

Natural-orifice transgastric endoscopic peritoneoscopy in humans: Initial clinical trial

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Abstract

Background Natural-orifice transluminal endoscopic surgery (NOTES) is a possible advancement for surgical interventions. We initiated a pilot study in humans to investigate feasibility and develop the techniques and technology necessary for NOTES. Reported herein is the first human clinical trial of NOTES, performing transoral transgastric diagnostic peritoneoscopy.

Methods Patients were scheduled to undergo diagnostic laparoscopic evaluation of a pancreatic mass. The findings of traditional laparoscopy were recorded by anatomical abdominal quadrant. A second surgeon, blinded to the laparoscopic findings, performed transgastric peritoneoscopy. Diagnostic findings between the two methods were compared and operative times and clinical course were recorded. Definitive care was based on findings at diagnostic laparoscopy.

Results Ten patients completed the protocol with an average age of 67.6 years. All patients underwent diagnostic laparoscopy followed by successful transgastric access and diagnostic endoscopic peritoneoscopy. The average time of diagnostic laparoscopy was 12.3 minutes compared to 24.8 minutes for the transgastric route. Transgastric abdominal exploration corroborated the

decision to proceed to open exploration made during traditional laparoscopic exploration in 9 of 10 patients. Peritoneal or liver biopsies were obtained in four patients by traditional laparoscopy and in one patient by the transgastric access route. Findings were confirmed by laparotomy in nine patients. Eight patients underwent pancreaticoduodenectomy and two underwent palliative gastrojejunostomy and/or hepaticojejunostomy.

Conclusions Transgastric diagnostic peritoneoscopy is safe and feasible. This study demonstrates the initial steps of NOTES in humans, providing a potential platform for incisionless surgery. Technical issues, including instrumentation, visualization, intra-abdominal manipulation, and gastric closure need further development.

Keywords Transgastric Surgery · Endolumenal Surgery · Natural Orifice Transluminal · Endoscopic Surgery

Minimally invasive surgery has evolved, allowing large operations to be performed without the trauma caused by large incisions for access alone. Despite advances, modern laparoscopy has not significantly changed in the last decade. The delivery of surgical interventions has evolved much slower than other areas of technologic led interventions such as cardiology. Recent advances in visualization and instrumentation in endoscopic and endolumenal technology now make it seem reasonable to consider obtaining access to body cavities via natural orifices. Natural-orifice transluminal endoscopic surgery (NOTES) is a newly described family of techniques that describe access to the abdominal cavity via transoral, transcolonic, transvesical or transvaginal routes. Human subjects have undergone transgastric appendectomy and tubal ligation performed endoscopically in India (unpublished) but not in the United States. Techniques have been described in a porcine model

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illustrating its feasibility in splenectomy [1], gastrojejunostomy [2] and the creation of an anastomosis [3], cholecystectomy with cholecystogastric anastomosis [4] and oophorectomy with tubal ligation [5, 6]. The safety, feasibility, and efficacy of this technique have not been studied in humans.

This field of study will require a large amount of supporting basic science, technologic, animal model, and human research to prove its desirability over standard surgical methods. With the initial ground work in animals described, we proposed to investigate the efficacy of transgastric endoscopic peritoneoscopy with endoscopic biopsy in patients undergoing diagnostic laparoscopy. Using this method all patients would be instrumented under the safety of laparoscopic guidance, eliminating potential risks of transgastric perforation. Patients also required a concurrent gastrotomy for gastrojejunostomy or gastric resection as part of their procedure eliminating the risk of an unnecessary gastrotomy for access.

Materials and Methods

Patients eligible for the study included those with a pancreatic mass who lacked a tissue diagnosis at presentation and required staging laparoscopy, as is the standard of care at our institution for biopsy and determination of resectability. Patients meeting the inclusion criteria and consenting to undergo diagnostic transgastric endoscopic peritoneoscopy were prepped, draped and placed under general anesthesia. Laparoscopic access was obtained in the traditional fashion and the abdomen was explored laparoscopically to determine evidence of metastatic disease and resectability in each patient. At laparoscopy, findings were recorded in a grid scoring each quadrant, the omentum and liver. All findings were recorded and biopsies taken if indicated. Once exploratory laparoscopy had been completed and the decision made by the laparoscopist as to the most appropriate treatment course (proceed with resection or palliation), a separate endoscopist performed the transgastric endoscopic peritoneoscopy. A single-channel therapeutic gastroscope was the most effective during transgastric endoscopic peritoneoscopy. A single-channel diagnostic gastroscope proved too flexible for effective transgastric passage and positioning of the endoscope. A dual-channel therapeutic gastroscope was too large and cumbersome to easily pass through a gastrotomy dilated with a 15-mm controlled radial expansion (CRE) balloon. In this technique, a gastroscope was passed transorally into the stomach and inflated. The laparoscopist visualized the anterior wall of the stomach ensuring the existence of a safe site for transgastric peritoneal access. Endoscopic access to the peritoneum was obtained under

direct laparoscopic visualization to ensure safety. An access site was chosen, a needle-knife used to puncture the wall of the stomach and a guide wire passed into the abdominal cavity under laparoscopic visualization (Fig. 1). This portal of access was dilated with a pyloric dilating balloon to allow passage of the endoscope through the stomach and into the peritoneum (Figs. 2 and 3). This technique for access to the abdominal cavity is described by Kalloo [1, 2, 6] and Swain [3, 4] and modified by our team. Intra-abdominal findings were recorded with a similar format to the laparoscopy and the results compared. Biopsies were taken if indicated and sent for frozen section using standard endoscopic biopsy forceps. No additional instrumentation was utilized to manipulate the tissues. The endoscopist then made a decision based on the endoscopic exploration as to the most appropriate way to proceed (resection or palliation) and the results were recorded for comparison. Once endoscopic and laparoscopic explorations were complete, the decision to proceed with palliation or resectional therapies was made by the laparoscopist according to our current standard of care. In the absence of obvious metastatic disease, the patient's abdomen was explored more thoroughly via standard laparotomy. Patients with resectable pancreatic tumors underwent an open pancreaticoduodenectomy, having their distal stomach, pancreas and duodenum resected to remove the tumor burden. The gastrotomy made during endoscopic peritoneoscopy was resected as part of the specimen. Patients with unresectable pancreatic tumors determined laparoscopically or after open exploration underwent palliative gastrojejunostomy to prevent an impending gastric outlet obstruction by incorporating the gastrotomy as part of the anastomosis. Hepaticojejunostomy was similarly created to palliate biliary obstruction. In each possible scenario, gastrotomy was necessary whether proceeding with resection for cure or palliation.

Data points collected include length of time necessary for laparoscopic exploration (from the initial incision to the laparoscopist's decision point) and endoscopic exploration (from scope in mouth to the endoscopist's decision point). Findings of the laparoscopic and endoscopic exploration were recorded based on the four quadrants of the abdomen, liver, and omentum. Patients' clinical course was followed to determine morbidity and mortality. This protocol was approved by the institutional review board (IRB) at the Ohio State University (protocol #2006H00120).

Results

Ten patients consented and underwent the protocol. All patients underwent diagnostic laparoscopy followed by successful transgastric access and diagnostic endoscopic

Fig. 1 Access to the abdominal cavity is created by passing a guide wire into the abdominal cavity through the stomach. The endoscopic view is depicted on the left and the laparoscopic view is depicted on the right

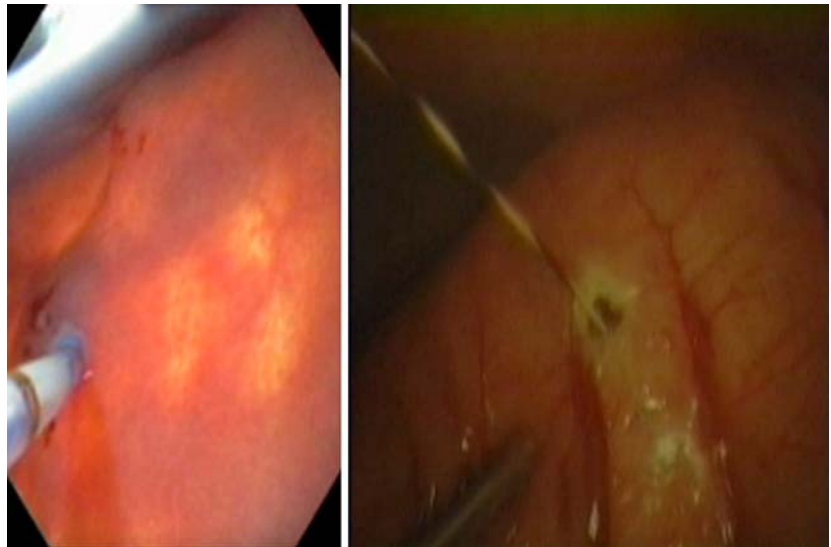


Fig. 2 The access site is dilated with an endoscopic dilating balloon to allow passage of the endoscope through the stomach. The endoscopic view is depicted on the left and the laparoscopic view is depicted on the right

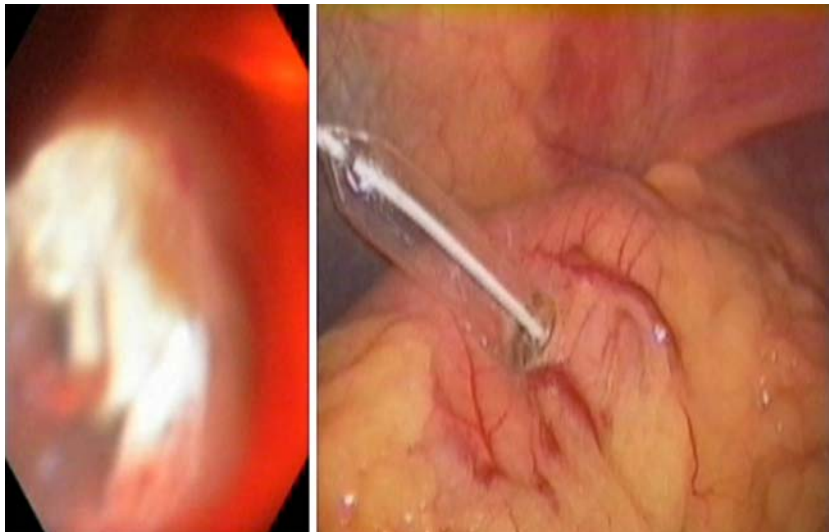
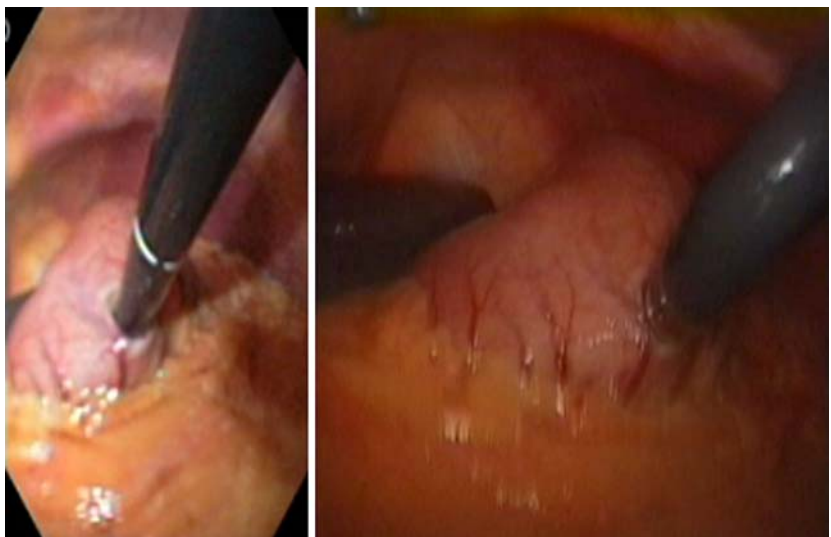


Fig. 3 The endoscope is passed through the stomach into the peritoneal cavity for abdominal exploration. The retroflexed view from the endoscope as it looks back to the access site from the stomach is shown. The endoscopic view is depicted on the left and the laparoscopic view is depicted on the right



peritoneoscopy. The average age of the patients was 67.6 years (range 49–79 years). Mean laparoscopic abdominal exploration time was 12.3 minutes (range 4–25 minutes) and the mean endoscopic abdominal exploration time was 24.8 minutes (range 15–34 minutes).

Although the decision to proceed to open abdominal exploration was corroborated between the endoscopic and laparoscopic exploration in nine of 10 patients, there was variability in adequacy of visualization of different structures and quadrants. Visualization of the anterior abdominal wall, omentum, left lateral segment of the liver, left upper quadrant, left lower quadrant, and right lower quadrant and the need for biopsy was corroborated in all 10 of the patients when comparing laparoscopic findings and endoscopic findings. In four patients, visualization of the right lobe of the liver and right upper quadrant structures was inadequate endoscopically with two patients in whom endoscopic biopsies were attempted but were unsuccessful due to inability to access these areas. Two patients had incidental small right inguinal hernias identified laparoscopically and endoscopically and a single patient had an incarcerated umbilical hernia identified endoscopically that was not identified laparoscopically.

Laparoscopic exploration generated biopsies in five patients with only one patient determined to have metastatic disease. The decision to proceed to open abdominal exploration correlated based on independent and blinded exploration of the peritoneum by the laparoscopist and endoscopist in nine of the 10 patients. Four of the five patients who had a laparoscopic biopsy had benign disease on biopsy and underwent a Whipple procedure for adenocarcinoma or an intraepithelial neoplasm.

Endoscopic exploration generated a biopsy in one patient, which proved to be a benign lesion. This patient also had a laparoscopic biopsy of a similar site, also found to be benign.

Eight of the 10 patients underwent an open pancreaticoduodenectomy based on the results of the laparoscopic exploration. Two patients underwent palliative procedures. One patient had a single peritoneal lesion identified and biopsied laparoscopically, which proved to be a metastatic lesion. The biopsy site was identified endoscopically but because the endoscopist was blinded to the laparoscopic findings and no lesion remained, the decision to palliate could not be made. Another patient had a high metastatic lesion over the dome of the right lobe of the liver that was not recognized at laparoscopic or endoscopic exploration. In two additional patients, endoscopic exploration identified suspicious lesions within the peritoneum but these could not be sampled due to inability to properly and safely orient or access the lesion. The inability to biopsy these sites had no bearing on whether to proceed with open abdominal exploration.

Of the eight patients who underwent pancreaticoduodenectomy, five had adenocarcinoma of the head of the pancreas. Two patients had benign disease and one patient had a pancreatic intraepithelial neoplasm.

Two patients experienced postoperative complications unrelated to the endoscopic exploration. One patient returned to the operating room postoperative day 1 for control of bleeding from the retroperitoneum at the site of resection of the uncinate process and another patient's wound dehiscence on post operative day number twelve requiring a return to the operating room for closure of the abdominal wall. There were no mortalities during the study period.

Discussion

Our pilot study investigates the feasibility of diagnostic transluminal endoscopic peritoneoscopy in a very select group of patients. Broad application of this technique to explore the abdominal cavity in patients who would otherwise not require a gastrotomy as part of their treatment requires additional investigation. Ability to reliably close a transluminal defect endoscopically is one of the more-significant stepping stones to widespread application of this technique as outlined in the natural-orifice surgery consortium for assessment and research (NOSCAR) white paper [7]. Scwab et al. have looked at three devices that may be used to close an enterotomy endoscopically but none have been used for this purpose in humans [8]. Prior to a standalone NOTES procedure, closure of an endoscopically created enterotomy using entirely endoscopic tools must be 100% effective to justify and safely perform transluminal access.

At the NOSCAR meeting in Phoenix in March 2006, and the working group of the American Society of Gastrointestinal Endoscopists (ASGE) and Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) on NOTES [7], a number of barriers were outlined and discussed by selected members of SAGES and ASGE. These include endoscopic access to the peritoneal cavity, endoscopic closure of a gastrotomy, prevention of infection, development of an endoscopic suturing device, development of an endoscopic anastomotic device (nonsuturing device), spatial orientation, development of a multitasking platform, management of complications, and outlining physiologic unanticipated events.

Bacterial contamination of the abdomen was of great concern in this study, as outlined in the NOSCAR white paper. To date, investigation of NOTES has been limited to animal models to establish feasibility and the techniques necessary to perform this type of procedure. Issues relating to infection and contamination of the peritoneal cavity

during transluminal access must undergo human studies. Prior to institution of this trial we investigated the bacterial contamination of the peritoneum that occurs while a gastrotomy is open to the peritoneum and instrumented during laparoscopic Roux-en-Y gastric bypass. Fifty patients were studied and, although contamination of the abdomen was documented, no clinically significant contamination of the peritoneal cavity was observed with no abscesses or infectious complications. Patients did experience an increase in the number of colony-forming units (CFU) after gastrotomy but in only five patients did cross-contamination between a gastric aspirate and the contaminated peritoneum occur [9]. This data, combined with the fact that all patients undergoing this protocol required a gastrotomy during the course of their palliative procedure or resection, ensures patient safety and eliminates the creation of an unnecessary gastrotomy and exposure to additional risk.

A number of lessons have been learned after application of this technique to 10 human subjects. The access site to the peritoneum through the gastric wall is the most important factor to determine ability to visualize the right upper quadrant. The gallbladder and right lobe of the liver are difficult to visualize unless the gastrotomy is created on the most distal aspect of the stomach. Ultimately, the site chosen for the creation of a gastrotomy was made by the endoscopist utilizing both endoscopic and laparoscopic views to direct safe access. The endoscopist realized that a trade-off exists between the creation of a site distally on the stomach to ensure incorporation in a gastric resection and adequate visualization of the right upper quadrant versus a more-proximal posterior site on the gastric wall for incorporation into a gastrojejunostomy. We have no ideal position to balance these issues when choosing a gastrotomy site.

Our ability to manipulate intra-abdominal organs with the endoscope is limited and may lead to a substandard abdominal exploration. Whether this is clinically significant needs to be studied further. In our study, in the single patient whose endoscopic exploration did not corroborate the laparoscopic exploration, the only visible lesion was biopsied laparoscopically and was not available to the endoscopist. Additionally, two patients had lesions of interest but these could not be sampled endoscopically due to difficulties with positioning of the endoscope within the peritoneum relative to the suspicious lesion. A single inline biopsy channel effectively limits the options available to the endoscopist for biopsy. Although of clinically incidental significance in this population of patients, we were able to recognize other intra-abdominal pathology, with the identification of a right inguinal hernia in two patients and an incarcerated umbilical hernia not recognized at laparoscopy in one patient. Visualization of the anterior abdominal wall is superior under endoscopic visualization

compared to standard laparoscopy. This is clearly due to the unique perspective allowing us to look up to the abdominal wall rather than looking back as required with standard laparoscopy and angled laparoscopes.

NOTES has several potential advantages over standard laparoscopy. These include less physiologic insult, improved cosmesis and offering therapies outside of an operating-room environment. Abdominal exploration may be considered in rural areas or facilities that do not have an operating suite. It may allow care providers other than surgeons to explore the abdominal cavity for diagnosis or staging. Application of these techniques will require the development of new technologies and instrumentation. The marriage of standard laparoscopy and endoscopy into a unique, flexible operating system to allow access through a single site will make NOTES techniques possible and advance laparoscopic techniques.

This pilot study serves as a first step towards the investigation of more-advanced techniques such as appendectomy, cholecystectomy or those that have yet to be envisioned. Instrumentation and technological advances must be made before this type of extirpative procedure can be performed. Careful consideration for patient safety and safe application of NOTES procedures through IRB protocols will effectively advance investigation in this area. Unnecessary risk avoidance is paramount as we must learn from mistakes made during the introduction of new laparoscopic procedures.

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