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Endoscopic applications of magnets for the treatment of gastrointestinal diseases

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Abstract

Endoscopic treatment of gastrointestinal diseases has developed rapidly in recent years, due to its minimally invasive nature. One of the main contributing factors for this progress is the improvement of endoscopic instruments, which are essential for facilitating safe and effective endoscopic interventions. However, the slow learning curve required in the implementation of many advanced endoscopic procedures using standard devices is associated with a high risk of complications. Other routine procedures may also be complicated by unexpected difficulties. Based on the ferromagnetic properties of many objects, both internal and external magnetic devices have been developed and applied for multiple endoscopic interventions. The applications of magnets, mainly including compression, anchoring and traction, facilitate many difficult procedures and make it feasible to operate procedures that were previously impossible. Other novel endoscopic applications, such as magnetic nanoparticles, are also under development. In this article, we reviewed published studies of endoscopic applications of magnets for the treatment of gastrointestinal diseases such as precancerous lesions and cancer, obstruction, stricture, congenital and acquired malformations, motility disorders, and ingestion of foreign bodies. Since several endoscopic applications of magnets may also be relevant to surgery, we included them in this review.

Key words: Anastomosis; Endoscopes; Endoscopic submucosal dissection; Magnets; Natural orifice endoscopic surgery; Traction

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Core tip: Endoscopic applications of internal and external magnets can facilitate or even help develop multiple endoscopic interventions for treating gastrointestinal diseases, by providing compression, anchoring, and traction. This article aims to review therapeutic

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INTRODUCTION

Due to the ferromagnetic properties, magnets have always been a focus of research in clinical practice. The initial application of magnets in the digestive tract can be traced back to the mid20th century^[1,2], when magnets played a promising role in removing ingested foreign bodies. However, due to the widespread recognition of the perils of magnet ingestion^[3,4], the therapeutic application of magnets has remained rare for a long time. In view of the safety associated with the extensive use of magnetic resonance imaging, many clinicians have reconsidered the roles that magnets could play in clinical medicine. Over the past 20 years, many innovative therapeutic uses of magnets have been reported, with early success, and the main applications of magnets include: compression anastomosis, compression without anastomosis, anchoring and traction. These applications, including endoscopic and surgical interventions for gastrointestinal diseases, have thus generated new attention. This article reviews the endoscopic applications of magnets in the treatment of gastrointestinal diseases. Surgical applications of magnets without endoscopes are excluded because they have been reviewed recently^[5]. In addition, diagnostic applications including magnetic capsule manipulation^[6] and magnetic navigation colonoscopy^[7] are also beyond the scope of this review.

MAGNETIC COMPRESSION ANASTOMOSIS

Esophageal

Applications of magnetic compression anastomosis in the esophagus include atresia^[8-10] and diverticula^[11-13].

In 1975, Hendren *et al*^[14] initially proposed the use of magnetic force for the treatment of esophageal atresia, and they used electromagnetic bougienage to lengthen esophageal segments to facilitate further surgical repair. The first application of magnets alone for esophageal atresia was reported by Zaritzky *et al*^[8] in 2009, in which magnetic anastomosis was achieved by a mean of 4.8 days (range, 2-7 days) in all five children after placement of two catheter-mounted magnets to the proximal end (by mouth) and the distal end (by gastrostomy) of the atresia, respectively (Figure 1). The procedure was performed under fluoroscopic guidance with or without endoscopic assistance. Using a similar technique, both Dorman *et al*^[9] and Ellebaek *et al*^[10] achieved good results later in one case, respectively. Magnetic compression anastomosis for esophageal atresia helps to avoid adverse events of thoracotomy, including tracheal injury, devascularization and denervation of the esophagus^[9]. Notably, esophageal stenosis could occur after magnetic compression anastomosis, and some of them may require repeated endoscopic dilation or even surgical intervention. The main cause of esophageal stenosis is the use of magnets with small diameters. Magnets with large diameters or self-assembling magnets may be applied to reduce stenosis. Preventative endoscopic dilation may also help to reduce the need for stenting or surgery^[10].

To date, there are only three reports including six cases of esophageal diverticulum (2 in the upper, 2 in the middle, and 2 in the distal esophagus) treated by magnetic compression anastomosis^[11-13]. During the procedure, the first magnet can be introduced into the stomach or distal esophagus with the help of a catheter or a clip, and the second magnet can be placed at the base of the diverticulum. The binding of the two magnets can be achieved by pulling back the first magnet under direct endoscopic visualization with or without fluoroscopic guidance (Figure 2). After 10-28 days, if a connecting hole is developed, diverticulotomy of the remaining part of the septum can be safely performed. Procedures can be repeated easily for better results if the diverticuloplasty is incomplete or if the diverticulum recurs. We first named this method "magnet-assisted diverticuloplasty (MAD)"^[13]. MAD resolves the

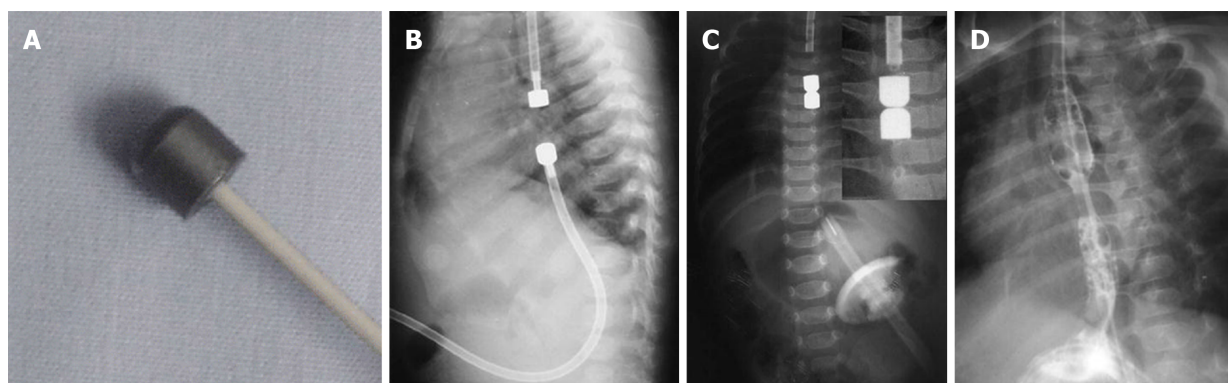


Figure 1 Magnetic compression anastomosis for an esophageal atresia^[8]. A: The device of the catheter-mounted magnet; B: Radiograph of the initial position of the devices (the proximal magnet is inserted from the mouth, and the distal magnet is inserted during gastrotomy); C: Radiograph of the devices after the union of the magnets; D: Esophagogram of the distal passage with stenosis and without leak. Used with permission from Springer Nature.

contradiction between complete transection of the septum and esophageal perforation when performing other endoscopic “clip and cut” diverticulotomy^[15,16], as well as the need for endoscopic experts to perform the peroral endoscopic myotomy (POEM)^[17-19]. Our limited experience suggests that this technique is easy, safe and effective, and that it would be especially suitable for high-risk patients with symptomatic esophageal diverticulum.

Gastrointestinal

Magnetic compression anastomosis in the gastrointestinal tract has been assessed by multiple animal studies. According to its anatomical position, anastomosis can be divided into gastrojejunal anastomosis^[20,21], gastrocolonic anastomosis^[22], duodenocolonic anastomosis^[22], jejunojejunal anastomosis^[23], jejunoileal anastomosis^[24], jejunocolonic anastomosis^[22,25], and colorectal anastomosis^[26]. Complete re-epithelization of the anastomosis rim can usually be achieved^[22-25,27], but leaks may also occur before anastomosis maturation^[23]. Endoscopic applications of these different types of anastomosis are for different clinical purposes, including treatment of gastric outlet obstruction^[28,29], obesity and type 2 diabetes^[30]. For gastric outlet obstruction, the distal magnet can be mounted on a catheter and advanced over a guidewire to the distal duodenum after balloon dilation of the stricture, and the proximal magnet can be inserted in the stomach along the introduction of the endoscope; the whole procedure should be performed under fluoroscopic guidance until the two magnets are coupled together. For obesity and type 2 diabetes, partial jejunal diversion can be selected so that the proximal magnet can be delivered to the proximal jejunum *via* enteroscopy, while the distal magnet can be delivered to the terminal ileum *via* colonoscopy simultaneously. Laparoscopy should also be performed to monitor or assist magnetic coupling. By using small disk or ring-shaped magnets, insertion of a stent may be needed to ensure the long-term patency of the anastomosis^[20,28,29], but this may cause severe stent-related complications, such as bowel perforation^[29]. Ryou *et al*^[21,24,25,30] developed the through-the-scope smart self-assembling magnets in 2011, and these magnets provide a wide opening for the anastomosis (with a mean maximum diameter of 30-35 mm)^[24,25]. **Figure 3** shows two typical magnetic compression anastomosis systems for endoscopic gastrointestinal anastomosis.

Hepatobiliary

Magnetic compression anastomosis is usually used for severe biliary stenosis^[31,32] and complete biliary obstruction^[33-36] that are difficult to manage using conventional nonsurgical interventions. Based on the specific situation, either biliobiliary anastomosis^[31,34,35] or bilioenteral anastomosis^[33,37,38] can be conducted. The proximal magnet (mother magnet) is usually inserted through the percutaneous transhepatic biliary drainage (PTBD) tract, while the distal magnet (daughter magnet) can be delivered in three ways: endoscopically (**Figure 4**), through a second PTBD tract, or through a surgically formed fistula^[39]. When inserting a magnet into the common bile duct (CBD), full sphincterotomy and/or sphincter balloon dilation is frequently required, and a metal stent may be inserted into the CBD to further facilitate magnet delivery^[34,39,40]. After recanalization and magnets removal, biliary stents can also be placed to prevent restenosis^[34,40]. In addition, an animal study showed the feasibility of a hinged metalloplastic anastomotic device for creation of a choledochoduod-

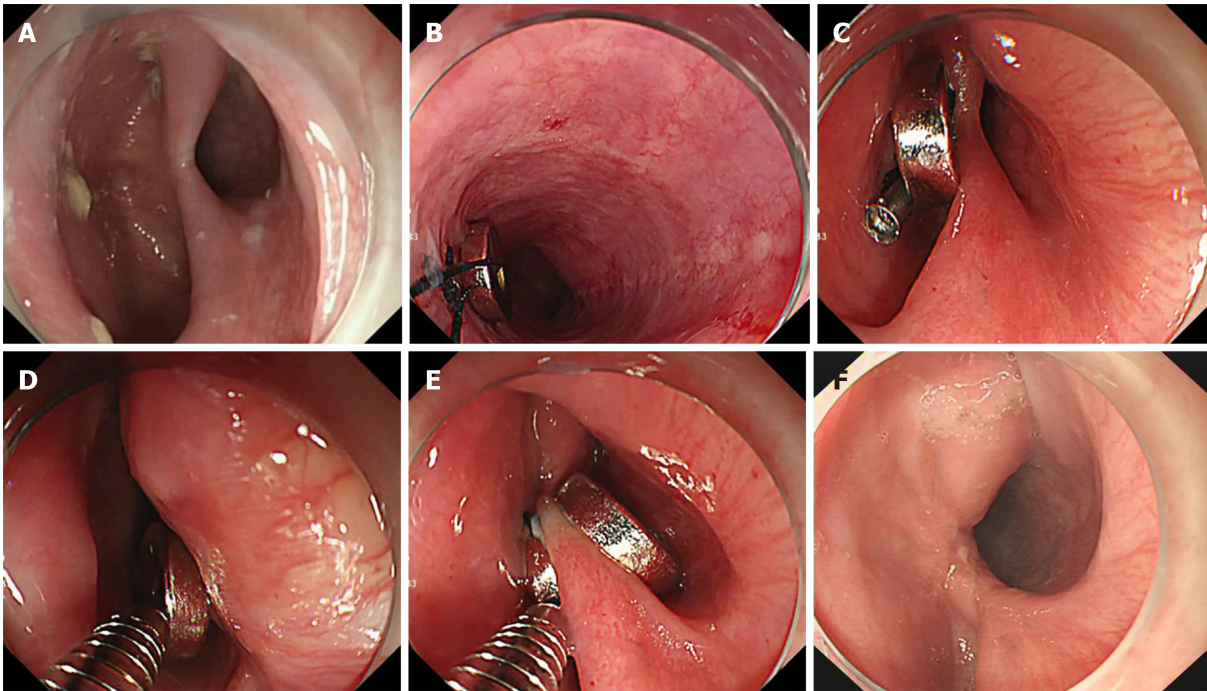


Figure 2 Magnetic compression anastomosis for a Zenker diverticulum^[13]. A: Retained diverticulum after endoscopic "clip and cut" diverticulotomy; B: The first magnet with string attached is fixed by clipping into the distal esophagus; C: The second magnet with string attached is fixed to the base of the diverticulum using the same technique; D: The first magnet is pulled back by the releasing device of the endoclip under direct observation; E: The two magnets are coupled together, sandwiching the septum; F: Improvement of the diverticulum. Used with permission from Georg Thieme Verlag KG.

denostomy above the papilla for large-diameter biliary drainage^[38], in which all procedures were performed endoscopically, and sphincterotomy was not needed for system deployment.

MAGNETIC COMPRESSION WITHOUT ANASTOMOSIS

Magnetic compression without anastomosis is mainly applied for improving gastroesophageal reflux^[41-47] or fecal incontinence^[48-50], but laparoscopic deployment of the Linx device [a system developed to augment the low esophageal sphincter (LES)] and surgical deployment of the Fenix device (a system developed to augment the anal sphincter) remain as the mainstream treatment (Figure 5). There are only two reports of endoscopic applications of magnets for preventing gastroesophageal reflux *in vitro* and/or *in vivo* in a porcine model^[46,47]. In 2009, Bortolotti *et al*^[46] deployed an endoesophageal magnetic device into the submucosal layer close to the LES to prevent gastroesophageal reflux. Although a high-pressure zone was achieved after insertion of the magnetic valve into the submucosal layer of the *ex vivo* porcine model (14.2 ± 1.27 mmHg *vs* 1.5 ± 0.26 mmHg, $P < 0.001$), mucosal breach could develop easily due to magnetic compression. After almost ten years, Dobashi *et al*^[47] published their modified endoscopic method, that is, endoscopic magnet deployment in the subadventitial space to augment the LES. They performed the procedures in both *in vitro* and *in vivo* porcine models, in which the two subadventitial tunnels (one in the right side and one in the left side) were created with a biliary stone extraction balloon using the POEM technique, allowing subsequent endoscopic placement and fixation of the magnets^[47]. Although this novel method by Dobashi *et al*^[47] appears to be more reasonable than that by Bortolotti *et al*^[46], erosion or fistula could also be developed. Fistula caused by magnetic compression after magnet ingestion has already been reported by many studies^[3,51,52]. The anatomical structure of the human esophagus is different from that of porcine esophagus^[53], with tight junctions to surrounding organs; thus, the feasibility of deploying magnets into the subadventitial space in the human body remains uncertain.

MAGNETIC ANCHORING AND TRACTION

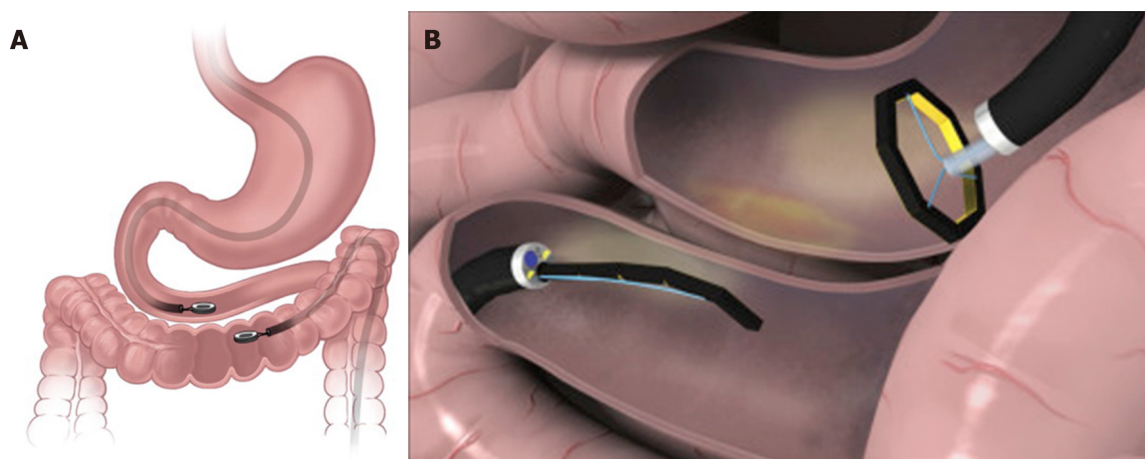


Figure 3 Application diagrams of two typical magnetic compression anastomosis systems for endoscopic gastrointestinal anastomosis. A: Over-the-scope ring-shaped magnets^[22]; B: Through-the-scope self-assembling magnets^[30]. Used with permission from Elsevier.

Endoscopic submucosal dissection

Currently, endoscopic submucosal dissection (ESD) is widely applied for en bloc resection of superficial gastrointestinal lesions^[54], but the procedure can be technically difficult if the cutting line and submucosal layer cannot be adequately exposed. Traction, like “the second hand” in surgery or laparoscopic operation, can facilitate safe and fast ESD by clearly exposing the field of vision^[55]. As one of those traction methods, magnetic-anchor-guided ESD (MAG-ESD) is thought to be more attractive due to dynamic tissue retraction independent of the endoscope (Figure 6)^[56]. In general, a small internal permanent magnet is applied to the edge of the lesion using an endoscopic clip, and a large external permanent magnet^[57-60] or electromagnetic control system^[61,62] is applied for retraction during MAG-ESD. The key point is that the external magnet can be moved to change the direction of traction as needed during the entire procedure. This technique has been reported for resecting both gastric^[57,58,60-62] and colonic^[59] lesions, helping to minimize technical difficulty and reduce the procedure time. Patient position changes can be replaced by using this technique, which is particularly valuable for obese patients under anesthesia. Despite its effectiveness, there are also some limitations for MAG-ESD^[56], including the coupling strength of magnets, the distance between the internal and external magnets (abdominal wall thickness and air insufflation during endoscopy are two key influencing factors), and the high costs of large magnets. In addition, the strong external magnetic field can lead to detachment of the internal magnet from the lesion^[60].

Based on the similar concept of MAG-ESD, Dobashi *et al*^[63] developed an internal magnet traction device (MTD) with weaker magnetic force. Using the second MTD (deployed to the opposite wall) for traction of the first MTD (deployed to the edge of the lesion), endoscopists do not need to worry about tissue tearing. The strength and direction of traction can also be easily adjusted during the ESD procedure by increasing or decreasing distention of the lumen and by removing and repositioning the second MTD. Neither the thickness of the abdominal wall nor the location of the lesion influence the procedure. The study by Dobashi *et al*^[63] used an *in vitro* porcine model and involved only gastric ESD; thus, its application *in vivo* and in other places with limited working space, such as the duodenum and colorectum, requires further investigation. In addition, as we reported previously^[64-66], magnetic bead-assisted ESD (MBA-ESD) can also be used to facilitate difficult ESDs in the duodenum and colorectum. However, as we mentioned previously^[64-66], the traction is mainly based on gravity. The magnetic force can play a role only when an additional magnetic bead is added to the same site to increase the weight and strength of the traction (Figure 7).

Natural orifice transluminal endoscopic surgery

As the next surgical frontier with objective incision-free abdominal surgery, natural orifice transluminal endoscopic surgery (NOTES) has attracted increasing attention but has not been widely accepted because of technical difficulties^[67]. The main limitation of NOTES is the loss of “the second hand” for tissue manipulation and visualization, where magnets may play a major role. According to reports involving *in vitro* and *in vivo* animal studies, NOTES that is facilitated with a magnetic anchor is feasible in different abdominal procedures such as cholecystectomy (Figure 8)^[68-70] and

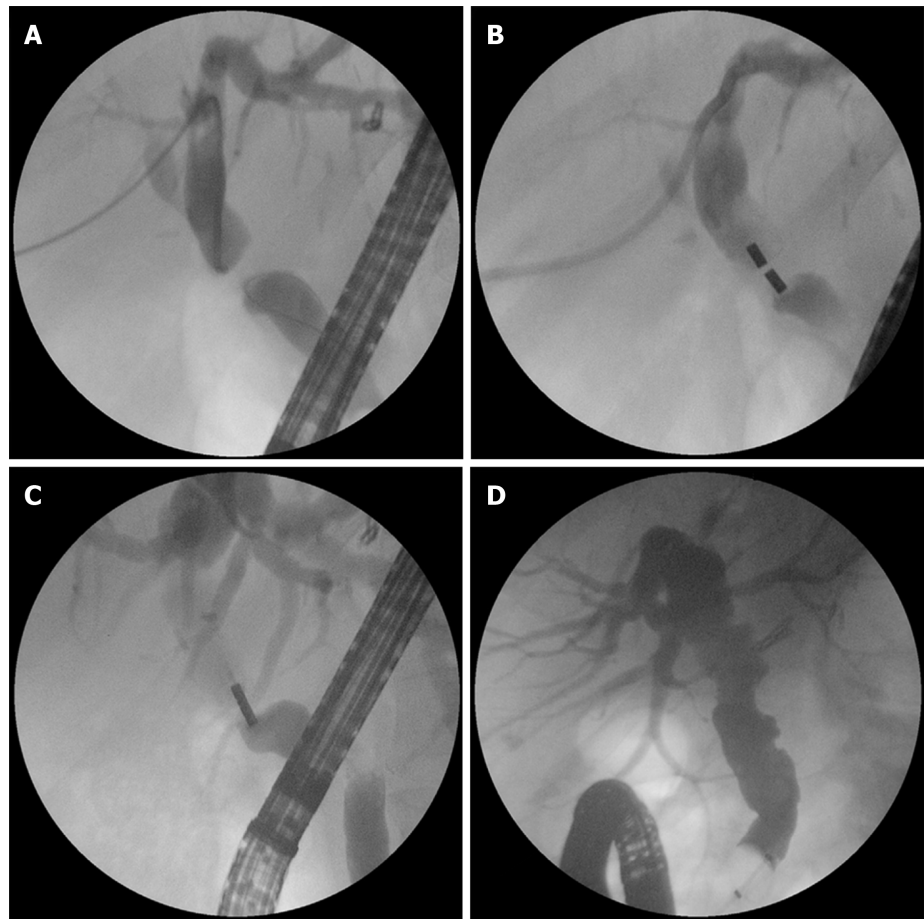


Figure 4 Magnetic compression anastomosis for biliary obstruction^[54]. A: Simultaneous percutaneous and balloon-occluded cholangiography shows the details of biliary obstruction; B: Two magnets were placed in the two sides of the obstruction (through the percutaneous transhepatic biliary drainage tract and endoscopic retrograde cholangiopancreatography, respectively); C: The coupling of the two magnets together and recanalization with stricture were achieved; D: Complete resolution of the stricture was achieved after periodical balloon dilation and insertion of multiple plastic biliary stents. Used with permission from Elsevier.

sigmoidectomy^[71,72], Transgastric^[71,72], Transcolonic^[68], and transvaginal^[69,70] approaches have been used for the access to the operation site. The internal magnet can be deployed to target organs or adjacent areas. However, there have been no reports of magnetic-anchor-assisted NOTES in humans thus far.

Other applications

Other endoscopic applications include magnet-assisted foreign body and pancreaticobiliary stent removal, preoperative tumor marking, and magnetic-anchor-assisted direct percutaneous endoscopic jejunostomy.

Magnet-assisted foreign body removal may be regarded as the first application of magnet in the treatment of the gastrointestinal diseases. In the past^[1,2], it was usually performed under fluoroscopic observation. A magnet inserted into a catheter was commonly used to remove ferromagnetic objects during the procedure. There is also a report on the blind removal of objects using such a device^[73]. However, these methods were under indirect visualization and thus were always cumbersome and hazardous. With the widespread application of endoscopes, many other retrieval devices, such as graspers, forceps, snares, baskets, and nets, have been developed for endoscopic foreign body removal^[74]. Despite their effectiveness, removal of foreign bodies in some cases remains difficult and time-consuming, especially when visualization of the objects is obscured^[75,76], when the objects are too small or numerous^[77], or when the objects are inaccessible^[78]. Magnet-assisted foreign body removal performed under endoscopic observation is reported to be beneficial for extracting various objects, including coins^[79,80], button batteries^[81], impacted magnets^[51], paperclips^[75], needles^[77], nails^[76,78,82], pins^[82] and safety pins^[82]. Forceps^[51], snares^[75], Roth nets^[76,77], and loop baskets^[79] are commonly used for magnet insertion. Limited data suggest that the use of magnets for foreign body removal helps to shorten the operation time, avoid additional injuries, and ensure a higher success rate.

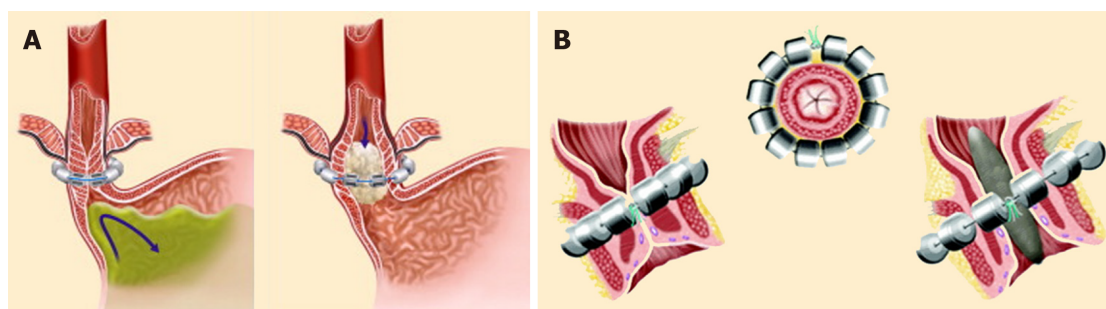


Figure 5 Application schemes of magnetic augmentation of lower esophageal and anal sphincter. A: The Linx device for antireflux^[41]; B: The Fenix device for fecal incontinence^[48]. Used with permissions from Elsevier and Wolters Kluwer Health, Inc.

An internal magnet with string attached can also be clipped to a tumor or its periphery using an endoscopic clip at preoperative endoscopy, allowing fast and precise orientation of the tumor using ferromagnetic instruments during laparoscopic surgery. Ohdaira *et al*^[83] selected a 4-mm cylindrical magnet and applied the magnet-string-clip system to gastric mucosa (20 mm away from the tumor periphery) in 15 patients with early gastric cancer; the tumor site was detected during laparoscopic gastrectomy in all cases. Warnick *et al*^[84] reported the use of a ring-shaped magnet (mounted on the tip of the scope by a cap), but tumor localization failed in 1 of 28 patients with small colorectal tumors (23 in the colon and 5 in the rectum) owing to system migration.

An external magnet can be applied to remove endoscopically placed ferromagnetic pancreaticobiliary stents^[85,86], which obviates the requirement for a second endoscopy for stent removal (Figure 9). This application involved only animal studies, but there are already reports of the use of a biodegradable stent^[87] or spontaneous dislodgement spiral stent^[88] in humans, in which additional endoscopy for stent removal is also not needed.

Applications of an internal magnet and an external magnet (*i.e.*, magnetic anchors) also help to fix the jejunal wall to the abdominal wall, facilitating direct percutaneous endoscopic jejunostomy (D-PEJ)^[89]. The D-PEJ is similar to conventional percutaneous endoscopic gastrostomy, except for the use of double-balloon enteroscopy (for access to the jejunum, insertion of an internal magnet, and placement of a tube) and magnetic anchors.

MAGNETIC NANOPARTICLES

Magnetic nanoparticles are a class of nanoparticles that can be manipulated by an external magnetic field and functionalized with bioactive agents; thus, they can be used for hyperthermia cancer therapy, guided drug delivery, and other applications^[90,91]. Currently, endoscopic application of nanotechnology and magnetic nanoparticles is in its infancy. Only a few *in vitro* and *in vivo* animal studies have primarily investigated their roles in the treatment of esophageal^[92], liver^[93], and pancreatic^[93] tumors by local or systemic injection.

CONCLUSION

Endoscopic applications of magnetic devices represent a further advancement in the field of minimally invasive intervention. Their use expands the indications of therapeutic endoscopy and makes it easier and safer to perform difficult procedures. Notably, many novel techniques have only been performed in *in vitro* and *in vivo* animal studies, and thus, applications in humans require further detailed evaluations to ensure their safety. For those techniques that have been initially applied in clinical practice, effective measures should also be taken to detect, treat, or even prevent the well-recognized complications. In addition, specific commercially magnetic devices need to be developed in this promising filed.

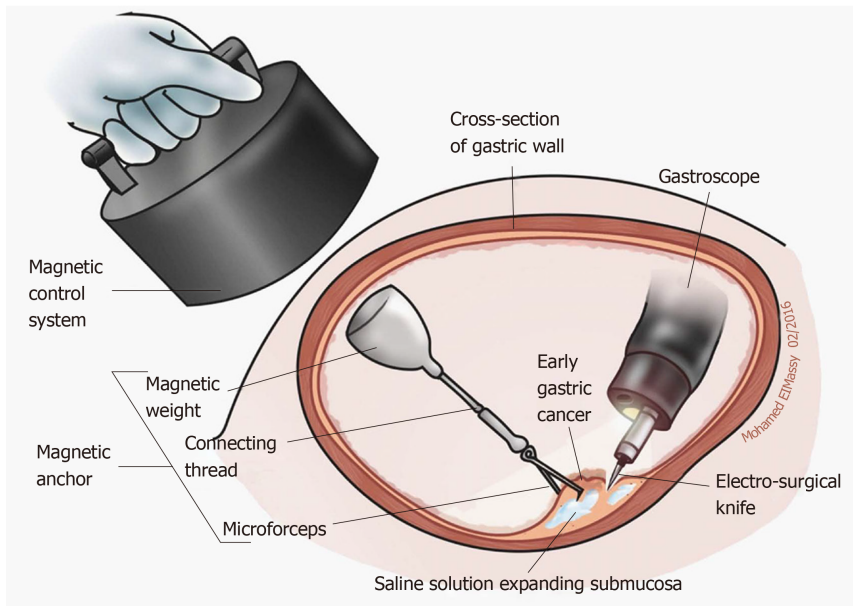


Figure 6 Application diagram of magnetic anchor guided endoscopic submucosal dissection^[56]. A small internal permanent magnet is attached to the edge of a partially dissected lesion, while a large external permanent magnet is applied for retraction (an electromagnetic control system can also be selected). Used with permission from Baishideng Publishing Group Inc.

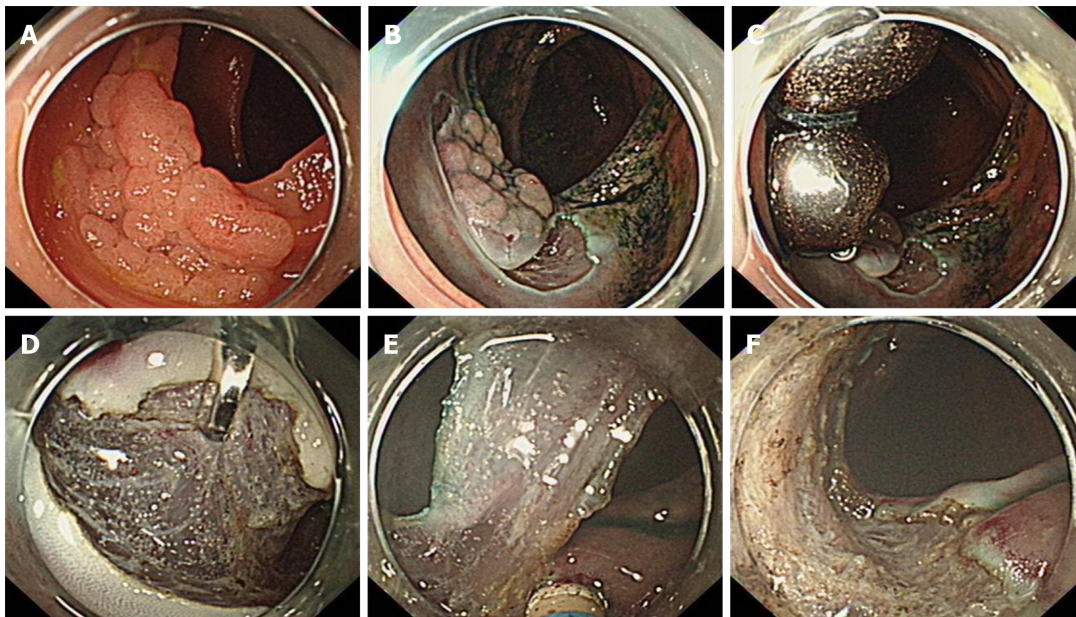


Figure 7 Magnetic bead-assisted endoscopic submucosal dissection for a lesion in the ascending colon. A: The lesion in the ascending colon; B: The submucosal layer was unclear after partial dissection; C: Application of two magnetic bead systems into the edge of the partially dissected lesion; D, E: The submucosal layer was adequately exposed for precise dissection; F: The mucosal defect after complete resection.

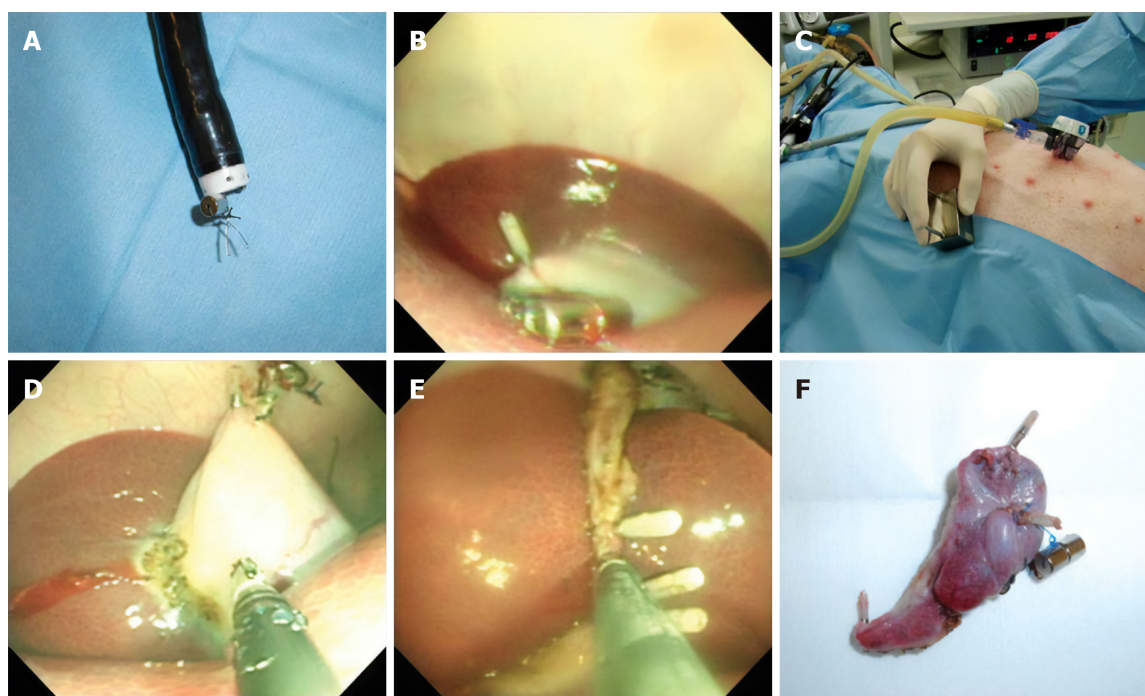


Figure 8 Transvaginal endoscopic cholecystectomy using a simple magnetic traction system in a porcine model^[70]. A: a small internal magnet was fixed to endoscopically deployed clips; B: the small magnet was attached to the apex of the gallbladder fundus; C: An external handled magnet was used for traction; D: the gallbladder was dissected from liver using hot claw forceps with the help of the magnetic traction system; E: The cystic duct and artery were ligated and dissected with the help of endoscopic clips; F: The dissected gallbladder. Used with permission from Taylor & Francis.

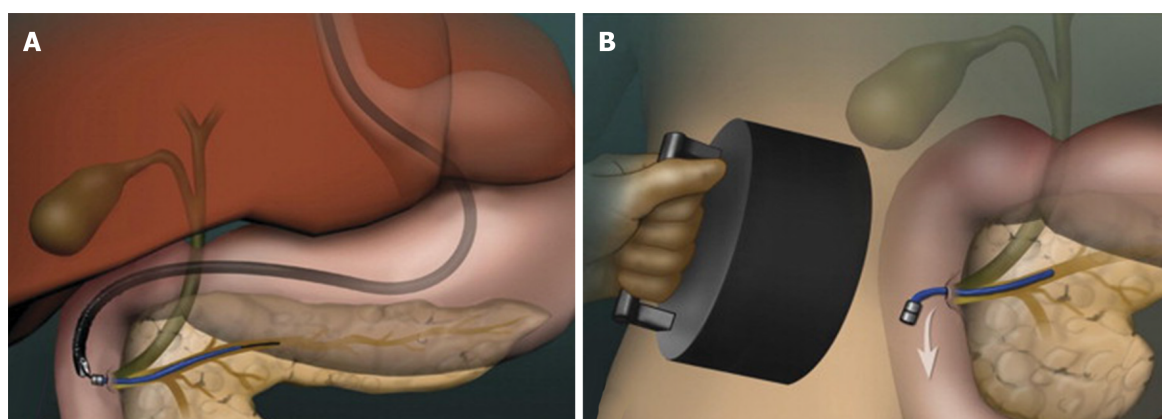


Figure 9 Magnetic pancreaticobiliary stents and retrieval system^[86]. A: endoscopic placement of a magnetic stent; B: stent retrieval using a large external magnet. Used with permission from Elsevier.

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