Natural orifice transluminal endoscopic surgery: New minimally invasive surgery come of age

Chen Huang, Ren-Xiang Huang, Zheng-Jun Qiu

Abstract

Although in the past two decades, laparoscopic surgery, considered as a great revolution in the minimally invasive surgery field, has undergone major development worldwide, another dramatic surgical revolution has quietly appeared in recent years. Ever since Kalloo’s first report on transgastric peritoneoscopy in a porcine model in 2004, interest in a new surgical procedure named natural orifice transluminal endoscopic surgery (NOTES) has blossomed worldwide. Considering that a NOTES procedure could theoretically avoid any abdominal incision, operation-related pain and scarring, many surgeons and endoscopists have been enthusiastic in their study of this new technique. In recent years, several NOTES studies have been carried out on porcine models and even on humans, including transvaginal cholecystectomy, transgastric appendectomy, transvaginal appendectomy, and transvesical peritoneoscopy. So what is the current situation of NOTES and how many challenges do we still face? This review discusses the current research progress in NOTES.

INTRODUCTION

Since the first laparoscopic cholecystectomy was conducted by Mouret in 1987[1], conventional surgery using laparotomy has been largely replaced in the two ensuing decades by laparoscopic surgery, due to its lower level of trauma and faster recovery. Currently, laparoscopic cholecystectomy has become a classical approach and laparoscopic surgery has become the standard treatment for many gastrointestinal conditions. Based on the minimally invasive surgery, a novel approach to the endoluminal endoscopic surgery named the natural orifice transluminal endoscopic surgery (NOTES) is currently emerging because it has the advantage of avoiding surface incision. This advantage could help reduce surgical pain, decrease anesthesia and analgesia, shorten recovery time, avoid hernia formation and adhesions, and eliminate any surgical site infection and visible scarring. Ever since Kalloo’s first report on transgastric peritoneoscopy in a porcine model in 2004[2], this dramatic surgical revolution has triggered many surgeons and endoscopists to study this new technique. This complex technique involves breaching the wall of the stomach, colon, vagina or bladder by endoscopic means to gain access into the peritoneum to perform the novel endoscopic therapy. In recent
years, several NOTES experiments have been carried out on porcine models and even on humans, including transvaginal cholecystectomy, transgastric appendectomy, transvaginal appendectomy and transvesal peritoneoscopy. In response to the clinical potential of NOTES, in 2005, a working group, named the Natural Orifice Surgery Consortium for Assessment and Research, composed of Society of American Gastrointestinal and Endoscopic Surgeons and American Society for Gastrointestinal Endoscopy was established. This working group generated a white paper that encouraged future NOTES research and outlined key research areas that needed to be addressed.

NOTES PROCEDURES

NOTES procedures are frequently performed with existing endoscopic techniques and a number of accessories, such as snares, endoscopic biopsy forceps, endoscopic grasping forceps, endoloops and endoscopic clips. An endoscope may be introduced through a natural external orifice such as the mouth, anus, vagina or urethra to visualize various cavities, or through incisions and sutures to create internal orifices for entry into the free peritoneal cavity and access different viscera.

Transesophageal route

This is probably used for transesophageal intracardiac and mediastinal procedures, including biopsies. Considering the high difficulty for thoracic NOTES technique nowadays, few surgeons and endoscopists have such experiences, with the notable exceptions of Fritscher-Ravens et al., who accessed the heart under endoscopic ultrasound (EUS) guidance through the transesophageal route, and von Delius et al., who reported transesophageal NOTES mediastinoscopy in eight porcine models.

Transgastric route

To date, most of the published clinical cases report experience with the transgastric approach. The anterior wall of the stomach is usually the ideal incision site for access to the peritoneal cavity, while the posterior wall may be selected to explore the retroperitoneum. After sterilization, a double-channel endoscope enters the stomach through a sterile overtube, and then an endoscopic needle knife is used to create a 2-4 mm incision with electrocautery. A dilation balloon is advanced over a catheter, and the incision is radially dilated to ensure free access of the endoscope to the peritoneal cavity. Previously, a wide range of NOTES procedures of various complexity were carried out on experimental porcine models, such as peritoneoscopy, lymphadenectomy, tubal ligation, oophorectomy, cholecystectomy, cholecystogastrostomy, gastrojejunostomy, distal pancreatectomy, and splenectomy. Lee et al. have successfully performed transgastric endoscopic cecectomy with laparoscopic assistance on three canine models. The first transgastric appendectomies in humans were performed by Rao and Reddy in India in 2004 (unpublished results).

Transcolonic route

Although transcolonic NOTES has been a rarely explored approach to the peritoneal cavity because of concerns related to rectal contamination and intra-abdominal infectious complications, a few surgeons and endoscopists still perform transcolonic cholecystectomy and transcolonic appendectomy. Bazzi et al. have successfully performed hybrid transrectal NOTES nephrectomy in three porcine models.

Transvesical route

Currently, transvesical access is the preferred approach in humans because this route obviates the risk of intestinal content leakage via an imperfectly closed access site. The first transvesical cholecystectomy in humans was carried out by Marescaux et al. in 2007. In 2009, Horgan et al. reported a series of successful transvaginal cholecystectomies in nine patients and one transvaginal appendectomy in a 24-year-old woman. Tarantino et al. have reported a study which aimed to evaluate the feasibility and safety of transvaginal rigid-hybrid NOTES anterior resection in 40 patients with symptomatic diverticular disease, and the results were satisfactory. Suzuki et al. have found that transvaginal cholecystectomy resulted in cardiopulmonary stability and well-preserved immune function similar to those in laparoscopic cholecystectomy in an experiment that involved 10 porcine models. Haber et al. have reported that hybrid robotic transvaginal NOTES pyeloplasty, partial nephrectomy and radical nephrectomy were feasible and safe in a porcine model.

Transvesical route

Considered as another novel surgical route, transvesical peritoneoscopy was performed by Lima et al. on a porcine model in 2006. In 2007, Gettman et al. have reported transvesical peritoneoscopy in a 56-year-old man.

All of these routes have their own advantages in NOTES procedures. However, no one is perfect to date. Although
the transgastric route is regarded as the easiest way to get into the abdominal cavity, and initially, many NOTES experiments were done via the transgastric route, a drawback limiting the use of the transgastric route is the lack of a secure and reliable way to close the gastrotomy, which is an essential step in the procedure. The transcolonic route is similar to the transgastric route except that the former has an increased risk of contamination due to the fecal bacterial load[38]. The benefits of transcolonic access include in-line endoscopic visualization and the ability to create and close the colotomy with existing transanal endoscopic microsurgery equipment[39]. The transvesical route allows straight access to the upper abdominal organs such as the gallbladder, which is mechanically more advantageous than the transgastric approach. By far, the most clinical experience has been obtained with transvaginal access used as an accessory entry point to the peritoneal cavity during cholecystectomy. Data from several NOTES registries show that this access is associated with a low complication rate (3%-8%) and has a low technical threshold[39,40]. Closure of the colpotomy can also be performed under direct vision using standard surgical techniques. However, this route is only suitable for female patients[29,38]. The urinary tract is normally sterile, therefore, using the transvesical route can reduce infection risk. Anatomical relationships of the lower urinary tract to the peritoneum and retroperitoneum appear to be in the direct line of sight. Thus, all abdominal structures can theoretically be accessed. Closure of bladder access is simplified because catheterization alone promotes healing with considerably less risk of fistula formation and no risk of bowel leak[37]. However, as the urethra is quite narrow and short, it is controversial to date whether it is possible to experience NOTES through the transvesical route, other than peritoneoscopy, and how surgical specimens can be taken out of the body through the narrow urethra.

**CURRENT CHALLENGES OF NOTES**

Although the potential benefits of NOTES such as no scarring, no pain and shorter hospitalization represent a new frontier of surgery, many technological challenges still exist. NOTES will not receive widespread adoption for clinical application until these problems are solved.

**Surgical platform**

The endoscopes that we use nowadays only offer small instrument and suction channels, which makes retraction and dissection of tissues difficult. Therefore, to develop a new platform that is larger, stronger and eventually articulated, instruments that can pass through large working channels are necessary. There are various operative platforms under investigation currently. Basically, all systems for performing NOTES-related procedures that are currently available can be classified into three different types[41]: (1) mechanical platforms such as EndoSamurai (Olympus, Tokyo, Japan); Anubis (Karl Storz, Tuttingen, Germany); Direct Drive System (Boston Scientific, Natick, MA, United States) and Endosurgical Operating System (EOS, USGI Medical, San Clemente, CA, United States), which allows passage of additional larger-caliber endoscopic instruments, without possibility of triangulation[42]; (2) computer-assisted platforms such as the master and slave transluminal endoscopic robot (University of Singapore) or da Vinci system (Intuitive Surgical, Sunnyvale, CA, United States); and (3) non-tethered systems such as mechanical or magnetic capsules. Cho et al[43] have successfully performed transgastric NOTES sigmoidectomy on a survival canine model with a custom-paired magnetic intraluminal device. Scott et al[44] have carried out complete transvaginal cholecystectomy using Magnetic Anchoring and Guidance System (MAGS) instruments on porcine models.

**Pneumoperitoneum**

Endoscopic insufflation may be used to maintain pneumoperitoneum, but this approach is more difficult to manage and measure than a standard laparoscopic port approach, which is specifically designed for intra-abdominal insufflation. A wider variation in pressure is observed than with laparoscopic insufflation[45]. On the other hand, a laparoscopic port and insufflation system ensures that any excess insufflation is noted and quickly addressed. The port also allows passage of a single laparoscopic instrument into the abdomen. Horgan et al[29] have suggested that, until better instruments are developed, having one port available for use with well-developed minimally invasive instruments is important for safe natural orifice surgery at this stage. However, in 2010, von Delius et al[46] performed pressure-controlled endoscopic insufflation and found that CO₂ insufflation for NOTES showed minor advantages compared with insufflation with room air, regarding intra-abdominal visualization, but resulted in an increase in cardiac afterload.

**Spatial orientation**

Orientation can be a challenge for NOTES in the peritoneum, because the triangulation used by surgeons during laparoscopy is impossible. Some organs appear relatively easy to find, such as the uterus and ovaries, while others are somewhat surprisingly difficult to localize (gallbladder and spleen)[3]. Some workers consider that the aid of EUS and miniprobes (MPs) can resolve this problem. Fritscher-Ravens et al[40] successfully accessed the heart under the guidance of EUS through transesophageal route in 2007. Varas Lorenzo et al[47] consider that EUS-guided pancreatic pseudocyst or abscess drainage represents a notable advance for NOTES, and in the future, distal pancreatectomy will probably require EUS support along the greater curvature of stomach to locate an entry point for distal pancreatic resection. MPs may also help in selecting an entry point. Fowler et al[48] have reported that their Queen’s NOTES group have devised a novel method of orientation by using a magnetic device that passes within an endoscope channel allowing for 3D imaging of...
the shape and orientation of the endoscope. Best et al have found that MAGS instrumentation for NOTES procedures did not cause tissue damage or adverse clinical outcomes in porcine abdominal walls. Fernández-Esparrach et al considered that it was helpful to use a CT-based image-registered navigation system to identify safe gastrointestinal access sites for NOTES and intraperitoneal structures.

**Triangulation of instruments**

To date, in NOTES experience, when the target tissue is reached, retraction and dissection are virtually impossible due to the lack of the triangulation of endoscopic instruments, which can provide efficient grabbing and dissection capabilities. Dallemagne et al have reported some novel instruments that are currently under investigation. One prototype of operating endoscope is known as Anubis (Karl Storz). This unique four-way articulating flexible endoscope, with a built-in light and video source, has a 16-mm diameter insertion shaft with an 18-mm diameter distal articulating vertebræ section and distal head. The distal head incorporates two opposing, movable arms with 4.2-mm working channels. Another instrument named as Direct Drive System (Boston Scientific) is an ergonomic, table-mounted, operative platform providing five degrees of freedom to the tip of the instruments. MAGS, which provides a longer access port (50 cm) that provides easier deployment of instruments and suitable reach, more robust cautery with a longer, more rigid, pneumatically deployed tip with better reach and sufficient torque to allow blunt dissection, and a more versatile tissue retractor with bidirectional dual flexible graspers, which provides excellent cephalad fundus retraction and inferolateral infundibulum retraction. EndoSamurai (Olympus) also aims at providing triangulation of the instruments, using a different operating mode. NOTES instruments are still developing and few researchers have compared these various instruments.

**Closure technique**

Among the challenges of the NOTES technique, closure and suture techniques are thought to be critical in view of perforation and infection risks, especially for the transgastric and transcolonic routes. To date, several animal cases of microabscesses, peritonitis and death have been related to unsatisfactory closure of the transmural access sites. Currently, clips are frequently used to close the defects, but these have proven to be inadequate. Ryoo et al have compared several gastric closure methods including endoclips, surgical suturing and a suction-based suturing device. The investigators were disappointed that mucosal closure with endoclips resulted in significant air and fluid leakage via the line of the endoclips. Shabbir et al have compared gastrotomy closure with either hand-sewn, endoloop or endoclip techniques in 24 ex vivo porcine stomachs, and found that endoclips seem to be better for gastrotomy closure than endoloops because of their potential to endure relatively higher pressure without any prolongation of application time. However, two leaks were still noted at the clip bite site. Meanwhile, other scholars have reported some positive experimental outcomes. McGee et al have demonstrated that the NDO Plicator, which is an endoscopic device designed to treat gastroesophageal reflux disease by reducing the inner diameter of the gastroesophageal junction, resulted in leak-proof gastric closure in a porcine model. Meireles et al have used an automated stapler (Surg ASSIST) for reliable closure of the gastrotomy incision in a live porcine model. Schoenberg et al have reported transgastric uterine horn ligations of porcine models with the specific absorbable NOTES loops, which are recommended for use during NOTES appendectomy. However, to date, a commercially available, simple, safe and effective endoscopic instrument for closing these puncture sites has not been created.

**Perioperative complications**

To date, the perioperative outcomes have been favorable in most reported studies. However, as closure technique is not mature enough, intraperitoneal infection remains a primary concern for NOTES. Yang et al have reported that 45 porcine models underwent transgastric or transvaginal NOTES peritoneoscopy and transumbilical laparoscopic cholecystectomy under NOTES view and found that, after antiseptic preparation such as gastric or vaginal lavage and antibiotic peritoneal irrigation, the bacterial load significantly decreased in the transgastric group, which seems as safe as the sterile transvaginal approach. von Delius et al consider that transesophageal NOTES mediastinoscopy carries a substantial risk of inadvertent development of pneumothorax after animal experiments. Biliary leaks have been reported in a NOTES study involving transvaginal cholecystectomy from Pugliese et al, which were treated successfully by endoscopic drainage and stenting. The risk of infertility after transvaginal NOTES procedures is unknown, but Horgan et al have suggested that avoidance of bleeding and inflammation of the pelvis should minimize this potential risk.

**NOTES AND LAPARO-ENDOSCOPIC SINGLE-SITE SURGERY**

Closely related to NOTES, laparo-endoscopic single-site surgery (LESS) describes minimally access surgical procedures that are performed through a single incision/location. Rane et al published the first true LESS experience in abstract form in 2007, performing a transumbilical laparoscopic nephrectomy. As a result of the lack of ideal novel endoscopic instruments, NOTES experiences have been much more limited than LESS, and clinical experience with LESS has been more extensively reported. However, Raman et al have reported a retrospective case-controlled study comparing the outcomes of 11 LESS nephrectomies to 22 matched, conventional laparoscopic nephrectomies, which failed to demonstrate any significant improvement in analgesic use or conva-
lescence. To date, although few studies have focused on the comparison between NOTES and LESS, we still believe that NOTES, considered as the developing terminal minimally invasive surgery, must have a promising future.

CONCLUSION

After the familiar laparoscopic surgical techniques, NOTES has become the next worldwide focus of minimally invasive therapy. The novel surgical procedures, with fast recovery and without general anesthesia, visible scarring, postoperative hernia formation and adhesions, are attractive for most surgeons and endoscopists. Although the novel procedure is far away from being mature and many technical problems have to be overcome before its widespread application in clinical cases, NOTES is undoubtedly a promising procedure for the future. More clinical studies and creation of new NOTES-specific instruments will make NOTES a reality.

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