NOTES: Past, Present & Future

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The concept of Natural Orifice Translumenal Endoscopic Surgery (NOTES) has grown in acceptance since 2000 at the time of its introduction. NOSCAR has outlined the major obstacles to ensure a safe transition to clinical practice providing a framework to tackle some of the hurdles and foster its growth. As a result, many investigators (Gastroenterologists and Surgeons) have developed innovative solutions to some of the problems facing this burgeoning field. Developments in techniques of peritoneal access, closure, surgical techniques and equipment modification have already been published and intensive research is ongoing. Current and future endoscopists will reap the benefit of this research since many techniques and devices that are developed for NOTES will enhance our ability to perform lumenal intervention including polypectomy, endoluminal hemostasis and submucosal resection.

The first human NOTES appendectomy by Rao and Reddy led the way to other pioneering work in humans. Transvaginal and transgastric cholecystectomies have been performed successfully in Europe, Latin America and the United States. Thus far these procedures were performed without any complications under an IRB approved protocol and supervision. These results are encouraging and are cause for enthusiasm for the future widespread application of NOTES.

Where do we go from here? What do we envision for NOTES? NOTES is not yet accepted into clinical practice and so is it untimely to predict its future role? However ideas that seemed possible only in Hollywood movie sets are close to becoming a reality. To predict the future, it is also important to look back at the past. The lessons garnered from laparoscopy have both forecasted the need for caution and for some, stimulated great enthusiasm for NOTES. The current popularity of laparoscopic intervention is a result of its less post operative stress, pain, short recovery and less scarring as compared to open surgery. NOTES with its potential for “scarless” surgery will be a strong driving force for its acceptance by the general population that is ever image conscious. The same benefits of laparoscopy over open surgical approach may be surmised when comparing NOTES to laparoscopy. Currently, advanced endoscopic procedures can be performed using deep sedation raising the possibility that, unlike laparoscopic and open surgery, transluminal procedures could be performed without general anesthesia and endotracheal intubation.

We will now attempt to predict the future of NOTES by describing potential applications for certain clinical scenarios and conditions. These concepts are for the most part early in laboratory evaluation.

**NOTES for Peritoneal Interventions in the Intensive Care Unit**

Patients in the intensive care setting have multiorgan dysfunctions that preclude transportation and major surgical interventions. NOTES may avoid the issue of transportation to an operating room allowing for bedside intervention. One example that has been described in the laboratory is diaphragmatic pacing for patients who are difficult to wean from ventilators. This has been shown by laparoscopy to benefit select patients. NOTES has already been performed to rescue a displaced PEG tube using the transgastric route in an ICU patient. NOTES may be a more practical approach to diagnose ischemic bowel in the ICU patient who have contraindications for a more definitive imaging study such as a CT or MRI.

**NOTES for Prehospital Management of Trauma**

Prehospital management of critical patients has resulted in improved outcomes. This is mainly due to the proper
resuscitation of patients and appropriating triaging. Despite these developments many patients with blunt or other urban related injuries do not make it to the hospital because of improper triaging and stabilizing measures. NOTES can become an integral and critical step in this setting since all instruments that are required are portable and can be fit into current emergency care vehicles. Imagine a scenario where a patient involved in motor vehicle accident with splenic trauma is given proper triaging and stabilizing hemostasis measures before reaching the hospital where traditional and more definitive surgical approaches can be performed. All these, of course could only be attained if there are more refined tools to enable easy access and closure of the access site with minimal risk of infection and without adding time needed to transport the patient to the hospital.

**NOTES for Acute Management of Blunt Trauma**

The use of NOTES as a method of achieving immediate assessment of organ injury and repair is theoretically possible. The minimally invasive nature due to the lack of abdominal incision and a need for a general anesthesia makes NOTES an attractive approach for use in the pre-hospital trauma/disaster setting.

In a preliminary study performed at our laboratory we were able to demonstrate the feasibility of NOTES in the assessment of penetrating abdominal injury. We performed a controlled injury to intraabdominal organs (liver, spleen, kidney and small bowel loops) under laparoscopic guidance using a laparoscopic shears. Transgastric peritoneal access was then attained using a PEG like approach by an operator blinded to the sites of organ injury. The finding of NOTES was compared to laparoscopic findings. The peritoneal cavity was systematically examined including the anterior abdominal wall, the diaphragmatic dome, liver, spleen and both kidneys was possible in all animals. The mean duration from the time of entry to the peritoneum to identification of lesion was 11 minutes. The mean duration of identification of site of injury based on the organ was 12 minutes to the liver, 15 minutes to the spleen, 17 minutes to the small bowel, and 6 minutes to the kidneys. The difference in the mean time in the identification of was significant in that injury to the anterior liver surface was identified more quickly as compared to injury to the small bowel. Based on these results we concluded that NOTES provided rapid and accurate identification of organ injury for penetrating wounds to the abdominal viscera.

Our group also assessed the feasibility of achieving hemostasis after organ injury using nonthermal hemostatic mechanisms. In this study three non thermal methods of achieving hemostasis were compared. The first group was randomized to QuikClot (QC; Z-Medica, Wallingford, CT) which is a granular zeolite powder with 1% residual moisture that, when placed on a bleeding wound, adsorbs water in an exothermic reaction, thereby concentrating platelets, erythrocytes, and clotting factors at the site of application. It has been tried in the battlefield with excellent success rate in achieving hemostasis. Several studies including a swine liver injury model have also shown its effectiveness as a hemostatic agent in life threatening bleeding. The second group was randomized to Oxidized regenerated cellulose is also used adjunctively in surgical procedures to assist in the control of capillary, venous, and small arterial hemorrhage when ligation or other conventional methods of control are impractical or ineffective. The third groups of animals were randomized to SHISH - a novel bioabsorbable hemostatic agent (Cook bioengineering prototype material).

The anterior liver surface was then lacerated using a laparoscopic shear to create a grade three (>3 cm) liver laceration. Modified endoscopic delivery systems were used for the delivery of the hemostatic agents. The oxidized regenerated cellulose (ORC) was placed effectively covering the site of injury in all animals. Delivery of the QC granules to the site of bleeding was also straightforward. Accurate placement of the granules to the site of injury was achieved in all animals. In the third group of animals SHISH was also able to be applied with resulting hemostasis in all animals. There was no statistically significant difference in the time to achievement of hemostasis between the QC and ORC group (p=0.33). The conclusion from these studies was that intraperitoneal hemorrhage can be easily and quickly controlled with these novel endoscopic therapies.
NOTES: Evolving Beyond the Traditional Operating Room

In today’s world where building the future operating room is a multibillion dollar industry, NOTES maybe a cost effective solution especially for procedures in the abdominal cavity. Given that the development of accessories and other integral components of NOTES needs to take place, by keeping the focus of sterility to the gastrointestinal tract, instruments and accessories, the need for the sterile operating room environment could be eliminated. The potential cost reduction is staggering since the cost of using an OR is obviated as is the use of transportation staff, operating room energy and operating costs. The fact that NOTES can also be performed not under general anesthesia but under sedation also will have a great impact in obviating the need for post operative ventilator complications including vent dependency.

NOTES in Developing Countries

Surgical care is not considered a priority in many developing countries due to scarcity of health care resources. Despite this many untreated conditions lead to preventable deaths and to chronic conditions that could have been managed effectively. Currently general surgical procedures are cost effective at the district level in most Southeast Asian and sub-Saharan African countries. Majority of the population though reside in the rural areas far from these districts hindered by poor road and transportation infrastructure. Due to these hurdles NOTES can play a major role in averting preventable surgical deaths since it does not require general anesthesia, a sterile operating room and may be performed by a highly mobile, portable easily disinfectable instruments. Other factors for the poor health care delivery in those countries, such as lack of trained healthcare personnel and economic ability need to be eliminated before this dream can be a reality.

Robots for NOTES

The concept of deploying a mobile robot via NOTES into the peritoneal cavity may appear very futuristic. This limitation may be solved by using robotics and this technique has been shown to be feasible by Rentschler et al. A 12 mm diameter in vivo robot was advanced into the gastric cavity using a sterile overtube and was able to traverse within the cavity under endoscopic guidance. The robot with its helical wheel was able to navigate the gastric lumen with no apparent tissue injury. In the peritoneal cavity, the robot successfully navigated and maneuvered several organs including the liver and small bowel. Development of an in vivo robot with camera and multipurpose arms capable of performing several tasks in addition to the endoscopic imaging will enable performance of moderately complex surgeries such as cholecystectomies. Furthermore, a robot with visual capabilities will help to overcome the problem of spatial orientation.

NOTES for Intrauterine Fetal Interventions

Although transabdominal, laparoscopic fetoscopy has proven to be a useful technique in human fetal surgery for such diseases as twin-twin transfusion syndrome and spinal meningomyelocele, it is still limited by rigid instruments and allowing only anterior access to the uterine cavity. In addition, the performance of intraperitoneal procedure by the traditional percutaneous route can have consequences of wound dehiscence and induction of preterm labor, NOTES can theoretically provide unlimited access to the uterus since the flexible nature and the straight shot direction from the transgastric route provide unparalleled access to the uterine cavity. Moreover, the absence of abdominal wall incision and general anesthesia also provide an added benefit to NOTES. Based on these assumptions our group evaluated the feasibility of NOTES in pregnant sheep. During this acute non survival experiment NOTES allowed visualization of the anterior, posterior and lateral walls of the uterus. In addition all intraperitoneal organs could also be identified and were easily accessible. Using endoscopic ultrasound the fetus, various body parts and placenta could be easily identified, Amniocentesis and intracardiac fetal interventions were
technically feasible with the EUS scope in the peritoneal cavity.17

NOTES for Spinal Procedures

Surgical spine procedures most commonly include trans-thoracic and posterolateral percutaneous approaches. Open surgical techniques require separation of musculoskeletal structures and traction of nerve roots to create an opening large enough to accommodate surgical tools. The morbidities associated with these surgical approaches include post-surgical neuralgia resulting from traction injuries to nerve roots, lacerations of the dura mater, scars from skin incisions, muscular atrophy or trauma. Minimal invasive surgical techniques including thoracoscopy and video-assisted thoracic spine surgery (VATS) have reduced the extent of percutaneous incisions and spreading open of the chest wall. Nevertheless, the consequences of a percutaneous access are not totally avoided and complications such as lung atelectasis and retropleural effusions from single lung ventilation are additional morbidities.19

NOTES provides a closer and direct anterior access to the vertebral column. In laboratory experiments we found that the proximity of the esophagus to the spine allowed immediate access to posterior mediastinum and excellent visualization of the entire thoracic vertebrae and intervertebral spaces via NOTES techniques. This innovative approach to the anterior vertebral column allows the development of novel spinal interventions under direct endoscopic guidance such as vertebroplasty and kyphoplasty for osteoporotic or pathological vertebral bone fractures, discectomies and interbody fusion for herniated discs, and release of the anterior ligament at different levels of vertebral column in patients with severe scoliosis. In addition, the lumbosacral spine could be also approached for anterior endoscopic procedures via trans-gastric access. The advantages of NOTES for spinal interventions are similar to anterior laparoscopic spinal surgery but without the limitations of rigid instrumentation. These benefits include maintenance and ease of restoration of intervertebral disc height, avoidance of removal of bone from the spine which is an integral component of posterior spinal surgery and preservation of normal spinal anatomy since this approach takes advantage of normal tissue planes with no removal of bone tissue. In addition the complications of posterior spinal surgery such as injury and damage of nerves from manipulation and retraction of nerves and hematoma around nerves that may cause scarring and chronic pain can be thwarted.20

Conclusion

Maybe it is premature to hypothesize on the future of NOTES when it yet has to reach clinical application. However NOTES offers exciting possibilities that cannot be ignored. It already has blurred the boundaries of specialties such as gastroenterology, surgery, gynecology and urology. It has challenged traditional principles which not only that have stood the test of time but have guided physicians for decades as to the boundaries of safe practice. The future of NOTES will be determined by the skill, imagination and ingenuity of physicians and engineers who dare to challenge conventional philosophy.

REFERENCES