

Endoscopic surgery - exploring the modalities

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Abstract

The adoption of endoscopic surgery continues to expand in clinical situations with the recent natural orifice transluminal endoscopic surgery technique enabling abdominal organ resection to be performed without necessitating any skin incision. In recent years,

the development of numerous devices and platforms have allowed for such procedures to be carried out in a safer and more efficient manner, and in some ways to better simulate triangulation and surgical tasks (*e.g.*, suturing and dissection). Furthermore, new novel techniques such as submucosal tunneling, endoscopic full-thickness resection and hybrid endo-laparoscopic approaches have further widened its use in more advanced diseases. Nevertheless, many of these new innovations are still at their pre-clinical stage. This review focuses on the various innovations in endoscopic surgery, with emphasis on devices and techniques that are currently in human use.

Key words: Transanal total mesorectal excision; Natural orifice transluminal endoscopic surgery; Endoscopic surgery; Submucosal tunneling technique; Endoscopic submucosal dissection; Endoscopic full-thickness resection; Endo-laparoscopic

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Core tip: This article is a comprehensive review of endoscopic surgery. It analyses the different types of endosurgery from endoscopic submucosal dissection, endoscopic full-thickness resection and natural orifice transluminal endoscopic surgery. This article highlights the relevant topics and recent advances in this area. In addition all the latest procedural devices such as the master and slave transluminal endoscopic robot endoscopic robot, multitasking endoscopes and other examples are described. Finally a clear and comprehensive review of the latest human clinical trials and their outcomes are outlined. Hence overall, readers will have a full understanding of endosurgery, the currently available as well as upcoming technology and their safety profiles.

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INTRODUCTION

Endoscopic resection has emerged as an alternative to many cases that were traditionally managed by surgery alone. Natural orifice transluminal endoscopic surgery (NOTES) has now offer truly scarless minimally invasive procedures for resection of abdominal organs. Since its introduction in 2000, more than 1000 reports have been published describing various applications NOTES in both animal and human^[1]. The concept is continuously expanding in parallel to the advancement in technology and innovation of mechanics.

Endoscopic surgery is becoming increasingly popular among surgeons especially in Asian countries because many surgeons here were capable of performing flexible endoscopy. The Asia Pacific NOTES working group was formed in 2006 by a group of endoscopists and laparoscopic surgeons from Hong Kong, China, South Korea, Japan, Singapore, India and Malaysia. Since its establishment, many collaborative efforts between these countries have produced innovative developmental breakthroughs that address the barriers faced and clinical application in NOTES^[2]. One example is the robotic endoscopic prototype named master and slave transluminal endoscopic robot (MASTER) that was developed in Singapore to perform complicated NOTES procedure.

Many novel endoscopic interventions have been described over the past decade, but none has been formally approved as standard of care. There are many preliminary data that suggest its feasibility and safety, but there are still at preclinical stage. This article aims to provide a comprehensive review on endoscopic surgery, focuses on various innovations in endoscopic surgery, with emphasis on devices and techniques that are currently in human use.

Endoscopic submucosal dissection

Endoscopic resection was first reported by Hirao *et al.*^[3], a surgeon, for the treatment of early gastric cancer using local injection of hypertonic saline-epinephrine. The ideal result of endoscopic submucosal dissection (ESD) is that the specimen is resected *en bloc* and has sufficient depth to ensure accurate histopathological assessment and achieve R0 resection, while avoiding hazardous complications, mainly perforation and bleeding. Colonic ESD is technically more difficult because of the colon has thin wall, narrow lumen, and acute bends. At times, this is further complicated with the lesions being situated at proximal colon or behind a mucosal fold^[4,5]. Various advances in the knives and other accessories have been developed to overcome these challenges (Table 1).

The devices used are generally divided into two broad categories: The needle-knife type and the grasp-

ing (scissors) type^[6,7]. The most commonly used are the Dual knife and the insulated-tipped knife. The grasping scissors may be used when there is inadequate elevation of the submucosa plane to allow safe dissection. EndoLifter is a novel innovation in which an additional external grasping forceps is used to provide countertraction and make the submucosal plane wider. This is widely used in gastric ESD.

One of the disadvantages of ESD is that it can be time consuming. To reduce procedure time by eliminating the need for frequent switching of instrument, a new hybrid knife that combines both submucosal injection and dissection facilities into a single instrument has been developed (HybridKnife by ERBE, Tübingen, Germany). HybridKnife allow fluid injection into submucosal plane under safe and preselected pressure *via* the tip of the knife. The operators can perform marking, circumferential cutting and submucosal dissection with just one instrument. This device have shown to decrease procedure time, perforation rate and increase the rate of en bloc resection^[8]. Another new water-jet system that also combines both submucosal injection and dissection known as the ENKI-2 has also recently been developed in France (by NESTIS, Lyon). The water jet is produced by a high pressure chamber. It is delivered *via* a flexible catheter hence enable ESD in retroflexion position. This system has proven its safety and efficiency in an animal study when compared to Dual knife^[9]. A prospective human trial is currently underway.

Endoscopic full-thickness resection

Endoscopic full-thickness resection is a new technique that involves en bloc resection of the tumor which resulting in perforation, and closure of the defect. Initial experience with endoscopic full-thickness resection (EFTR) involves secondary defect closure using either over-the-scope-clip (OTSC), conventional clipping, T-tags or endoloops^[10-12]. This may potentially cause peritoneal contamination or seedling of early cancer. Sarker *et al.*^[13], Fähndrich and Sandmann^[14] have separately reported the successful use of grasp-and-snare techniques with preresection closure using OTSC system in human studies. The key aspect of this technique is to apply the clip at the base of the target lesion, and followed by resection above the ensnared lesion (Figure 1). There was no complication reported in their case series and all specimens had achieved complete resection margin. A significant disadvantage of using the OTSC system is that the size of the cap limits the size of the lesion that can be resected. Schmidt *et al.*^[15] described another preresection closure method using suturing devices (Plicator and GERDIX) in which it was found feasible for tumor of approximately 4 cm.

EFTR procedure still need to be investigated as current available evidence is mainly of animal models or from small series of human studies. EFTR could have a great impact in management of gastrointestinal stromal tumour and neuroendocrine tumor that would currently

Table 1 Characteristic of various endoscopic submucosal dissection knives

Type	Manufacturer	Description	Comments
Needle-knife type			
Insulated tip knife	Olympus	Ceramic ball attached to the tip of the knife	Insulator helps to prevent perforation. Small ceramic ball is suitable to operate on thinner submucosal plane; <i>e.g.</i> , in the esophagus and colon
Hook knife	Olympus	Tip of the knife is right-angled	Submucosal tissue is hooked and pulled before incision, lessen the risk of perforation
Flex knife	Olympus	Knife formed by soft, flexible loop cutting wire with adjustable length	Less risk of perforation. Distal end of the sheath is thick to serve as stopper to allow precise control of incision depth
Dual knife	Olympus	Small ball-like process on the tip, knife can be fixed in two positions - retracted or extended	Ball tip prevents slipping
Flush knife	Fujinon	Short needle knife that comes in 5 different projection lengths	Water jet is activated by a foot pedal, helps to washout blood at operative field and debris at the tip of knife. Provide better visualization and less time consuming without having to switch instruments
		Water emission through the lumen of the needle	
Splashneedle	Pentax	Similar to Flush knife	
Mucosectomy	Pentax	Circumferentially insulated knife with single cutting wire on the side of the tip	Insulated plastic sheath can lie on the muscular layer, allowing safe dissection by cutting wire on the submucosal plane
Grasping type scissor forceps			
SB knife	Sumitomo Bakelite	Rotatable monopolar scissors, surrounded with no-conductive coating. Clawed and curved tip	Large insulated claw prevents injury to the muscular layer
Clutch Cutter	Fujinon	Thin serrated cutting scissor, insulated on the outer forcep, rotatable	Serrated edges help to grasp tissue better

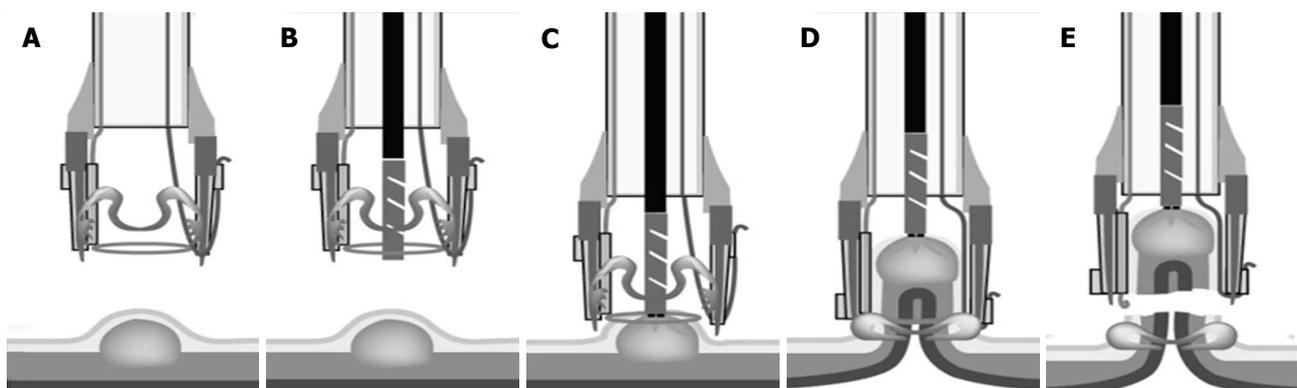


Figure 1 Endoscopic full-thickness resection of a submucosal lesion by application of an over-the-scope-clip followed by snare polypectomy. A: Endoscope is equipped with a cap mounted with clip; B: Identified lesion grasped; C: Pulled into the cap; D: Clip applied at the base; E: Full-thickness of the targeted lesion resected with closure of snare.

be treated by surgical resection.

NATURAL ORIFICE TRANSLUMINAL ENDOSCOPIC SURGERY

Endoscopic surgery has in recent years achieved yet another breakthrough, going beyond the boundaries of the gastrointestinal lumen, and entering into the peritoneum to perform intra-abdominal intervention. This concept, widely known as NOTES, was first introduced by Kalloo *et al*^[16]. In 2004 whereby he reported the success of transgastric peritoneoscopy using a flexible endoscope in an animal model 3 years later, Rao *et al*^[17] performed the first ever human NOTES procedure, which was a transgastric appendectomy. Since then NOTES has been increasingly adopted to

perform intra-abdominal exploration and extraction of various organs.

One of the most common NOTES access route is transvaginal access. Its accessibility and safety has long been proven through the use of culdoscopy in gynaecology and of the vaginal route to extract surgical specimen. However, in clinical practice, transvaginal NOTES is mostly facilitated with the help of abdominal wall entry, hence these surgeries are sometime known as hybrid procedures. One of the most studied procedures is transvaginal cholecystectomy (TVC). To date, TVC has been put up against laparoscopic cholecystectomy on a few prospective studies, and the results have favor TVC being associated with decreased risk of port site hernia, less postoperative pain and shorter recovery time (Table 2)^[18-20]. Many intra-abdominal operations have now been undertaken *via*

Table 2 Randomised controlled trials that reported on no significant difference in major outcomes between transvaginal cholecystectomy and conventional laparoscopic cholecystectomy

Ref.	Study type	Type of TVC	Outcome					
			Median/min Duration of surgery (min)		Median/min Length of stay (d)		Median/min Pain score	
			TVC	CLC	TVC	CLC	TVC	CLC
Kilian <i>et al.</i> ^[18]	RCT	Hybrid	68	55	3	4	1	3
Noguera <i>et al.</i> ^[19]	RCT	Hybrid	64.85	47.04	1	1	3.94	4.65
Borchert <i>et al.</i> ^[20]	RCT	Hybrid	65.1	64.2	2.81	2.81	1.81	2.03

These studies proved that TVC is not inferior to CLC. RCT: Randomised controlled trials; TVC: Transvaginal cholecystectomy; CLC: Conventional laparoscopic cholecystectomy.

this route. The drawbacks to transvaginal access are its associated risk of bladder and urethra injury, potential risk of infertility, and it is only applicable to female. It may be less acceptable in Asian countries due to cultural differences^[21].

NOTES *via* gastrointestinal lumen have been proven to be virtually possible for every type of surgery in animal models. Despite this breakthrough, there are reservations of utilizing this route among patients mainly due to fear of introducing infection from gut wall penetration. A transcolonic approach carries the highest risk, followed by transgastric, transesophageal, transvaginal and transvesical approaches. Over the past years, evidence from experimental and clinical studies have shown that infectious complication from NOTES is low (< 3%)^[22-24]. At present, the transvaginal and transgastric approaches are the most relevant for intraperitoneal NOTES procedures in human.

Pure NOTES is technically challenging. Conventional flexible endoscopes are inadequate to perform complex transluminal surgical procedures. They lack a multitasking platform that allows more variety of surgical manipulation. Like in any laparoscopic procedures, the key element to successful pure NOTES is triangulation. The evolution of NOTES devices has seen many efforts put into developing devices and platforms that simulate triangulation and surgical tasks (*e.g.*, suturing and dissection) in a laparoscopic procedure. Presently, all multitasking system developed for NOTES procedures can be broadly classified into two different types: (1) Mechanical platforms, which includes the dual channel endoscope (DCE) (Olympus, Japan), R-Scope (Olympus, Japan), the ANUBISCOPE (Karl-Storz, Germany), the EndoSAMURAI (Olympus, Japan), incisionless operating platform (IOP) (USGI Medical, United States), and DDES system (Boston Scientific, United States). DCE, R-Scope (a modified DCE), EndoSAMURAI and the ANUBISCOPE are integrated system comprising of the visual and the instrument manipulation function. The IOP and DDES systems serve as multitasking platforms that have multiple operating channels and they rely on conventional endoscopes for visualization. Generally, these systems have an average diameter of not more than 22 mm in order to be able to intubate pass the pharynx. Triangulation is achieved by having two or more working arms and therefore increases the degree

of freedom of the end effectors. To date, DCE, R-scope and the IOP have data published on human studies. The EndoSAMURAI, the more advanced platform, has two independently movable arms with an additional non-articulating arm. The moveable arms are mechanically cable actuated. They serve to provide traction and counter-traction on dissecting tissue, and perform more advanced maneuvers such as suturing. The non-articulating arm allows insertion of generic endoscopic instruments meant dissection, cautery and clipping. This system has console very similar to conventional laparoscopic instruments. During the early stage, Spaun *et al.*^[25] compared between DCE and EndoSAMURAI, and found that EndoSAMURAI has significant advantage over the conventional endoscopes in regards to accuracy and efficiency in performing complex surgical task. This device has been used successfully to perform transgastric small bowel full thickness resection in animal studies^[26,27]. Another promising multitasking endoscope prototype is the ANUBIScope, which has a special tulip shaped tip that allow two deflectable instrument channels to be positioned for instrument triangulation, and a third central channel for suction. These instruments are controlled through a trigger handle that is similar to that seen in laparoscopic instruments. In 2012, Perretta *et al.*^[28] successfully completed a cholecystectomy on a human in 60 min using the ANUBISCOPE. Of the available integrated endoscope platforms, the ANUBIScope is likely to be the most successful.

IOP is another promising device which was first designed specifically to perform intraperitoneal NOTES procedures. One of the unique features of this multi-lumen access device is that its flexible over-sheath is equipped with ShapeLock function. ShapeLock function is formed by a series of titanium rings that are connected by wire, and the rings lock into position when the connecting wires are tightened. The stiffened over-sheath ensures a stable platform while articulating the instruments. As such, many extraluminal intraperitoneal procedures including those that require significant retroflexion such as transgastric cholecystectomy, fundoplication, gastric restriction and diaphragmatic repair have been performed in animal and human cadaveric study^[29]. The IOP has since been used by surgeons in the Europe and Middle East for the novel primary obesity surgery

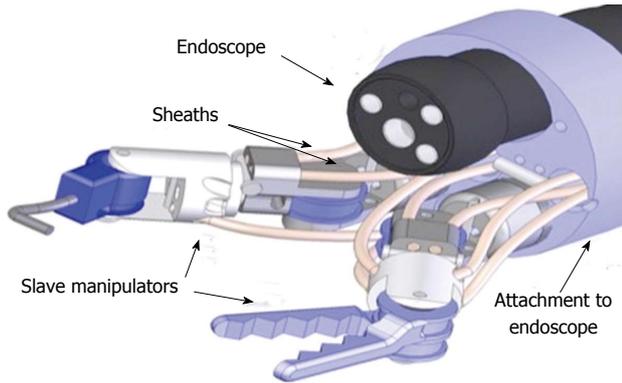


Figure 2 Design of prototype slave manipulator.



Figure 3 Master console controlled by surgeon.

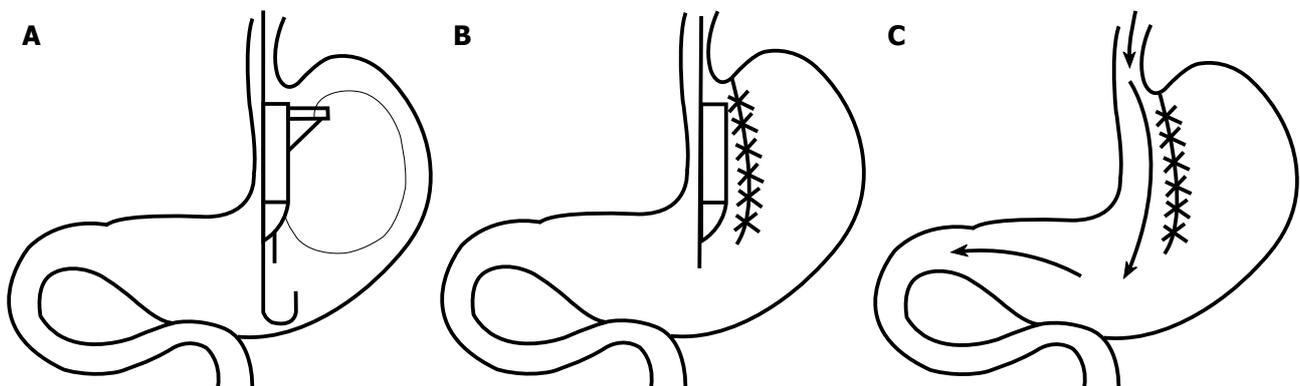


Figure 4 Endoscopic creation of restrictive pouch with transoral gastroplasty device. A: TOGA system deployed within the stomach, and having the endoscope at retroflex view; B: Anterior and posterior gastric mucosa brought into the suction chamber and stapled on; C: A restrictive luminal tube created within the stomach. TOGA: Transoral gastroplasty.

endoluminal (POSE) procedures. With this technique, multiple transmural plications are placed in the fundus and the distal body using specialized suture anchors that is facilitated by the IOP device. Espinós *et al.*^[30] has demonstrated clinical safety and effectiveness of POSE with IOP in 45 obese patients; (2) Robotic platforms: At present, two state-of-the-art robotic systems have been developed, namely the MASTER (Nanyang University, Singapore) and the ViaCath (Hansen Medical, United States). Master and slave transluminal endoscopic robot is an endoscopic robotic platform that is composed of a human-master robotic interface, a telesurgical workstation, and slave manipulator. This system works with a front-viewing endoscope equipped with two cable-actuated robotic arms (Figures 2 and 3). The robotic arm prototypes are designed with four "joints" which allows them to supinate, pronate, hyperextension, and flexion. One arm has a grasper and the other arm a cauterizing hook. The MASTER robotic system requires an endoscopist and a surgeon to operate. Once the endoscopist had positioned the endoscope, the surgeon then controls the finer motion of the robotic arms to perform surgery (Figure 4).

The MASTER system has been used to perform ESD in *ex vivo* and *in vivo* porcine models and was found to be comparable to standard endoscopic therapy

in terms of operation time^[31]. In 2014, Chiu *et al.*^[32] demonstrated that full thickness resection with MASTER for the treatment of gastric submucosal tumors in animal models with and closure of the defect with Overstitch is safe and feasible. First reported use of MASTER in clinical setting was a multicenter prospective study of 5 patients with early-stage gastric neoplasia^[33]. All submucosal dissections were performed using the MASTER system, and no perioperative complications encountered. The resection margins were clear of tumors in all 5 patients. From these studies, the MASTER system has shown to have met its objectives on successfully performing true NOTES procedures. We are still awaiting further studies to assess its capability and safety to perform other surgical procedures.

ViaCath system is another robot driven actuator that consists of a flexible overtube that runs alongside a standard endoscopes with two distal articulated robotic instruments. It functions similar to the IOP except it is robotic assisted hence allow more precise manipulation of the operating arms. ViaCath is yet to be fully utilized for NOTES procedures in human.

Although the most common access route for NOTES procedures is the vagina, selective indications have emerged for each different access techniques, including submucosal tunneling techniques *via* the transesophageal

approach, staging, gastric restriction and small tumor resection *via* the transgastric approach, and colorectal resections *via* the transanal/transcolonic approach.

Transeophageal approach: Submucosal tunneling techniques

Submucosal tunneling technique was first developed at the Mayo clinic with the intention to create a mucosal flap prior to penetration through the deeper layer and subsequent entry into the peritoneal cavity^[34]. In this technique, the submucosal layer is endoscopically tunneled into with the resulting space that can be used either for dissection onto the deeper layer, or an offset exit into the peritoneal cavity. The mucosal flap serves as a sealant valve that minimizes the risk of intraperitoneal soiling with the luminal contents. Experimental studies on animal models have shown safe entry *via* the submucosal tunnel into the mediastinum and peritoneum, resulting in successful transesophageal approach for epicardial coagulation and transgastric cholecystectomy, respectively^[35,36].

This submucosal tunneling technique has been adapted into the esophageal myotomy procedure to treat achalasia. The procedure, first introduced in 2008 by Inoue *et al*^[37] as per oral endoscopic myotomy (POEM), involves dissection and division of the inner circular muscle layer of the esophagus through a submucosal tunnel created endoscopically by a small proximal opening in the esophageal mucosa. The submucosal entry point is usually created at 10-15 cm from the gastroesophageal junction (GEJ). Once the submucosal layer is exposed, the dissection is carried out using electrosurgical ESD technique. The mucosal layer is separated from the underlying circular muscle fibers, and this dissection is extended until the endoscope is 2-3 cm beyond the GEJ. Myotomy then begins from 2 cm distal to the entry point up to the GEJ. Once completed, the mucosal closure can easily be performed with clips or endoscopic suturing device. Five years later, Inoue *et al*^[38] published the largest series of POEM with overwhelming success. Out of 300 patients, dysphagia was relief following one session of POEM in 98.2% of the subjects. There were only 2 patients with perforation that resulted in pneumomediastinum and pneumoperitoneum, one each respectively. In another prospective, multicentre study, 6 and 12 mo symptom remission rates was reported as 89% and 82%, respectively^[39]. All current studies have indicated that POEM is a safe and effective treatment for esophageal achalasia.

The success in POEM has led to the further use submucosal tunneling technique for resection of subepithelial tumor. Usually, the submucosal tunnel begins at 5 cm proximal to the lesion. A short tunnel approaching the lesion is created by additional submucosal dissection with CO₂ or air insufflations. Subepithelial tumour is excised using needle-knife and removed completely through the tunnel. Mucosal entry flap is then approximated using endoclips. To date, successful

attempts were reported for submucosal tumors in the esophagus and cardia that is ≤ 4 cm in size^[40-42]. Resection of gastric lesion distal to cardia appears to be technically difficult, and endoscopic full thickness resection, as described above is the more preferred treatment of choice.

Transgastric access: Peritoneoscopy, gastric restriction surgery, full-thickness gastric tumor resection

Transgastric NOTES access is typically *via* gastrostomies performed in the anterior stomach with needle knife puncture and balloon dilation. Currently, its role in clinical practice is mainly for staging peritoneal exploration, small bowel tumor resection and gastric tumor resection. A study involving a series of 130 patients who underwent transgastric NOTES by Nau *et al*^[43] found that endoscopic peritoneoscopy is not inferior to laparoscopic exploration for assessment of peritoneal metastasis. Interestingly, the former was also found to be equally effective and safe in a subgroup of patients with previous abdominal surgery. Transgastric peritoneoscopy can be performed with conventional flexible endoscopes, but the gastrostomies would require a specialized closure device. Since the development of abovementioned multitasking platforms, full thickness resections of gastric and small bowel tumors are currently performed *via* transgastric route.

Novel endoscopic gastric restriction surgery is the new frontier in bariatric surgery, to offer a less invasive approach which can be performed without general anesthesia. In theory, this may potentially reduce the risks commonly associated with laparoscopic bariatric surgery such as cardiopulmonary event, anastomotic leak, marginal ulcer formation and wound related complications. Endoscopic approach can serve either as a bridge to surgery or as "stand-alone" procedure for patients who are poor surgical candidates especially in super-obese (BMI > 50). Currently, there are two established techniques and, known as the transoral gastroplasty (TOGATM) and endoluminal vertical gastroplasty. Table 3 provides a summary of reported outcome for these endoscopic restrictive gastroplasty procedures. TOGA uses an endoscopic full-thickness stapling device to create a pouch along the lesser curve. The device uses vacuum suction to oppose the anterior and the posterior gastric wall prior to deploying the staplers. A restrictor is used to clamp the gastric folds, and the process can be repeated to achieve the desired luminal narrowing (Figure 4). A multicentre trial of 67 patients showed that this procedure resulted in substantial weight loss after 1 year without severe complications and no mortality^[44]. Endoluminal vertical gastroplasty uses a endoscopic suturing device (Bard EndoCinch) to create a sleeve intraluminally. The suturing device is contained within a capsule that is attached at the end of the gastroscope. Tissue is sucked into the capsule and a needle is advanced through the captured tissue. Several sutures are deployed in a

Table 3 Summary of reported outcome data for endoscopic restrictive gastroplasty

Technique	Study design	Excess BMI/weight loss (%)	Effects of comorbidities	Postoperative complications
Transoral gastroplasty ^[44]	Prospective multicentre study with 67 patients enrolled Average BMI: 41.5 (range 35.0-52.7) Follow up period: 12 mo	52.2% for patients with baseline BMI < 40; 41.3% for patients baseline BMI > 40	Successful reduction of HbA1c to 5.7% (baseline of 7%), improvement in triglyceride level	2 patients had respiratory insufficiency and asymptomatic pneumoperitoneum, respectively. Both were successfully managed conservatively
Endoluminal vertical gastroplasty using Bard EndoCinch suturing system ^[45]	Prospective, single centre observational study Average BMI: 39.9 (range 28.0-60.2) Follow up period: 12 mo	Overall EWL of 58.1% Patients with BMI < 35 have highest EWL of 85.1%	NE	No serious adverse events reported
Endoscopic transmural gastric plication using Incisionless Operating Platform ^[30]	Prospective single centre Average BMI: 36.7 (range 28.1-46.6) Follow up period: 6 mo	49.4% EWL at 6 mo	NE	Minor postoperative side effects, <i>i.e.</i> , fever, sore throat, stomach pain, nausea, vomiting and chest pain

NE: Not evaluated; BMI: Body mass index; EWL: Excess weight loss.

continuous and cross-linked fashion from the proximal fundus to the distal stomach. Once the suture is fixed, a vertical sleeve is created. Fogel *et al.*^[45], the first to describe the use of EndoCinch for this procedure, reported a 12 mo excess weight loss of 58.1 ± 19.9 in 64 patients. The main concern with this technique is its durability, for which additional studies are needed to evaluate its long-term efficacy. Recent modifications to this technique is the use of the restoring suturing system that enabled suture reloading without device withdrawal and provide greater depth of suturing. The incisionless operating platform has also being used for this procedure.

Transanal/transcolonic natural orifice transluminal endoscopic surgery: Transanal endoscopic microsurgery

From experience derived from transanal endoscopic microsurgery (TEM), surgeons have expanded the utilization of the transanal route for complete rectal and colonic resection. In 2007, Whiteford *et al.*^[46] described the first transanal NOTES radical sigmoidectomy in human cadavers. Various attempts by others were successful in swine and cadaveric models, but all has found significant technical difficulty for dissection of the mesentery and more proximal colon using solely the TEM platform. This has led to the use hybrid technology that uses transabdominal laparoscopy to provide camera visualization, triangulation by assisting grasper, dissection with energy source device. Ever since, this approach has made it to clinical application for treating rectal cancer and inflammatory bowel disease^[47-49]. Transanal approach has two distinct techniques: (1) Using origin TEM technique to dissect the lower rectum and perform colorectal resection and rectal anastomosis; and (2) abdominal cavity is entered *via* transanal route or *via* transcolonic approach at the desired anastomotic

site. Currently, pure transanal NOTES colorectal resection is still at preclinical stage.

CONCLUSION

The innovation in endoluminal techniques and development of endoscopic instruments encouragingly implies that it is now possible to perform fully incisionless surgery. The progress of endoscopic surgery is still at an experimental stage. Further development of multitasking platforms and surgical instruments is necessary to allow safe and widespread application of endoscopic surgery for more complex procedures, especially for malignant tumors. Despite its current limitations, endoscopic surgery has met with considerable success and has proven to be not inferior to conventional laparoscopic surgery in numerous areas. The future of NOTES seems promising and may one day provide the ultimate version of minimally invasive surgery.

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