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ASGE/SAGES Working Group on Natural Orifice Translumenal Endoscopic Surgery

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The growing capabilities of therapeutic flexible endoscopy have ushered in a new era in the treatment of gastrointestinal conditions. Refinements in laparoscopic surgery have progressed to the point that complex surgical procedures, such as gastric bypass, can now be performed in a minimally invasive fashion. These trends have set the stage for the development of even less invasive methods to treat conditions in both the gut lumen and in the peritoneal cavity. It seems feasible that major intraperitoneal surgery may one day be performed without skin incisions. The natural orifices may provide the entry point for surgical interventions in the peritoneal cavity, thereby avoiding abdominal wall incisions. In the first published description, Kalloo et al. [1] demonstrated the feasibility and safety of a per-oral transgastric endoscopic approach to the peritoneal cavity with long-term survival in a porcine model. This was soon followed by other transgastric peritoneal procedures in the porcine model, including tubal ligation, [2] cholecystectomy, [3] gastrojejunostomy, [4] splenectomy, [5] and oophorectomy with tubectomy [6, 7]. Although there are no publications, Rao et al. have described transgastric appendectomy in humans (personal communication). There have been two excellent editorials on this potentially emerging field. [8, 9]

To discuss this vision, 14 leaders from the American Society of Gastrointestinal Endoscopy (ASGE) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) met in New York City on July 22 and 23, 2005. The participants are listed in Table 1. All agreed that Translumenal Endoscopic Surgery could offer significant benefits to patients such as less pain, faster recovery, and better cosmesis than current laparoscopic techniques. The group identified the barriers that needed to be surmounted for the development of translumenal endoscopic intraperitoneal surgery and developed a list of next steps and guidelines to move this concept ahead.

Taxonomy

Although initial procedures have been performed via a transgastric route, it is conceivable that other routes of access to the peritoneal cavity may be preferable (such as transvaginal or transcolonic). The group therefore agreed that the term Natural Orifice Translumenal Endoscopic Surgery (NOTES) best described the emerging field. Inclusion of the word Surgery was felt to be essential because tissue resection and repair is the ultimate goal of accessing intraperitoneal organs. The participants of the retreat named the working group as the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR). It was immediately acknowledged by all that many key investigators in this growing field were not present at this initial meeting and the intent was to expand participation in NOSCAR to those meeting the following criteria:

1. Must have a multidisciplinary team, such that the team possesses both advanced therapeutic endoscopic skills and advanced laparoscopic skills.
2. Should be SAGES and/or ASGE members.
3. Must have animal laboratory facilities to perform research and training.
4. Must agree to share lab results with other NOSCAR members at semiannual group meetings.
5. Must agree that any and all human procedures be performed only after obtaining Institutional Review Board approval (IRB).

*Group members and affiliations are listed in Table 1 on page 330.

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Table 1. SAGES/ASGE Working Group on Natural Orifice Translumenal Endoscopic Surgery

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Case Western University School of Medicine
William Richards, MD
Vanderbilt University Medical Center
Richard Rothstein, MD
Dartmouth-Hitchcock Medical Center
Nathaniel Soper, MD
Northwestern University School of Medicine
Lee Swanstrom, MD
Oregon Health Sciences University
Christopher Thompson, MD
Brigham & Womens Hospital

6. Must submit all cases to an outcomes registry that will be maintained by the sponsoring societies.

Fundamental challenges to the safe introduction of NOTES

The group was surveyed prior to gathering in New York about the potential barriers to performing NOTES, and each of these barriers was discussed in depth (Table 2). There were significant differences of opinion between surgeons and endoscopists of the importance of certain barriers, particularly prevention of intraperitoneal infection, the need to maintain spatial orientation, the need for a stable platform, and the management of intraperitoneal complications. There was immediate consensus on the criticality of a secure gastric closure, understanding the physiologic changes likely to be caused by NOTES, and the need to train adequately before performing these procedures. Over the course of the meeting, views were exchanged and consensus was achieved on nearly all items.

Peritoneal access

Achieving access to the peritoneal cavity in and of itself was not felt to be a barrier, but the optimal techniques to do so as well as the optimal location for access are unknown. Most investigators are using a modified PEG technique, entering the peritoneal cavity through the anterior gastric wall and then dilating the tract to 18 mm with a balloon dilator. Other investigators are tunneling through the gastric wall in a manner that creates a flap valve to simplify gastric closure or are using an endoluminal grasping technique to cut through the stomach. The optimal puncture site for performing a cholecystectomy is likely to be different than for performance of a splenectomy or gastrojejunostomy. It is even conceivable that a transcolonic (i.e., hepatic flexure) approach may be the best route for performing a cholecystectomy. These are important considerations to be worked out as procedure development occurs.

Gastric closure

If NOTES is to reach human trials, a 100% reliable means of gastric closure must be developed. The puncture site(s) can be closed by sutures, clips, or a technically simple closure device. Animal work to date would suggest that a solitary puncture site can be closed fairly readily by any of the above methods. However, if two or more instruments are passed through the gastric wall at different sites, there is potential for shearing forces to develop and complicate closure. Surgeons in the group noted that anastomotic leaks are seen in up to 10% of laparoscopic gastrojejunostomies when tested in the operating room and thus felt evaluation of the integrity of the gastric closure should be part of the intraoperative protocol to ensure safety of the first transgastric procedures. A 1% to 2% leak rate is not acceptable given the safety of other minimally invasive approaches to cholecystectomy, tubal ligation, etc. Therefore, this is a critical area of very active research and development at the moment. Most animal experiments have been performed in porcine models, and it is possible that other models are more suitable to test gastric closure devices prior to human use.

Prevention of infection

The use of a transgastric route to access the peritoneal cavity may increase the risk of intraperitoneal contamination and infection. In early laboratory work, intraperitoneal abscesses were occasionally observed; however, maneuvers to sterilize the stomach prior to gastric puncture, as well as use of a sterile overtube, seem to have reduced the incidence of intraperitoneal abscesses, provided that the gastric closure is secure. To date, no one has quantified the bacteriologic load that the peritoneum is exposed to during a transgastric procedure. There is extensive surgical experience with bacteriologic contamination of the peritoneum during bowel surgery, and this is usually well tolerated, provided the patient receives prophylactic antibiotics and gross spillage is avoided. Therefore, the group felt that although more study of this problem is needed, it was unlikely to pose a major barrier to procedure development.

Suturing and anastomotic devices

This topic created perhaps the widest diversity of opinion among the working group. Many felt that the

Table 2. Potential barriers to clinical practice

Access to peritoneal cavity
Gastric (intestinal) closure
Prevention of infection
Development of suturing device
Development of anastomotic (nonsuturing device)
Spatial orientation
Development of a multitasking platform to accomplish procedures
Control of intraperitoneal hemorrhage
Management of iatrogenic intraperitoneal complications
Physiologic untoward events
Compression syndromes
Training other providers

ability to suture would ultimately be an essential skill. Suturing would provide maximal flexibility for the therapist to handle a wide variety of problems. However, the group acknowledged that laparoscopic cholecystectomy was introduced prior to the widespread adoption of laparoscopic suturing capabilities and that the initial translumenal procedures would likely be those that did not require this capability. Some working group members remained concerned that for gastric closure to even be ready for human trials, suturing capability will be needed for correcting inevitable (even if rare) failures of mechanical device closures. The early devices for endoscopic suturing have been cumbersome, but there is active research and development in this area. The group felt that it was essential to remain open to other methods of tissue approximation such as biologic glues and laser welding. As more complex procedures develop, there will be a need for anastomotic devices. Because suturing appears as though it will be cumbersome, mechanical devices that create an air- and water-tight anastomosis will ultimately be needed. The ability to use modifications of current stapling devices delivered via flexible endoscopes would seem a desirable goal.

Maintaining spatial orientation

Gastroenterologists are accustomed to working in line with their camera and light source because all instruments pass through working channels on the endoscope. Laparoscopic surgeons working in larger spaces and with multiple instruments and access ports, however, are acutely aware of the problems that develop when working off the axis of the camera angle (i.e., off axis). Many NOTES procedures will be performed with the endoscope in a retroflexed position and require secondary (perhaps even percutaneous) access sites creating situations in which the image is upside down and an off-axis manipulation is required. With experience, some of this spatial incongruity may be overcome, though it will prevent complex procedures from being performed with the speed and facility that total in-line visualization would allow. This was perceived as a major barrier to performing advanced procedures (i.e., those procedures that would require two or more instruments and assistants). Potential solutions include incorporating visualization systems into the platform technology discussed below, electronic image stabilization/inversion, and the use of multiple cameras to achieve the appropriate in-line view of the working area. *If* the principles learned in advanced laparoscopic operations are applicable to NOTES, then orientation, as well as triangulation, will be fundamental requirements for any NOTES surgical system.

Development of a multitasking platform

For the simplest transgastric procedures (e.g., peritoneoscopy, specimen retrieval) a multitasking platform may be unnecessary. However, for NOTES to develop further, a multitasking platform is critical. Many important maneuvers for manipulating tissue are difficult to perform, even with a two-channel endoscope. For example, aggressive grasping of tissue to set up traction and counter-traction for exposure and division of structures is currently not possible. The flexibility of the endoscope, which provides a great advantage for traversing the gut lumen, is a disadvantage when applying force to tissue because it is very difficult to both push and pull at the same time. Fixation and stiffening the endoscope will be essential for translumenal procedures. Because these procedures will require a team to manipulate instruments, devices with multiple ports are likely to be important. The role of robotics in this area seems promising, though a great deal of development work remains to be done. Voice activation technology may ultimately play a role in giving the therapist control of multiple devices, but initial development should focus on manual tools that ultimately can be modified for robotic control.

Management of intraperitoneal complications and hemorrhage

Clearly the best way to manage complications is to perform procedures in such a fashion as to minimize risk. However, it seems inevitable that as more complex procedures are performed, intraperitoneal complications such as bleeding, bowel perforation, and splenic injury will occur. The management of significant complications solely with current transgastric devices would be difficult. The working group felt it essential that surgeons and gastroenterologists perform these procedures as a team in a fully equipped operating room with the patient under general anesthesia. Managing these complications requires recognition and timely intervention. With refinement of endoscopic suturing techniques, repair of injured organs may take place via the translumenal platform. Until that time, however, it seems prudent that procedures be performed either as hybrid procedures (i.e., combined translumenal and laparoscopic) or that laparoscopic backup is instantly available. Although it is anticipated that many of the complications will be those that surgeons have experienced in laparoscopic and open surgery, there may be a new set of complications that are unique to NOTES. Therefore, it is essential that all cases are reported to a

central registry that can track complications and spot trends or unique complications that an individual investigator might not appreciate. Rapid dissemination of this information is felt to be one of the key functions of NOSCAR.

Physiologic untoward events caused by NOTES

The physiology of pneumoperitoneum has been extensively studied, but it is not known whether pneumoperitoneum during NOTES will behave in an identical fashion to laparoscopy. One participant in the working group reported wide fluctuations in intraperitoneal pressure during a recent animal experiment. Insufflation through flexible endoscopes is currently not pressure controlled, and the flow rate is much less than that of a typical laparoscopic insufflator. The tightness of the seal by the stomach around the flexible endoscope may vary with tissue characteristics and, hence, the flux of gas and maintenance of pneumoperitoneum may require better instrumentation. Another concern is loss of domain if the bowel is opened because air or CO_2 can enter the bowel, causing massive bowel distention. Because intraperitoneal pressures in excess of 15 mm Hg are detrimental, systems that control intraperitoneal pressure are needed. The working group also discussed whether or not insufflation should occur with CO_2 or room air. Although room air does not support combustion and hence is probably safe, CO_2 offers the advantage of rapid absorption and therefore is probably the gas of choice for establishing and maintaining pneumoperitoneum.

Training

Clearly the boundary between GI surgery and therapeutic GI endoscopy is already blurred. Although some institutions are developing training programs for digestivists incorporating both surgical and gastroenterologic training, it seems likely that in the short term, a multidisciplinary team is needed for any institution that wants to perform NOTES. In the long term, there may be turf and credentialing issues for people performing NOTES, but for the near term, teamwork and communication among interested parties is critical. It is too early to establish guidelines for training when the NOTES procedures barely exist and there is very little human experience. However, the fundamental skill set necessary to perform NOTES is apparent and, therefore, the working group requires that training should occur as a team in a facility with good animal resources and equipment. The initial cadre of NOTES physicians will likely need to train each other. Their experiences need to be carefully documented and reported Poor outcomes by physicians not thoroughly trained in NOTES procedures could lead to premature regulatory intervention, preventing development of a technology that would ultimately benefit many patients. As procedures are developed and subsequent safety and efficacy are established, guidelines for training, as well as courses, can be developed by SAGES and ASGE.

Table 3. Recommended initial animal laboratory studies for NOTES

- Bacteriologic assessment of gastric fluid after irrigation with antibiotics versus saline solution
- Assessment of intraperitoneal pressures during various insufflation and surgical techniques
- Assessment of security of various gastric closure devices
- Evaluation of postoperative gastric motility and function after NOTES

NOTES: moving forward

For NOTES to mature into a viable technology, both procedure and device development must continue. At this stage, NOTES must be performed by a team that has the skills of an advanced therapeutic endoscopist and a laparoscopic surgeon, who in many instances will bring unique but complementary skills. There are a number of other fundamental issues, many of which are detailed above, that need to be understood prior to the safe introduction of NOTES. These are best addressed in laboratory settings (Table 3). Having supportive laboratory data is an essential step prior to approval from regulatory agencies like the FDA or IRBs for performing initial NOTES in humans. The most important areas for initial study are the following: gastric sterilization/intraperitoneal contamination, safe peritoneal access and secure gastric closure, image display and maintenance of spatial orientation, development of stable working platforms, physiologic perturbations, and tissue approximation methods (suturing and others). NOSCAR believes that these efforts ought to be coordinated in order to achieve results in the most efficient manner. SAGES and ASGE are organizationally suited to obtain funding and coordinate grants to address the specific issues above. Funding for this research should come from a combination of industry and governmental agencies with the research committees of the Societies acting as grant reviewers.

The first human procedures must be IRB-approved and recorded in a registry. Results of such work, even if unfavorable, should be reported at the Societies' national meetings and at related programs. If deemed feasible, then early comparative trials of NOTES versus laparoscopic alternatives should be encouraged.

The leadership of SAGES and ASGE is hopeful and enthusiastic about this burgeoning new field and is committed to safely developing and introducing a technology that may benefit patients as the next wave of minimally invasive therapy.

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