Asia Pacific NOTES: Where are we?

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Abstract

Over the past decade, the development of natural orifice transluminal endoscopic surgery (NOTES) has progressed from preclinical animal studies to clinical human trials in Asia. Due to the difference in culture and disease prevalence, most of these human studies focused on NOTES-related procedures, including endoscopic full-thickness resection and peroral endoscopic myotomy as well as submucosal endoscopic tumor resection. This article reviews the research works on NOTES originated from Asia to obtain insight into future development.

Keywords: Endoscopy, Natural orifices transluminal endoscopic surgery, Surgery

Introduction

The concept of natural orifices transluminal endoscopic surgery (NOTES) was first proposed in 2000 when Kalloo et al reported the success of transgastric peritoneoscopy with a flexible endoscope in an animal model.1 One of the potential advantages of NOTES is that surgical procedures could be performed through the gastrointestinal tract without skin incision. Theoretically, the pain induced would be significantly lowered, which would hasten recovery. The first human NOTES procedure was reported by Rao et al,2 who performed transgastric appendectomy using a flexible endoscope in 2003. The American Society of Gastrointestinal Endoscopy (ASGE) and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) jointly organized the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) consortium and published a white paper that listed the important barriers to clinical application of NOTES.3 These included access to the peritoneal cavity, gastric (intestinal) closure, development of suturing and anastomotic devices, development of a multitasking platform to accomplish procedures, management of intraperitoneal complications, and spatial orientation. The Asia Pacific NOTES working group was formed in 2007 to address the issue of rapid development in NOTES among Asian Pacific countries. Upon discussion in our first meeting, we believe that there were some advantages in developing NOTES among Asian countries because many surgeons were capable of performing flexible endoscopy. Moreover, surgeons and gastroenterologists were working in a very close relationship.

Since 2007, numerous workshops and symposia were held to discuss the development of NOTES. Researchers in the group from different Asian countries had conducted innovative developmental studies to address these barriers listed in the white paper. This article reviews the research on NOTES that originated from Asia, to acquire an insight into future development.

Access to the peritoneal cavity

Access to the peritoneal cavity through the gastrointestinal tract is an important first step toward successful performance of NOTES. Direct access using needle-knife incision coupled with balloon dilatation is the conventional method used for peritoneal access in animal experiments.4 With the goal to improve ease of peritoneal access, a one-step needle sphincterotomy was developed in conjunction with Olympus Co Ltd, Tokyo, Japan.5 The device allowed direct incision using the needle-knife part and subsequent carbon dioxide insufflation through the channel after withdrawal of the needle to avoid adjacent organ injury. Eventually, gastrointestinal access would be extended with the sphincterotome. In a randomized study, Teoh et al showed that direct access using the new combined needle sphincterotomy hastened gastrointestinal access compared with balloon dilatation.5 Sumiyama et al pioneered an innovative method to access the peritoneal cavity through a submucosal tunnel.7 In four survival porcine models, mediastinoscopy was successfully performed using the submucosal tunneling technique, whereby a submucosal tunnel was created.

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between the mucosal entrance and the mediastinal access. The feasibility of gastric access with submucosal tunneling was examined in another study reported by Yoshizumi et al. In seven porcine models, a 50-mm submucosal tunnel was created prior to peritoneal access and the mucosal incision was closed with clips. All the pigs survived without evidence of leakage. The submucosal tunneling became the most promising method toward peritoneal access through the gastrointestinal tract.

**Gastrointestinal closure and development of suturing and anastomotic devices**

Closure of the gastrointestinal access after NOTES is important, as failure to securely close the access will lead to catastrophic events. Endoscopic clipping is the most common method used for closure of the gastrointestinal access. In an ex vivo experiment, researchers from Singapore created 24 gastrotomies in a porcine stomach that were randomly closed with either a hand-sewn, endoclip, or endoloop technique. The group receiving endoclip closure endured a significantly higher bursting pressure before leakage when compared with the endoloop group. The surgical hand-sewn closure, however, had a significantly higher bursting pressure when compared with closure with endoclips and the endoloop technique. Indeed, surgical suturing is a time-honored method for tissue approximation. Endoscopic suturing devices were thus developed to achieve tissue approximation through suturing within the confined gastrointestinal lumen. The Eagle Claw (R&D division, Olympus Co Ltd, Tokyo, Japan) is a prototype endoscopic suturing device that can achieve knot tying using a flexible endoscope to perform complex surgical dissection such as endoscopic submucosal dissection (ESD). The difficulties in performing these complex endoluminal procedures is related to the fact that dissection was performed using a single device coaxial to the endoscope, and there is no other device for retraction. The endoscope should be redesigned with a view to achieve complex endoluminal procedures using two or more effectors in a triangulation approach. EndoSamurai (R&D division, Olympus Co Ltd, Tokyo, Japan) is a novel multitasking endoscopic platform that can achieve dissection and suturing through the two arms attached to a flexible platform. Ikeda et al reported on the performance of endoscopic full-thickness resection (EFTR) using EndoSamurai and compared to that performed with ordinary double channel endoscope in ex vivo porcine models. The performance of EFTR was shown to be faster, more precise, and more efficient using EndoSamurai as compared with conventional endoscope. Although the EndoSamurai was shown to be effective and safe, there is a lack of clinical studies to evaluate its performance.

In Singapore, a novel endoscopic robotic platform named Master and Slave Transluminal Endoscopic Robot (MASTER, EndoMaster Pte Ltd, Singapore) was developed. The MASTER is composed of a human–master robotic interface, a telesurgical workstation, and slave transluminal endoscopic robot. In preclinical Erlangen (a model used for endoscopic training) and porcine models, MASTER was shown to be effective in performing ESD with comparable surgical time to the use of an ordinary insulated tip knife. This preclinical study showed that MASTER can achieve good tissue handling and dissection ability. The world’s first multicenter clinical study on gastric ESD using MASTER confirmed the safety and efficacy in treating early gastric neoplasia in five patients. The mean submucosal dissection time was only 18.6 minutes, and no perioperative complication was encountered. Further study will be conducted to evaluate the feasibility and safety of other potential surgical procedures using MASTER.

**Clinical NOTES procedures in Asia**

In Western countries, the NOTES procedure reported most often in humans is transvaginal cholecystectomy. Due to cultural variations and differences in disease prevalence, the acceptance of transvaginal procedures is much lower in Asian countries. Clinical NOTES procedures in Asia can be subclassified into pure/hybrid...
NOTES and NOTES-related procedures. We consider pure/hybrid NOTES as translumenal surgical procedures focusing on management of intraperitoneal pathologies. NOTES-related procedures are complex, innovative endoluminal procedures developed from the concept of NOTES. Rao et al first reported the performance of transgastric appendicectomy in humans.2 Subsequently, the feasibility of various NOTES procedures was explored in an animal model.4 The technique of transgastric peritoneoscopy had been widely examined; numerous studies were recently conducted to investigate its feasibility in humans. Lee et al20 reported their experience in performing transgastric peritoneoscopy through a submucosal tunnel in a patient with suspected malignant ascites under conscious sedation. Niu et al21 performed transvaginal cholecystectomy with single umbilical trochar assistance in 43 patients. All the procedures were successfully performed, and a retrospective comparison showed the advantages of transvaginal cholecystectomy in comparison with conventional laparoscopic cholecystectomy related to postoperative pain and hospital stay.

With the high prevalence of upper gastrointestinal pathologies, NOTES-related procedures were explored in Japan and Korea, looking at the management of upper gastrointestinal malignancies. EFTR was examined in numerous clinical studies for treatment of gastrointestinal neoplasia. Cho et al22 reported the performance of EFTR and laparoscopic regional lymph node dissection in 14 patients. These patients were contraindicated for treatment with ESD alone, because most of them had submucosal carcinomas. The EFTRs were successfully performed with negative resection margins and the defect was closed by laparoscopic suturing. This approach potentially reduces the need of gastrectomy, which leads to significant morbidities. Inoue et al23 combined the technique of endoscopy and laparoscopy to achieve full-thickness resection for gastric cancer using the gastric cancer with nonexposure technique (CLEAN-NET, combination of laparoscopic and endoscopic approaches to neoplasia with non-exposure technique). The gastric tumor was first marked with ESD technique using the endoscope. After circumferential mucosal incision, laparoscopic full-thickness resection was performed and the luminal defect was closed by laparoscopic suturing. Zhou et al reported on the results of EFTR of gastric submucosal tumors without laparoscopic assistance in 26 patients.24 The complete resection rate was 100% and the mean surgical time was 105 minutes. The mean tumor size was 2.8 cm, and most of these were gastrointestinal stromal tumors. There was no complication or recurrence after the EFTR.

Perhaps one of the most important developments in NOTES-related procedure is Per Oral Endoscopic Myotomy (POEM). Inoue et al25 were first to perform endoscopic myotomy via a long submucosal tunnel in 16 patients with achalasia. The POEM procedure was achieved using ordinary endoscopic instruments, and the essential elements to its success included the use of step-by-step dissection with a triangle tip knife, carbon dioxide insufflation, and general anesthesia with positive ventilation.26 Currently, more than 250 POEM procedures have been performed in Japan. POEM was quickly adopted from other Asia countries. In a prospective study for treatment of achalasia among 16 patients in Hong Kong, POEM achieved significant improvement in dysphagia and Eckhart score, as well as lower esophageal sphincter pressure after the surgery27 (Fig. 3). Ren et al28 reported the results of 119 cases of achalasia treated with POEM. In this series, a substantial rate of complications was reported, including surgical emphysema at 27% and pneumothorax at 2.5%. The high rate of complications was not observed in other series. All the complications, however, were treated nonsurgically. Inoue et al29 extended the techniques of submucosal tunneling to resect subepithelial tumors using the submucosal endoscopic tumor resection (SET). Through a submucosal tunnel created with the same POEM technique of 5 cm above the tumor, the submucosal tumor was resected using a triangle tip and insulated tip knives. Seven patients with subepithelial tumors underwent complete resection using this technique. With the success in submucosal tunneling, access to the peritoneal cavity and closure of the gastrointestinal entrance in NOTES will become safe and feasible.

Conclusion

Over the past decade, the development of NOTES has progressed from preclinical animal experiments to clinical human trials. In Asia, numerous research studies were conducted to address the various barriers to performance of NOTES. These included the access and closure of the gastrointestinal tract using submucosal tunneling and the development of endoscopic suturing devices, as well as multitasking endoscopic and robotic platforms. Currently in Asia, most of the clinical procedures performed were an extension of the concept of NOTES. These NOTES-related operations included EFTR, POEM, and SET. In the future, we will expect a routine performance of these NOTES-related procedures, and a higher number of NOTES procedures performed via the concept of submucosal tunneling with novel multitasking platforms.

Conflict of interest

The author has no conflict of interest to declare. This manuscript was written based on a presentation to the SGI 2011 conference held in Seoul, Korea.
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References