discharged on the 2nd day. An abdominal radiograph obtained on the day of discharge showed all three clips in the left iliac fossa. Flexible rectosigmoidoscopy 30 days after repair showed ulceration in the sigmoid colon (Fig. 3d) and no residual clips.

Case 3

A 49-year-old woman underwent surveillance colonoscopy. After an en-bloc endoscopic mucosal resection of two flat lesions of the descending colon, an iatrogenic perforation measuring 35×10 mm became apparent (Fig. 4a). Complete closure was obtained in 35 min using four TriClips (Fig. 4b). Upright plain abdominal radiography showed absence of free air. The patient was subsequently admitted and kept on intravenous fluids, broad-spectrum antibiotics and nothing by mouth. On the first day after the procedure the white blood cell count was 11,000/mm^3 and repeat abdominal radiography confirmed the absence of free air. No signs or symptoms of peritoneal irritation developed. On the 3rd day, the WBC count was normal, the patient resumed oral intake, intravenous antibiotics were stopped and she was discharged after 6 days. Histological examination confirmed two tubular adenomas

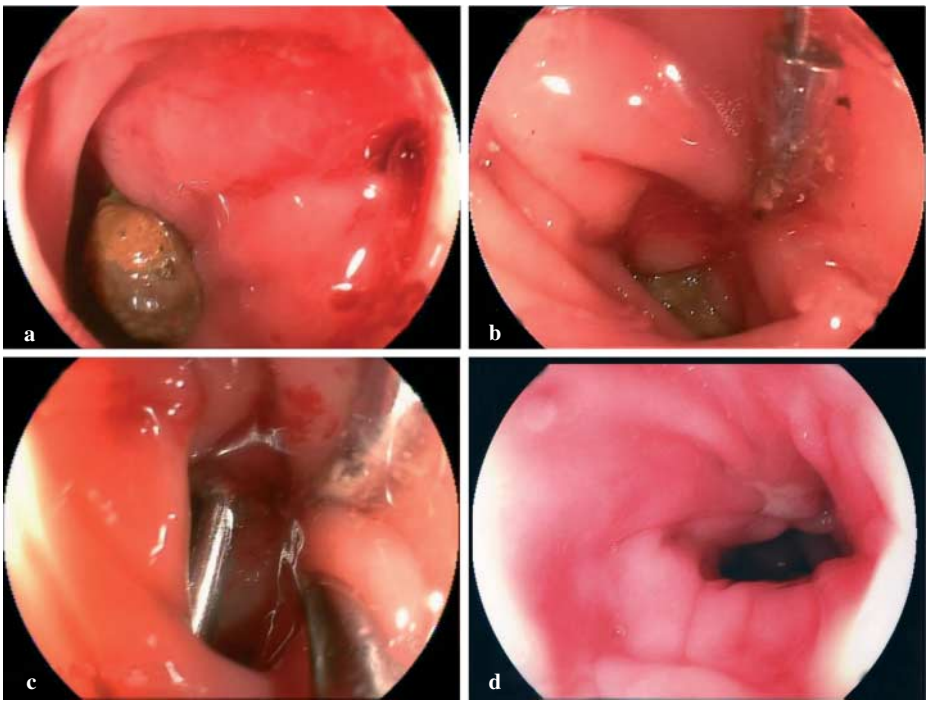

Fig. 3 a A 12-mm perforation of the sigmoid colon with bleeding edges. **b** After placement of the first clip bleeding stops and the edges of the defect are approximated. **c** Two additional clips are placed to secure the closure. **d** At colonoscopy after 30 days an epithelialized ulceration is visible at the site of the repair

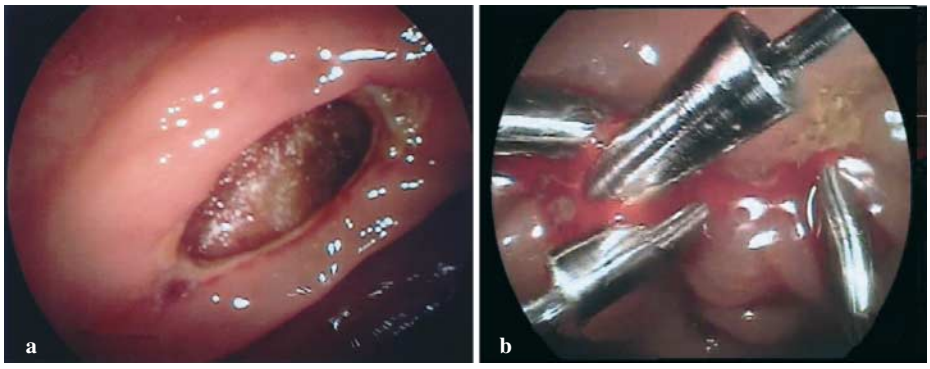

Fig. 4 a Iatrogenic perforation at the site of endoscopic mucosal resection with a diameter of 35×10 mm. **b** A total of four clips are required for endoscopic closure of the parietal defect

with high-grade dysplasia in one, with full-thickness muscle layer included in the specimen. At the time of this report the patient had been asymptomatic for 22 months.

Review of the literature

In 1997 Yoshikane [13] reported the first successful repair of a colonic perforation after an endoscopic mucosal resection using a HX-600-135 clip fixing device (Olympus America, Center Valley, PA). Following the report of Yoshikane, other 73 cases of endoscopic repair of colonoscopic perforations have been described [10-20] giving a total of 75 cases including the present report (Table 1). Among them, 71 (95%) were after therapeutic colonoscopy, 15 (21%) after endoscopic submucosal dissection, 41 (58%) after endoscopic mucosal resection, 13 after polypectomy (18%), 1 after hot biopsy (1.5%) and 1 after Argon Plasma Coagulator (1.5%). It is of note that four perforations, including two in the present report, were repaired after diagnostic colonoscopy [11, 18, 20] which has so far been considered a contraindication to nonoperative management.

The endoclip devices used are listed in Table 1. All of the devices are rotatable except TriClip and the over-the-scope clip (OTSC) system (Ovesco Endoscopy, Tübingen, Germany). The size of the perforations was less then 10 mm in all patients except the three patients in our series and the patient reported by Barbagallo et al. [14]. Some authors consider a perforation diameter greater than 10 mm (the size of most clips being 11 mm) a contraindication to endoscopic repair [12, 18]. Perforations involved all segments of the colon and rectum. Of 19 patients for whom direct abdominal radiography results were described, free air was present in 13 (68%) and absent in 6 (32%), including all of our patients. One report describes CT scan findings at the time of the perforation as positive in 7 of 13 patients treated successfully without surgery [19]. When abdominal free air is seen on the first radiograph, most authors perform serial follow-up radiography until the air is seen to have disappeared. Taku et al. [12] recommends prompt aspiration of the bowel contents and positioning the patient in such a way as to avoid further spillage.

No insufflation during endoscopic repair should be used. If tension pneumoperitoneum occurs, percutaneous transabdominal air deflation with an 18- or 20-gauge needle may be beneficial [9, 10]. In one patient an abdominal compartment syndrome resolved after placing a 14-gauge needle at the epigastrium [18]. The use of 50 ml intravenous contrast material injected after the procedure has also been reported and leakage of the repair was excluded by plain abdominal radiography and CT scan [9]. Most patients were fasted until bowel movement and disappearance of any evidence of peritonitis. Parenteral nutrition was used in three patients [13, 14, 16]. Different combinations and durations of broad-spectrum intravenous antibiotics were used in all patients. Of the 18 patients in whom symptoms are clearly described there was initial abdominal pain or rebound in 6 (33%) but it quickly diminished and disappeared in all. In one study all patients asymptomatic or with localized peritoneal signs were treated with endoscopic clips while development of diffuse peritoneal signs was an indication for surgery [19]. White blood cell count was not always normal and was as high as 16,000/mm^3 in one report [10]. C-reactive protein (CRP) was monitored in 23 patients and reached a maximum value of 14 mg/l, gradually decreasing to normal. Intensive monitoring, serial abdominal examinations and 12-h checks of laboratory values is recommended by most authors. Checking the site of repair before resuming oral feeds is not recommended [10].

How long should the clips stay in place to ensure closure is not known. Repeat colonoscopy was systematically performed in one study [20] and in three patients clips were present on day 31 and day 1 and absent on day 33, respectively. In one patient colonoscopy was performed 5 days after closure showing half of the clips and an ulcer at the perforation site [31]. Our follow-up abdominal x-rays showed no residual clips on the fourth day in one patient while clips were still present on the third and fifth day in the other 2. Colonoscopy at 30 days showed a small ulcer without clips (Fig. 2d). It is therefore likely that clips just temporarily bridge the mucosal gap limiting peritoneal spillage and allowing healing to occur as demonstrated by Raju et al. in pigs [16]. In the early series the majority of patients were hospitalized for at least 7 days, but in one of the recent series mean hospital stay was 3.5 days (range 2–6 days).

Feasibility and success rate vary between series. In a recent report of 4,000 polypectomies, among 26 perforations 12 (46%) were managed without surgery, 5 (19%) by endoscopic clipping, and 7 (26%) by observation [17]. Of the nine perforations recognized immediately five (55%) were clipped [17]. Taku et al. attempted endoscopic closure in 13 of 16 patients (81%) with immediate perforations, 9 of which (69%) were successful; diffuse peritoneal signs developed in none of the 9 patients with successful closure and in 5 of 7 patients in whom closure was either not attempted or unsuccessful [19]. Magdeburg et al. [18] attempted endoclip closure of perforations in 27 of 28 patients (96%), and they successfully managed 25 of 27 patients (93%) without surgery, while 2 patients had peritoneal signs and symptoms and underwent surgery. At surgery 1 of the 2 patients had negative findings and was simply drained. None of the

Table 1 Summary of previous reports of endoscopic repair of colonoscopic perforations

Reference	No. of patients	Age (years)	Cause of perforation	Size (mm)	No. of clips	Device used	Site	Abdominal air on radiography	Signs/symptoms and laboratory values	Hospital stay (days)
10	9	mean 65[a] (54–76)	ESD (9)	2.5–5[a]	Median 3 (1–8)[a]	HX-5QR, HX-600-090L (Olympus)	Caecum 2, ascending 2, transverse 2, sigmoid 1, rectum 2	No 2, yes 7	No signs or symptoms; mean maximum T 37.3 (36.5–38.9)[a], mean maximum WBC 9.7 (4–16)[a], mean maximum CRP 5 (0.1–14)[a]	mean 12.1 (7–18)[a]
14	1	48	Polypectomy	20	2	Olympus	Sigmoid	Yes	Modest right sided pain; T normal, WBC normal	8
11	1	91	Diagnostic	"Small"	3	Itx-600-135 (Omnilobo, Belgium)	Sigmoid	Yes	Initial abdominal pain, no peritonism; T normal, maximum WBC 13	n.a.
16	1	49	EMR	"Small"	6	n.a.	Ascending	Yes	Initial abdominal pain, no peritonism; T normal, WBC normal	5
12, 19	23	Mean 66.4 (43–82)	EMR (12), ESD (6), hot biopsy (1), polypectomy (4)	n.a.	n.a.	HX-600-090L (Olympus)	n.a.	CT yes 7[b], CT no 6[b]	Localized peritoneal symptoms or asymptomatic; mean maximum WBC 10.2 (5.2–13.4)[b], mean maximum T 37.8 (36.5–42)[b], mean maximum CRP 7.6 (0.3–19.6)[b]	Mean 9.1 (3–18)
18	27	n.a.	EMR (25), APC (1)	n.a.	1–4	Resolution (Boston Scientific)	n.a.	n.a.	n.a.	Mean 3.5 (2–6)
17	5	n.a.	Polypectomy (5)	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
13	1	48	EMR	4	5	HX-5QR (Olympus)	n.a.	Yes	Slight tenderness and rebound; T normal, WBC normal, maximum CRP 6.7	14
9	1	78	Polypectomy	6	2	HX-600-135 (Olympus)	Caecum	Yes	Abdominal pain	9
20	3	62, 74, 67	Polypectomy (2), diagnostic (1)	8, 4, 4	1 each	OTSC system (Ovesco Endoscopy, Germany)	Splenic flexure 1, n.a. 2	No 1, yes 1, n.a. 1	Asymptomatic 1; n.a. 2	n.a.
15, and present report	3	49, 75, 78	EMR (1), diagnostic (2)	12, 35, 30	4, 3, 3	TriClip	Descending 1, sigmoid 2	No	Rebound tenderness 1; T normal, WBC 11 in 1, normal in 2	3, 8, 6

APC, argon plasma coagulation; *CRP*, C-reactive protein expressed in milligrams per litre (normal <5); *CT*, computed tomography; *EMR*, endoscopic mucosal resection; *ESD*, endoscopic submucosal dissection; *n.a.*, not assessed; *OTSC*, over the scope clip; *T*, body temperature in degrees Celsius; *WBC*, white blood cell count expressed in no. of cells $\times 10^3/mm^3$

[a]Results mixed with gastroesophageal perforations

[b]Includes a few perforations treated conservatively

patients initially managed with clips who subsequently underwent surgery developed a postoperative complication. In the animal model, endoscopic closure was technically successful in 92% of cases and only one animal (8%) in the clip closure group showed signs of peritoneal inflammation at necropsy [21]. Besides avoiding the trauma and the morbidity of surgery, one report suggests that an advantage of endoscopic clip closure may be the shorter length of hospitalization in patients successfully treated by clips (mean 3.5 days, range 2–6 days) compared to patients who underwent immediate surgery (mean 12.2 days, range 6–12 days) [18].

Discussion

We have previously reported of a 35×10-mm. perforation of the left colon after endoscopic mucosal resection successfully closed with the TriClip endoscopic clipping device [15]. We now report two new cases of large perforations occurring after diagnostic colonoscopy closed using TriClip. Endoscopic closure in all three patients was carried out immediately after diagnosing the perforation. Closure took 35 minutes or less in all three patients (range 8–35 minutes). While in patient 2 the cause of the perforation was obvious, patient 1 had no predisposing factors to colonic perforation such as previous abdominal surgery or diverticular disease, and therefore the cause of perforation was uncertain and was possibly the result of a sharp angulation in the redundant sigmoid and/or of unsuspected adhesions. Performing colonoscopy under deep sedation could have been a contributing factor [22], but this is unclear. The omental patch repair, a technique first described during endoscopic repair of iatrogenic perforation of the stomach wall [23–25], was not possible in either patient because of the absence of visible omentum through the perforation site. Neither of our patients had intraperitoneal free air on radiography. It is possible that all three perforations in our series were “covered”, i.e. occurring on the mesenteric side of the colon or retroperitoneally. The absence of free air may also reflect the prompt diagnosis of perforation and the limited use of insufflation. However, from our review of the literature it seems that the presence of free air does not mandate a surgical procedure.

Large parietal defects after diagnostic procedures were easily repaired with the use of TriClip. This new device has so far only been used for the treatment of colonic haemorrhage [26]. This device differs from the two-pronged clip appliers in the following features: (1) the clip diameter is 12 mm vs 11 mm of other clips; (2) because of the three equidistant prongs it is not necessary to rotate the device to better bridge the defect (all the two-pronged devices used for closure of perforations must be rotatable and appropriately oriented); (3) the three prongs grasp a larger amount of tissue on a wider surface compared to two-pronged devices and may therefore have more chance of closing a wide gap with the first clip deployment, thereby facilitating the application of further clips; (4) the three prongs provide pressure from three directions, potentially increasing the strength of the repair; and (5) the distal part of the prongs is at a more acute angle compared to other endoclips resulting in a hook shape which may be an advantage in this clinical situation. The recently developed OTSC system has the advantage of the largest size of clip, not limited by the diameter of the working channel with a unique trap-like design, and allows the simultaneous use of a grasper [20]. Because of the superelasticity of nitinol clips the force is permanently applied to the tissue, but disadvantages are the lack of visualization when the clip is applied and the need to extract the endoscope to mount the device at the tip of it.

Traditionally colonoscopic perforations have been managed by open or laparoscopic surgical intervention with closure of the perforation, intestinal resection and primary anastomosis or with resection and a diverting stoma, depending on the intraoperative findings [27, 28]. For small perforations occurring during therapeutic colonoscopy, and in the absence of signs and symptoms of peritoneal irritation, nonoperative management has been selectively used with a success rate from 60% to 100% [5, 29–31]. From the growing experience and good results of endoclip closure of perforations highlighted in our review, we can predict that a higher percentage of colonoscopic perforations will be managed without surgical intervention. For small perforations occurring during therapeutic endoscopy, it is likely that clip closure effectively contributes to successful nonoperative management. In addition, our experience shows that endoscopic clipping may also be curative in large perforations or in perforations occurring during diagnostic colonoscopy. However, because of the small number of reported cases these data must be interpreted with caution.

From our review it seems that endoscopic clipping may be successful even in the presence of free air, peritoneal signs, moderately elevated WBC count and elevated CRP, providing that signs, symptoms, and laboratory and radiographic findings rapidly improve. Just as with conservative management of perforations, patients should be kept fasting or on clear liquids and on intravenous broad-spectrum antibiotics until bowel movement, complete disappearance of pain and peritoneal signs as well as normalization of the WBC count.

Although the use of the rotating clip applier has been recommended [12], we have found the TriClip device to be very useful for this application. In all three of our patients the edges of the perforation were approximated after application of the first clip making completion of the closure easier. A dedicated rotating multiclip applier to close colonoscopic perforations has been used by Raju et al. on animals but is not yet available commercially [21].

In conclusion, closure of colonoscopic perforations with endoclips is a viable therapeutic option. Immediate closure of colonoscopic perforations has been achieved with endoclips irrespective of size and aetiology. There are not enough data to draw conclusions as to the risks of this type of management, but so far no complications have been reported. We therefore believe that endoscopic repair should be attempted in the majority of cases of colonoscopic perforation. If further prospective studies confirm these early findings every endoscopist will have to be trained in the use of clips for closure of the bowel wall and new dedicated clipping devices will need to be developed.

Acknowledgements The authors thank their nurse Mrs. Astrid Gurrieri for her kind assistance and Mr. Giuseppe Azzarita for his clinical support.

Conflict of interest statement The authors declare that they have no conflict of interest related to the publication of this article.

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Invited comment

In the current issue of this journal, Trecca and colleagues describe three cases of large colonic perforation and review the literature [1]. All of their cases were successfully treated conservatively after endoscopic repair with the new TriClip device. This report is remarkable as it includes two large perforations associated with insertion, and all perforations were able to be closed with the TriClip rather than with conventional endoclips.

Perforation during colonoscopy is a rare but severe complication, which has been treated surgically. Perforations associated with endoscopic resection, however, are often as small as 10 mm or even less, and these can be repaired by endoscopic closure with endoclips [2, 3]. Compared with perforations after endoscopy, the defects induced by insertion are usually larger. Whether defects larger than 1 cm are also endoscopically manageable is still an open question, as the larger the defect, the more difficult clipping becomes due to the limited open width of commercially available endoclips. Therefore, perforations larger than 10 mm are generally treated surgically, as such patients benefit more from surgical intervention [4]. To overcome the problems of closing large defects, however, the endoloop/metal clip method, the eight-ring/resolution clip method and the over-the-scope clip system have been designed [5–7].

Endoclipping should be performed with as little air insufflation as possible, as a distended lumen often makes it difficult to close the perforation site. Moreover, air leakage will create extensive pneumoperitoneum, which can lead to circulatory and/or respiratory collapse. In such cases, early identification and prompt treatment with abdominal puncture are important to avoid serious sequelae leading to multiple organ failure [8]. Instead of air insufflation during colonoscopy, carbon dioxide insufflation is also safe and effective [9]. The authors emphasize that prompt complete endoscopic repair can result in successful conservative treatment. However, we emphasize that good bowel preparation is a prerequisite. Poor bowel preparation is associated with longer and more difficult insertion, and thus leads to a low diagnostic yield. Furthermore, poor bowel preparation may result in spillage of contaminants into the peritoneal cavities causing serious peritonitis when perforation occurs.

The choice of conservative or surgical treatment for iatrogenic colonic perforation remains controversial. Needless to say, nonsurgical treatment after complete endoscopic closure should be based on a stable clinical course including stable vital signs and localized nonprogressive abdominal pain with good surgical support [10].

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