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Development of Transvesical Port for Scarless Surgery

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Development of Transvesical Port for Scarless Surgery

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“Every great advance in science has issued from a new audacity of imagination”

John Dewey

À minha Mãe Virginia Rodrigues

À memória do meu avô Estêvão Rodrigues

À minha irmã Felicidade Lima e família

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Desenvolvimento da Porta Transvesical para Cirurgia Sem Cicatriz

RESUMO

A cirurgia endoscópica transluminal por orifícios naturais (N.O.T.E.S.) é uma área de investigação que está no limiar das novas técnicas cirúrgicas com aplicação em Humanos. Após a descrição do acesso transgástrico, e do seu inesperado sucesso como nova porta para acesso abdominal, duas evidências sobressaíram: i) a qualidade da imagem fornecida pelos gastroscópios é suficiente; ii) mas, o conceito de instrumentos usados através dos gastroscópios (flexíveis e paralelos) revelaram-se inapropriados. Nesta sequência, levantámos a hipótese de usar um acesso abdominal pélvico com o objectivo de superar muitas das limitações descritas para a porta transgástrica. Assim, ao descrevermos a porta tranvesical por um método rápido e seguro, criámos as condições necessárias para introduzir instrumentos rígidos de 5 mm na cavidade peritoneal por um acesso estéril. Embora o tamanho da porta transvesical seja restrito, o que nos limita o seu uso como porta isolada para realizar procedimentos cirúrgicos em que seja necessário remover orgãos ou estruturas de maiores dimensões, a porta transvesical revelou-se particularmente útil como porta acessória ao acesso transgástrico. Tal permitiu-nos desenvolver o conceito de 'acesso N.O.T.E.S. combinado transgástrico-transvesical', que nos permitiu executar procedimentos experimentais moderadamente complexos, exclusivamente por N.O.T.E.S., tais como a nefrectomia. Além disso, esta porta também foi testada como um acesso à cavidade torácica, o que prevemos possa ser praticável após o desenvolvimento de instrumentos mais apropriados (mais longos e articulados). Estas experiências demonstraram que quase todos os procedimentos intra-abdominais são exequíveis por acesso N.O.T.E.S. isolado ou combinado, mas demonstraram também, que não são facilmente aplicáveis em Humanos presentemente, porque o encerramento das portas transgástrica, transvesical e transcolónica não estavam ainda bem definidos. Nesta sequência, o nosso grupo investigou um novo método de encerramento endoscópico de perforações transvesicais usando 'T-tags' com suturas absorvíveis. A eficácia revelada por este método de encerramento permite-nos concluir que a porta transvesical está total e completamente caracterizada, havendo neste momento evidência suficiente para propor a sua aplicação em Humanos.

Development of Transvesical Port for Scarless Surgery

ABSTRACT

Natural Orifices Translumenal Endoscopic Surgery (N.O.T.E.S.) is an exciting field that is clearly pushing the boundaries of surgery as we know it. After description of the transgastric access and its unexpected success as a novel port for abdominal surgery, two major conclusions come out: i) the quality of the image provided by the gastroscopes is reasonable good for surgery; ii) but the concept of gastroscope-instruments (flexible and parallel) is not appropriate. In this sequence, we hypothesized that a lower abdominal acces such the transvesical approach would overcome many of the transgastric limitations. Thus, we could describe an easy and safe method to create a tranvesical port that allows the surgeons to introduce 5 mm rigid instruments into the peritoneal cavity through a sterile pathway. Although the limited size of the transvesical port does not allow us to use it as an isolated access for intra-abdominal procedures where organ removal, it revealed particularly useful as an accessory port to the transgastric access allowing us to develop the concept of 'transgastric-transvesical combined access', which revealed efficacious to perform experimentally pure N.O.T.E.S. scarless moderately complex procedures, such as nephrectomy. Moreover, this port was even tested as an access to the thoracic cavity, what we predict to be more feasible after development of proper instruments (longer and articulated). These experiments had demonstrated that almost all intra-abdominal procedures are feasible by pure isolated or combined N.O.T.E.S., but they also demonstrated that they are not easily translated for Humans because both creation and mainly closure of transgastric, transvesical and transcolonic ports are not well defined. In this sequence, we pursued the idea to discover a novel method to closure the transvesical hole endoscopically. This was reasonably achieved using T-fasteners with locking cinch using absorbable sutures. This methodology increases not only the viability of transvesical port in N.O.TE.S., but it also can have application in endoscopic urinary urology in Human field.

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Chapter 1

General Introduction

Minimally invasive surgery: a brief revision

The early history of laparoscopy is unknown to many surgeons, but endoscopy was first described by Hippocrates in Greece (460-375 BC) (Rosin et al., 1993). He made reference to a rectal speculum. The first simple speculum for gynecological endoscopy dates from about the same time. The Talmud refers to a siphopherot made of lead, bent at its tip with a mechul (wooden mandarin) used for inspection of the vagina. Roman medicine also produced instruments with which they could inspect internal organs (Bento and Hewlett, 1944). In Pompeii's ruins (70 AD), a three-bladed vaginal speculum was discovered; this instrument was similar to the current vaginal speculum (Gorden, 1993). Greek also transferred the teachings of medicine to the Arabs included the use of speculums. The Arabian Abulkasim (936-1013 A.D.) improved upon Hippocrates´ method by using reflected light to examine the cervix of utero (Bento and Hewlett, 1944). The next evolutionary step was fostered by Tulio Caesare Aranzi in 1585. Aranzi was the first to use a light source for an endoscopic procedure, focusing sunlight through a flask of water and projecting the light into the nasal cavity (Organ, 1933; Saleh, 1988; Gunning and Rosenzweing, 1991; Philipi et al., 1991). Thus, the interest for physicians to look into the "internal organs" has existed since the early days of medicine.

The credit for modern endoscopy belongs to Philipp Bozzini of Frankfurt - German (1773-1809) (Bozzini, 1806). He developed a light conductor which he called "Lichtleiter" to avoid the problems of inadequate illumination. This early endoscope combined reflecting mirrors, candles, and an urethal cannula to direct light into the internal cavities and then redirects it to the eye of the observer. This brilliant and unconventional pioneer was officially reprimanded by the local medical community for undue curiosity, having been so audacious as to place this instrument into the uretra of a patient and attempt direct bladder inspection. Although he died at age 36 of typhoid fever, Bozzini's invention established the principles that guided the development of endoscopy, and it inspired others to forge ahead in this new field. John D. Fisher (1798-1850) in Boston descrived an endoscope initially to inspect the vagina, but later he modified it to examine the bladder and urethra (Picatoste et al., 1980). In 1853, Antoine Jean Desormeaux, a French surgeon, invented the first endoscope that enabled the physician to actually see (Desormeaux, 1867). For many he is considered the "Father of Endoscopy." This instrument had a system of mirrors and lens, with a lamp flame as the light source; the endoscope burned a mixture of alcohol and turpentine. Burns, as might be imagined, were the major complication of these procedures. Desormeaux had initially contemplated using electricity, but abandoned that idea. This endoscope was mainly used for urologic cases. In 1869, Commander Pantaleoni used a modified cystoscope to cauterize a hemorrhagic uterine growth. Pantaleoni thus performed the first diagnostic and therapeutic hysteroscopy (Gunning and Rosenzweig, 1991).

Thomas Edison proved a new technologic breakthrough in 1879 with the invention of the electric light bulb. This allowed Maximilian Nitze of Dresden - German (1848-1906) and Josef Leiter of Vienna - Austria, in the same year, to introduce a rigid cystoscope with a built-in light source formed from an electrically heated platinum wire, a multilens system, and a separate water circulation system for cooling. Like the Lichtleiter from Bozzini, this instrument was only used for urologic procedures (Rather, 1976; Hausmann, 1987). Then, Newman in 1883 described using a miniaturized version of the incandescent bulb in a cystoscope and Boisseau de Rocher in 1890 introduced a Mignon lamp cystoscope that offered the first double channel for ureteral catheterization (Newman, 1888; De Rocher 1890).

In gastrointestinal field, in 1868, Kussmaul performed the first esophagogastroscopy, initiating efforts at instrumentation of the gastrointestinal tract (Haubrich, 1987). Mikulicz and Schindler, however, are credited with the advancement of gastroscopy, having designed gastroscopes equipped with both an optical system and a means to insufflate air (Haubrich, 1987). The use of rigid endoscopic instruments severely limited access to the gastrointestinal tract. A flexible instrument was requied to gain entrance into the duodenum or the colon proximal to the rectosigmoid junction. The necessary technology took over 100 years to be developed until Georg Wolf and Rudolph schindler (1932) introduced the first useful semi-flexible gastroscope to the market ready for use (Haubrich, 1987). All these developments were restricted to the inspection of organs through natural external access.

Laparoscopy has been evolving for more than 100 years, with the first experimental laparoscopy reported in 1901 by George Kelling a German surgeon from Dresden who was the first to apply Nitze´s cystoscope in combination with pneumoperitoneum in peritoneal cavity of a living dog. The pneumoperitoneum was created by injecting air through a sterile cotton filter in abdominal cavity with high-pressure air insufflation with the goal of stopping intra-abdominal bleeding (ectopic Pregnancy, bleeding ulcers, pancreatitis), but these studies did not find any response or supporters.. He noted that the abdominal cavity could store more than 2.5 liters of blood and he also considered intra-abdominal adhesions a contraindication for the procedure. George Kelling coined the term "*celioscopy*" to describe the technique (Kelling, 1901). Also in 1901, Dimitri Ott, working in Petrograd described "*ventroscopy*", a technique in which a speculum was introduced through an incision in the posterior vaginal fornix. Ott wore head mirrors to reflect light and augment visualization (Ott, 1901).

During late 1910 and early 1911, Hans Jacobaeus, from Stockholm, used the term "*laparothoracoscopy*" for the first time (Jacobeus, 1911). By 1912 he had performed closed-cavity endoscopy with a Nitze cystoscope in over 100 patients with ascite and also described liver pathology, peritoneal tuberculosis, and tumours. He also suggested employing similar techniques to examine body cavities endoscopically. Following this he devoted most of his attention to thoracoscopy. He published his report on laparoscopy and thoracoscopy in humans in *Münchener Medizinische Wochenschrift*. A response by Kelling appeared two months later in the same journal, disputing Jacobaeus' claim to be the first to perform the procedure in humans, stating that he had successfully used celioscopy in two humans between 1901-1910. Unfortunately, Kelling had made a mistake: he did not publish his work. Interestingly, in Jacobaeus' paper in 1911, he viewed thoracoscopy as a more promising procedure than laparoscopy. He also reported in 1923 the first bleeding complication requiring laparotomy (Harrell and Heniford, 2005).

In 1911 Bertram Berheim, an assistant surgeon at Johns Hopkins, performed the first laparoscopy in the United States, before he learned of the work of Kelling and Jacobaeus. He published his laparoscopic experiences entitled, "*organoscopy*", in the Annals of Surgery (Bernheim, 1911). The instrument was a proctoscope of a half-inch diameter, and he used ordinary light for illumination. Orndoff, an internist from

Chicago, reported the first large series of peritoneoscopies (42 cases) in the United States in 1920 (Orndoff, 1920). One of his innovations was a sharp pyramidal trocar point. In 1923, Kelling reported his 22 years of experience with laparoscopy to German Surgical Society. Kelling became one of the earliest advocates of minimally invasive surgery. He encouraged surgeons to use diagnostic laparoscopy in order to spare patients the prolonged and costly stay of a laparotomy.

Over the next 40 years, specific instruments were developed to allow for an accurate and complete examination of the peritoneal cavity. Pneumoperitoneum was maintained initially through syringe injections until Otto Goetze developed a manual insufflator with a foot pump in 1921 (Harrell and Heniford, 2005). Zollikofer a Swiss gynecologist used carbon dioxide to obtain a pneumoperitoneum in 1924 because it was absorbed faster and minimized the risk for explosion (Gaskin et al., 1991). In 1929 Heinz Kalk, a German gastroenterologist considered the founder of the German School of Laparoscopy developed a 135-degree lens system and a dual trocar approach (Kalk, 1929). He used laparoscopy as a method of diagnosis for liver and gallbladder disease. Therapeutic applications began in 1930. Fervers, a gynaecologist, initiated this process with the laparoscopic adhesiolysis using electrocautery (Harrell and Heniford, 2005). In 1934 an American internist, John Ruddock, described laparoscopy as a good diagnostic method, many times superior to laparotomy. His developed a specific lens system and biopsy forceps to be used in laparoscopy (Ruddick, 1934). Then he reported his results in 500 patients (Ruddick, 1937). Boesch of Switzerland performed a tubal ligation using endoscopic electrocoagulation in 1936. Internists also appreciated the usefulness of this technique to provide biopsy speciments of liver pathology (Harrell and Heniford, 2005).

A major advance occurred in 1938 when Janos Veress of Hungary developed the spring-loaded needle for draining ascites and evacuating fluid and air from the chest. Its main purpose was to perform therapeutic pneumothorax to treat patients suffering from tuberculosis (Varess, 1938). He used it in over 2000 cases. He did not suggest that it be used for laparoscopy. Its current modifications make the "Veress" needle a perfect tool to achieve pneumoperitoneum during laparoscopic surgery. In 1944, Raoul Palmer of Paris performed gynecological examinations using laparoscopy and placing the patients in the Trendelenburg position so air could fill the pelvis (Palmer, 1947). He also stressed the importance of continuous intra-abdominal pressure monitoring during a laparoscopic procedure. Harold Hopkins was responsible for the two most important inventions in endoscopy after World War II: the rod-lens system and fiberoptics. These improvements allowed a brighness and the true color to the endoscopes that had not been possible before. In addition, the light source was removed from the tip of the insruments, and this decreased the risk for intra-abdominal thermal injuries (Harrell and Heniford, 2005). Hasson, a gynecologist from the Grant Hospital of Chicago, Augustana Hospital and Columbus-Cuneo Medical Center, published in the American Journal of Obstetrics and Gynecology on July 15, 1971 his paper named: "A modified instrument and method for laparoscopy." He developed a technique performing laparoscopy through a miniature laparotomy incision (Hasson, 1971).

Despite such advances in laparoscopic imaging and technique, several troublesome problems persisted. Bowel and vascular injuries during trocar insertion continued to occur. No scientific knowledge existed regarding the dangers of increased intraabdominal pressure. These dangers severely restricted the use of laparoscopy. Few surgeons judged that the advantages of laparoscopy outweighed the inherent’s risks of the technique. Additionally, remarkable discoveries were made that created modern surgery in this same period of time. Anesthesia and antisepsis made elective surgery a reality. Antibiotics decreased the mortality of surgeries and as a result complex surgeries never before realistically attempted became possible. As the complexity of surgeries increased, the doctrine of surgical exploration expanded exponentially. It was the begining of the aforism “*Big Surgeon Big Incision*”.

During the 1960s, Kurt Semm, a German gynecologist, invented the automatic insufflator for monitoring the pressure of CO2 pneumoperitoneum. His experience with this new device was published in 1966 (Harrell and Heniford, 2005). But, Semm also made and designed many new instruments included tissue morcellators, suction-irrigation systems, laparoscopic endocoagulation, and laparoscopic scissors. He played a major role in the development of laparoscopy. He called his procedure "*Pelviscopy*” to avoid the negative connotations laparoscopy seemed to be attracting. He performed the first laparoscopic appendectomy in 1983 during a gynecological procedure and opened a large door for a new surgery, although he was almost removed from the Germany Physician Society because of that procedure (Semm, 1983). Although Semm was not recognized in his own land, on the other side of the Atlantic, both American physicians and instrument makers valued the Semm insufflator for its simple application, clinical value, and safety.

In England, in 1980, Patrick Steptoe started to perform laparoscopic procedures in the operating room under sterile conditions. In 1981, rules and requirements to perform laparoscopy were adopted by many hospitals and surgical societies. The American Board of Obstetrics and Gynecology made laparoscopy training a required component of residency training (Phillips et al., 1974; Reich, 1989).

In 1985, Erich Muhe reported the first laparoscopic cholecystectomy but the procedure was rejected by the German Surgical Society, and scepticism remained until 1993 when his pioneering efforts finally were recognized formally by the German Surgical Society (Reynolds, 1989; Litynski, 1998).

The first solid state camera was introduced in 1982. This was the start of "video-laparoscopy." The modern era of laparoscopy really started when the French general surgeon Philippe Mouret realized that laparoscopy could be used for more than just exploration, and in 1987 he performed the first video-guided laparoscopic cholecystectomy (Mouret, 1996). Within a year, Dubois (Paris), Perissat (Bordeaux), and Barry Mckernan and William Saye (United States) had performed laparoscopic cholecystectomy at their respective institutions on both sides of the Atlantic (Dubois et al., 1990; Mckernan, 1990; Litynski et al., 1999; Harrell and Heniford, 2005).

Only five years later, this procedure was acknowledged as the “gold standard” technique for the removal of the gallbladder (NIH Consensus Conference, 1993). Progress in acknowledging the laparoscopic potential in urology followed the same course, although the time scale was markedly truncated. Schuessler, in Texas reported his initial experience in pelvic lymphadenectomy (Schuessler et al., 1991). Although laparoscopic explorations for undescended testis had been done previous to this reported, its impact was marginal, with the procedure being dismissed as amenable to few patients with little other clinical applicability (Silber and Cohen, 1980). Soon afterward, techniques for the extraction of solid organs, including the adrenal, kidney, prostate and bladder, soon were developed (Clayman et al., 1991; Gagner et al., 1992; Schuessler et al., 1997; Guillonneau et al., 1999; Abbou et al., 2000; Gill et al., 2000; Rassweiler et al., 2001; Turk et al., 2001). Nowadays, practically all surgeries with exception of transplantation can be made by laparoscopy with advantages for the patients.

Basis for Natural Orifice Translumenal Endoscopic Surgery (NOTES)

The introduction of laparoscopic surgery will stand as the revolutionary episode that marked the end of the twentieth century. This new approach has completely revolutionized modern surgical practices, significantly changing the surgical way of thinking, surgical techniques, and all other aspects of modern surgical patient care (Harrell and Heniford, 2005).

Simultaneously, the endoscopy has changed progressively and dramatically over the last few decades and the evolution of this technique has been from simple diagnostic procedures to progressively more invasive one (Vitale et al., 2005). In this sequence, one of the last achievements of surgical endoscopy was the aggressive and efficacious gastric endoscopic mucosal resection. These procedures were progressively invading the visceral wall, and some anecdotally reports began to describe safe endoscopic procedures beyond the visceral wall, ie. transgastric drainage of pancreatic pseudocyst (Vitale et al., 2005). Supported by these reports, Reddy and Rao, and Kalloo et al described a new port to the peritoneal cavity through a transgastric approach in humans and pigs, respectively (Kalloo et al., 2004; Rattner and Kalloo, 2006). This was the dawn of a new era that open new perspectives for those dealing with abdominal minimally invasive surgery, making them to pursue novel audacious goals such as avoidance of incisions and even pain. In fact, the visceral wall is no longer a barrier for endoscopic intervention.

Subsequently, various authors described more complex intra-abdominal procedures such as ligation of fallopian tubes, cholecystectomy and cholecystogastric anastomosis, gastrojejunostomy, partial hysterectomy and oophorectomy (Jagannath et al., 2005; Park et al., 2005; Kantsevoy et al., 2005; wagh et al., 2005). The continuous evolution of new instruments and the unexpected success reported by those authors in porcine models with transgastric surgery seems to open a new era in surgical field: Natural Orifice Translumenal Endoscopic Surgery (N.O.T.E.S.). These techniques are likely less invasive than even laparoscopy because we don't have to cut through the skin and muscle of the abdomen, and it may prove a viable alternate to existing surgical procedures.

In this sequence, the development of other transvisceral approaches remained to be defined. This was the call for our experiments on transvesical surgery with or without combination with other natural orifices approaches in order to help the implementation of new intra-abdominal scarless procedures in what seems to be the 3rd generation surgery.

Objectives of the Thesis

This project aims to test the hypothesis that common abdominal and thoracic surgical procedures might one day be performed by natural orifices. In addition to avoidance of scars, the major rationale for this project emerges from the knowledge that viscera walls do not have sensitivity to cut. Furthermore, the increasing development image technology gives support to believe this goal is attainable soon. For all these reasons, it make sense to explore the hypothesis to perform surgery by natural orifices in what will be for sure a further step on minimally invasive surgical field. Thus, using the pig model and current instruments from urology and gastroenterology fields, we planned this PhD Thesis with the following objectives:

1) To develop novel strategies to introduce surgical instruments into peritoneal cavity sparing abdominal wall through transvesical pathway;

2) To test the feasibility, usefulness and safety of this peritoneal access alone or in combination to perform either abdominal or thoracic surgery;

3) To describe novels Natural Orifice Transluminal Endoscopic Surgical techniques for commom procedures such as peritoneoscopy, liver biopsy, thoracoscopy, lung biopsy and nephrectomy;

4) To assess the feasibility and safety of the new endoscopic closure method for transvesical perforations.

Chapter 2

Transvesical endoscopic port for abdominal surgery

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Transvesical Endoscopic Peritoneoscopy: A Novel 5 mm Port for Intra-Abdominal Scarless Surgery

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Purpose: Recently various groups reported successful attempts to perform intra-abdominal surgery through a transgastric pathway. We assessed the feasibility and safety of a novel transvesical endoscopic approach to the peritoneal cavity through a 5 mm port in a porcine model.

Materials and Methods: Transvesical endoscopic peritoneoscopy was performed in 8 anesthetized female pigs, including 3 nonsurvival and 5 survival animals. Under cystoscopic guidance a vesical hole was created on the ventral bladder wall with an open-ended ureteral catheter. An over tube with a luminal diameter of 5.5 mm was placed in the peritoneal cavity, guided by a 0.035-inch guidewire. In all animals we performed peritoneoscopy of the entire abdomen as well as liver biopsy and falciform ligament section. A vesical catheter was placed for 4 days in all survival animals, which were sacrificed by day 15 postoperatively.

Results: After a learning curve in the first 3 nonsurvival animals the creation of a vesical hole and placement of the over tube were performed without complication in all survival animals. In these animals we easily introduced an EndoEYE™ into the peritoneal cavity, which provided a view of all intra-abdominal viscera, as well as a 9.8Fr ureteroscope, which allowed simple surgical procedures without complications. In survival experiments all pigs recovered. Necropsy examination revealed complete healing of the vesical hole and no signs of infection or adhesions into the peritoneal cavity.

Conclusions: Transvesical endoscopic peritoneoscopy was technically feasible and it could be safely performed in a porcine model. This study provides encouragement for additional preclinical studies of transvesical surgery with or without combinations with other natural orifices approaches to design new intra-abdominal scarless procedures in what seems to be third generation surgery.

Key Words: swine, endoscopy, laparoscopy, peritoneal cavity

Since the late 1980s, a revolution has begun with the implementation of laparoscopic techniques that have gained progressive acceptance as the gold standard for an increasing number of intra-abdominal procedures.[1] In fact, there are many advantages to the laparoscopic approach, such as smaller incisions, decreased postoperative pain and more rapid patient recovery.

Recently Kalloo et al described a new port to the peritoneal cavity through a transgastric approach in a porcine model.[2] Subsequently various groups described more complex intra-abdominal procedures, such as fallopian tube ligation, cholecystectomy and cholecystogastric anastomosis, gastrojejunostomy, partial hysterectomy and oophorectomy.[3–6] The continuous evolution of new instruments and the unexpected success reported by these investigators in porcine models with transgastric surgery seems to have opened a new era in the surgical field, that is endoscopic transvisceral surgery.[7–11]

In this sequence the development of new transvisceral approaches remains to be defined. In this pilot study we assessed the feasibility and safety of the transvesical endoscopic approach to the peritoneal cavity with liver biopsy and falciform ligament section in a porcine model.

MATERIALS AND METHODS

This study was approved by the ethical review boards of Minho University, Braga, Portugal. Transvesical procedures were performed in 8 female pigs, including 3 in nonsurvival studies. Survival studies were done in 5 consecutive 35 to 45 kg female pigs (Sus scrofus domesticus). These 5 pigs were followed after surgery for 15 days before sacrifice and necropsy examination.

Pig Preparation

The animals were withdrawn from food for 24 hours and from water for 6 hours before the surgical procedure. All procedures were performed using general anesthesia with 6.0 mm endotracheal intubation with a Ruschelit® Super

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Study received approval from the ethical review boards, Minho University, Braga, Portugal.

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Safety Clear Tracheal Tube and mechanical ventilation. Pre-anesthesia medication consisted of intramuscular injection of 32 mg/ml azaperone (Stressnil®) reconstituted with 1 mg/ml midazolam (Dormicum®) at dose of 0.15 to 0.2 ml/kg.

Venous access was obtained through an intravenous line placed in the marginal ear vein. Anesthesia was induced with 3 μg/kg fentanyl (Fentanest®), 10 mg/kg thiopental sodium (Pentothal®) and 0.2 mg/kg vecuronium (Norcuron®). For infection prophylaxis all animals received an intramuscular injection of 1 gm ceftriaxone (Rocephin®) before endoscopy. Anesthesia was maintained with 1.5% to 2% sevoflurane (Sevorane®) and a perfusion of 1 mg/kg per hour vecuronium (Norcuron®).

Surgical Technique

An Olympus® A2281 cystoscope with an A22001A telescope was introduced through the urogenital sinus and urethra into the bladder with hydrodistention. Before any further procedure the bladder was emptied of urine and refilled with saline. The vesicotomy site was selected on the ventral bladder wall caudal to the bladder dome. Figure 1 shows the procedures. The cystoscope was then replaced by an Olympus® A2942A ureteroscope guided through a Terumo® guidewire to achieve the bladder. A mucosal incision was made with Olympus® A2576 scissors introduced by the working channel of the ureteroscope. Subsequently a 5Fr Selectip™ open-ended ureteral catheter was pushed forward through the incision into the peritoneal cavity (fig. 2).

A 0.035-inch flexible tip Terumo® guidewire was then inserted into the peritoneal cavity through the ureteral catheter lumen. Guided by the flexible tip guidewire the vesical hole was enlarged with the dilator of a ureterorenoscope sheath (Microvasive-Boston Scientific Corp., Natick, Massachusetts) enveloped by a flexible over tube. We designed this equipment with a length of 25 cm, internal diameter of 5.5 mm and wall thickness of 1 mm. Dilator passage over the guidewire and through the bladder wall spared muscle cutting. The ureteroscope was introduced into the peritoneal cavity in the over tube and allowed to create pressure controlled CO_2 pneumoperitoneum up to 12 mm Hg using an Olympus® UHI-3 Insufflator.

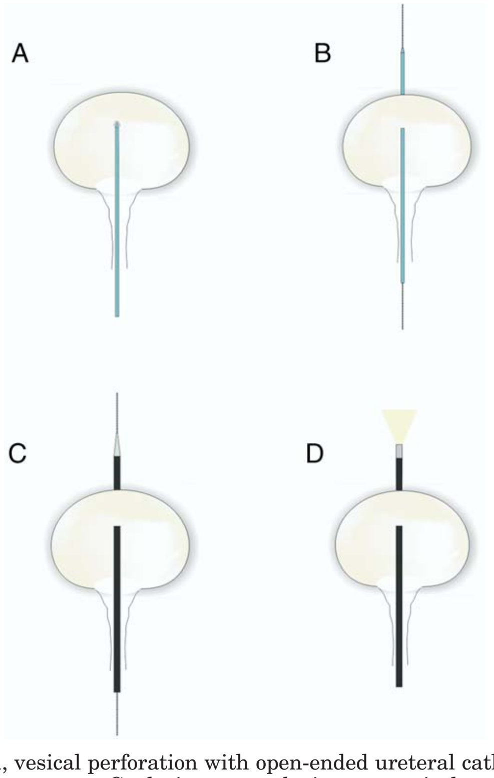

FIG. 1. *A*, vesical perforation with open-ended ureteral catheter, *B*, guidewire passage. *C*, placing over tube in transvesical position. *D*, video telescope inside abdominal cavity, inserted through over tube.

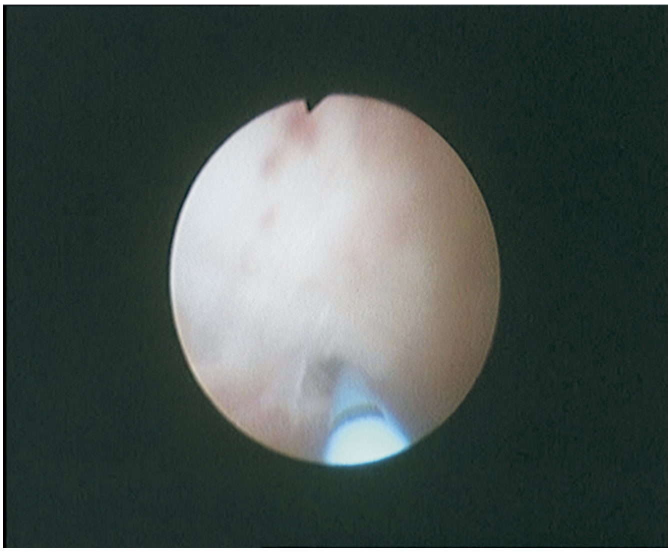

FIG. 2. Endoscopic view of vesical wall perforation with open-ended ureteral catheter.

The peritoneal cavity was examined, biopsy specimens were obtained from the liver with an Olympus® A2423 endoscopic biopsy forceps and the falciform ligament was sectioned with an Olympus® A2576 device (fig. 3). The ureteroscope was withdrawn. It was then possible to introduce into the peritoneal cavity a 5 mm Olympus® EndoEYE™ video telescope with chip on the tip and a 0-degree direction of view. The endoscope was removed and the peritoneal cavity was decompressed through the over tube. At the end of this procedure the cystoscope was again introduced to observe inner bladder wall morphology. At the end of the operation a 14Fr Foley catheter was inserted into the bladder and the balloon was inflated with 10 cm^3 saline.

At the beginning of this protocol the first 3 animals were sacrificed immediately at the end of the procedure by anesthetic overdose and the peritoneal cavity was examined grossly. In the 5 survival animals oral feeding was started within the following 24 hours. They were evaluated daily and followed for 15 days. The bladder catheter was removed

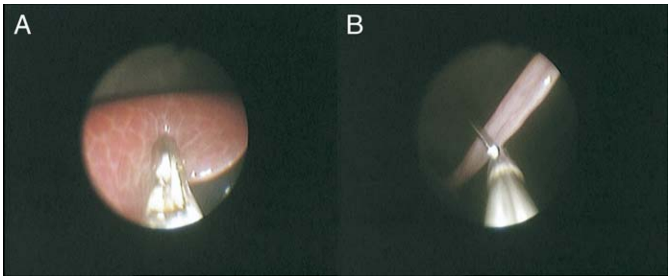

FIG. 3. Representative endoscopic views. *A*, transvesical liver biopsy. *B*, transvesical falciform ligament section.

4 days after surgery except in 1 animal, in which the vesical catheter exteriorized accidentally 12 hours after surgery. Necropsy was performed at the end of followup with particular attention to the vesical incision site.

RESULTS

Through a rapid learning curve the first 3 nonsurvival pigs were used to acquire the necessary skills to perform transvesical endoscopic peritoneoscopy. In the subsequent survival animals all procedures involved in creating the vesical hole, including cystoscopy, bladder mucosal incision, vesicotomy and transvesical over tube passage, were performed without complications. The ureteroscope was introduced easily into the peritoneal cavity and CO_2 insufflation was performed without incident. The view of the internal organs provided by this instrument was reasonable, mainly for organs of the upper abdomen, including the liver, gallbladder, stomach, spleen and diaphragm. The length of the ureteroscope used allowed us to perform simple surgical procedures, such as liver biopsy and falciform ligament section, in all animals without difficulty. The over tube allowed us to easily introduce the EndoEYE™, which provided a detailed view of all intra-abdominal organs (fig. 4). After over tube removal the cystoscope showed obvious signs of contraction, making the vesical hole appear like a puncture hole. Operative time from cystoscope introduction to the completion of surgery was between 20 and 40 minutes.

After recovery from anesthesia the pigs tolerated a regular diet within 24 hours, ate heartily and thrived for the next 14 days. Any adverse events occurred in the survival period. Until postoperative day 4 the pigs tolerated the bladder catheter well. After its removal the pigs voided normally.

Necropsy 15 days after surgery revealed complete healing of the bladder wall incision. The vesical perforation location was detected on the inner surface of the bladder as a small dimple (fig. 5). At necropsy the liver biopsy sites were completely healed. There were no signs of infection or adhesions in the peritoneal cavity.

FIG. 4. Endoscopic view of upper abdominal organs, that is liver and gallbladder, provided by video telescope with chip on tip inserted through over tube. Over gallbladder note sectioned falciform ligament. Bleeding point on liver edge represents liver biopsy.

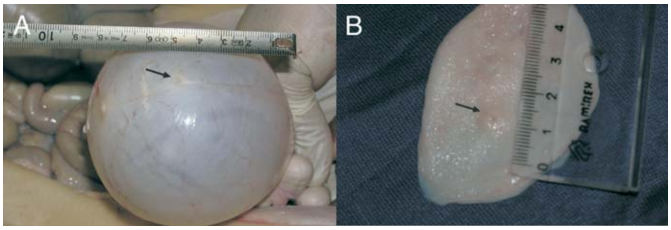

FIG. 5. Bladder necropsy. *A*, external surface of air filled bladder with closed hole (arrow). *B*, inner bladder surface with small residual dimple at surgical perforation site (arrow).

DISCUSSION

Since Kelling used a Nitze cystoscope combined with pneumoperitoneum to examine the peritoneal cavity in a dog in 1902, many advances in endoscopic intra-abdominal surgery have occurred.[1] In fact, the rationale for the current study comes from constant technological advances making better and more reliable instruments available for endoscopic procedures and from the recent, unexpected success of transgastric surgery described in porcine models.[2–6] These facts led us to predict that an additional transvisceral approach positioned diametrically opposed to the stomach might be helpful for performing complex intraperitoneal endoscopic procedures.

In this sequence we tested the possibility of creating a transvesical 5 mm port. Our study reveals that it was easy to perform it while handling the current instruments used for urological purposes. We began all procedures with a cystoscope, mainly to facilitate the perception of anatomy, which in the porcine model is different from that in humans since the urethra opens in a urogenital sinus. Additionally, the larger vision field supplied by the cystoscope compared to a ureteroscope allowed us to easily define the bladder point to perforate. We selected this point in the ventral wall to achieve a peritoneal cavity above the level of the bowel loops. Perforation of the bladder wall with the open-ended ureteral catheter was rapid, efficient and safe. It should be emphasized that the incision performed in the bladder mucosa was essential to fix the catheter tip and prevent easy looping of the catheter inside the bladder. To date with this technique we have never injured any bowel loop since this catheter is nontraumatic.

Passage of the over tube with the ureteral dilator guided by the guidewire was also an easy operation. The ureteroscope working channel allowed the creation of pressure controlled CO_2 pneumoperitoneum. Although it has limited width, the view provided by a 9.8Fr ureteroscope allowed us to perform simple procedures, such as liver biopsies and falciform ligament section.

In our point of view a transvesical 5 mm port could be particularly useful for complementing other transvisceral ports. In fact, a group that performed complex abdominal procedures through a transgastric pathway detected problems in working with decreased triangulation and many times with retroflexion.[4] The position of a transvesical port could easily overcome some of these limitations with additional advantages for performing those complex operations. In fact, it easily achieved by introducing a rigid 5 mm instrument or a video telescope, which can be particularly useful in those procedures. It should be emphasized that the transvesical port provides frontal access to the upper abdominal organs, allowing better instrument position for working on these organs.

During creation of the vesical hole in our protocol the risk of bowel perforation was never neglected. However, in our limited number of experiments we never damaged any bowel loop. The explanation of these results might be related to several aspects. 1) Bowel loops in contact with the bladder wall are free into the abdomen, likely making them run ahead of the ureteral catheter as it perforates the vesical wall. 2) Subsequent procedures to position the over tube were performed while guided by the hydrophilic guidewire with atraumatic equipment.

Vesical perforation has potential complications, such as peritoneal urine leakage with secondary infection (peritonitis). This commonly occurs as a delayed complication of undiagnosed vesical perforation in trauma or pathological bladder conditions, such as neoplasms.[12] In fact, we had reservations about leaving the transvesical entry site unclosed. Interestingly we did not note any of those complications in our study, suggesting that suture or approximation of the vesical wall was unnecessary. In our understanding this might be related to various reasons. 1) The technique that we used to perforate the bladder wall spared muscle fiber section. It seems that muscle fibers contract around the hole immediately after over tube removal. At the end of the procedure we could see through the cystoscope that the vesical hole became immediately and virtually closed. 2) Bladder decompression provided by the vesical catheter surely helped prevent peritoneal leakage, enhancing all healing processes. In this regard we stress that in the last pig in our study the vesical catheter exteriorized within 12 hours after surgery and even in these circumstances no intra-abdominal complications were observed. 3) We did not deal with abnormal bladder tissue invaded by neoplasm or infiltrated by inflammatory cells.

The possibility of installing a 5 mm port, which might allow the introduction of a 5 mm rigid instrument or a video telescope with chip on the tip offering an excellent view of the upper abdominal organs, makes this approach appealing for a combination with a transgastric pathway for future intra-abdominal scarless surgery. In addition to cosmesis, we predict that these procedures performed via a transvisceral pathway may have easier recovery than traditional surgery. We think that postoperative pain might be significantly decreased since the density of pain receptors on the viscera is significantly lower than that in the abdominal wall.

CONCLUSIONS

This study demonstrates that the transvesical endoscopic approach to the peritoneal cavity is feasible without any further complications in a porcine model. This series provides encouragement for additional preclinical studies of transvesical surgery with or without combinations with other natural orifice approaches to design new intra-abdominal scarless procedures in what seems to be the third-generation surgery.

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REFERENCES

1. Harrell, A. G. and Heniford, T.: Minimally invasive abdominal surgery: lux et veritas past, present, and future. Am J Surg, **190:** 239, 2005
2. Kalloo, A. N., Singh, V. K., Jagannath, S. B., Niiyama, H., Hill, S. L., Vaughn, C. A. et al: Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc, **60:** 114, 2004
3. Jagannath, S. B., Kantsevoy, S. V., Vaughn, C. A., Chung, S. S. C., Cotton, P. B., Gostout, C. J. et al: Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model. Gastrointest Endosc, **61:** 449, 2005
4. Park, P. O., Bergstrom, M., Ikeda, K., Fritscher-Ravens, A. and Swain, P.: Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc, **61:** 601, 2005
5. Kantsevoy, S. V., Jagannath, S. B., Niiyama, H., Chung, S. S. C., Cotton, P. B., Gostout, C. J. et al: Endoscopic gastrojejunostomy with survival in a porcine model. Gastrointest Endosc, **62:** 287, 2005
6. Wagh, M. S., Merrifield, B. F. and Thompson, C. C.: Endoscopic transgastric abdominal exploration and organ resection: initial experience in a porcine model. Clin Gastroenterol Hepatol, **3:** 892, 2005
7. Ponsky, J. L.: Gastroenterologists as surgeons: what they need to know. Gastrointest Endosc, **61:** 454, 2005
8. Hochberger, J. and Lamade, W.: Transgastric surgery in the abdomen: the dawn of a new era? Gastrointest Endosc, **62:** 293, 2005
9. Vitale, G. C., Davis, B. R. and Tan, T. C.: The advancing art and science of endoscopy. Am J Surg, **190:** 228, 2005
10. Weickert, U., Jakobs, R. and Riemann, J. F.: Diagnostic laparoscopy. Endoscopy, **37:** 33, 2005
11. Liu, R., Chand, B. and Ponsky, J.: The future of surgical endoscopy. Endoscopy, **37:** 38, 2005
12. Cass, A. S. and Luxenberg, M.: Features of 164 bladder ruptures. J Urol, **138:** 743, 1987

Chapter 3

Transvesical endoscopic port for thoracic surgery

Lima E, Henriques-Coelho T, Rolanda C, Pego JM, Silva D, Carvalho JL, Correia-Pinto J. Transvesical thoracoscopy: a natural orifice transluminal endoscopic approach for thoracic surgery. *Surg Endosc*; 21: 854-858, 2007.

Original Articles

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SURGICAL ENDOSCOPY
and Other Interventional Techniques

Transvesical thoracoscopy: A natural orifice translumenal endoscopic approach for thoracic surgery

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Abstract
Background: Recently there has been an increasing enthusiasm for using natural orifices translumenal endoscopic surgery (NOTES) to perform scarless abdominal procedures. We have previously reported the feasibility and safety of the transvesical endoscopic peritoneoscopy in a long-term survival porcine model as useful for those purposes. Herein, we report our successful experience performing transvesical and transdiaphragmatic endoscopic approach to the thoracic cavity in a long-term survival study in a porcine model.
Methods: Transvesical and transdiaphragmatic endoscopic thoracoscopy was performed in six anesthetized female pigs. A 5 mm transvesical port was created on the bladder wall and an ureteroscope was advanced into the peritoneal cavity. After diaphragm inspection, we introduced through the left diaphragmatic dome a ureteroscope into the left thoracic cavity. In all animals, we performed thoracoscopy as well as peripheral lung biopsy. Animals were sacrificed by day 15 postoperatively.
Results: We easily introduced a 9.8 Fr ureteroscope into the thoracic cavity that allowed us to visualize the pleural cavity and to perform simple surgical procedures such as lung biopsies without complications. There were neither respiratory distress episodes nor surgical complications to report. Postmortem examination revealed complete healing of vesical and diaphragmatic holes, whereas no signs of infection or adhesions were observed in the peritoneal or thoracic cavities.
Conclusion: This study demonstrates the feasibility of transvesical thoracoscopy in porcine model. However, although this study extends the potential applications of NOTES to the thoracic cavity, new instruments and further work are needed to provide evidence that this could be translated to humans and with advantages for patients.

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Key words: Swine — Endoscopy — Laparoscopy — Peritoneal cavity — Thoracic cavity

Background

Since the early 1990s, it has been proposed that thoracoscopy is less invasive than open procedures [6]. Whereas its use as a definitive therapeutic tool in many pulmonary diseases is still controversial, its use as a diagnostic tool in pleural and pulmonary diseases is already well established [2, 17]. Indeed many prospective, randomized studies confirmed that thoracoscopy reduces postoperative pain, minimizes pulmonary dysfunction and shortens hospital stay [1, 18, 21].

Recently, there is an increasing enthusiasm for using natural orifice approaches to perform abdominal scarless surgery. In fact, Reddy and Rao (N. Reddy, V. G. Rao, oral communications, May 15 and 19, 2005; N. Reddy, oral communication, May 2004) and Kalloo et al. [8] described a new port to the peritoneal cavity through a transgastric approach in humans and pigs, respectively. Subsequently, various authors described more-complex intra-abdominal procedures in porcine models, opening a new era in surgery that is being considered third generation surgery: the natural orifice translumenal endoscopic surgery (NOTES) [7, 9, 11–14, 19–20]. Building on these findings, our group described transvesical endoscopic peritoneoscopy as a complementary and safe approach to the abdominal cavity in a porcine model [10, 16].

The aim of this study was to assess the feasibility and the safety of transvesical endoscopic approach to the thoracic cavity with lung biopsy in a porcine model.

Materials and methods

The ethical review board of Minho University (Braga, Portugal) approved this study. Survival studies of thoracoscopy by transvesical approach were performed in six consecutive 15–20 kg female pigs (*Sus scrofus domesticus*). Pigs were followed after surgery for 15 days before sacrifice and postmortem examination.

Pig preparation

The animals were restrained from food (24 hours) and water (6 hours) before the surgical procedure. All procedures were performed under general anesthesia, with 6.0-mm endo-tracheal intubation (Super Safety clear tracheal tube, Ruschelit®) and mechanical ventilation. Pre-anesthesia medication consisted of an intramuscular injection of 32 mg/ml azaperone (Stressnil®, Esteve Farma) reconstituted with 1 mg/ml midazolam (Dormicum®, Roche) at dose of 0.15–0.2 ml/kg.

Venous access was obtained through an IV line placed in the marginal ear vein. Anesthesia was induced with 3 μg/kg fentanyl (Fentanest®, Janssen-Cilag), 10 mg/kg thiopental sodium (Pentothal®, Abbott) and 1 mg/kg vecuronium (Norcuron®, Organon). For infection prophylaxis, all animals received intramuscular injection of 1 g ceftriaxone (Rocephin®, Roche) before endoscopy. Anesthesia was maintained with 1.5–2% sevoflurane (Sevorane®, Abbott) and a perfusion of 1 mg/kg/h vecuronium (Norcuron®, Organon).

Surgical technique

An ureteroscope (Olympus A2942A) was introduced through the urogenital sinus and urethra into the bladder with hydro-distension. Before any further procedure, the bladder was emptied from urine and refilled with saline. The vesicotomy site was carefully selected on the bladder dome. A mucosal incision was made with scissors (Olympus A2576) introduced through the working channel of the ureteroscope. Subsequently, a 5 Fr open-ended ureteral catheter (Selectip, 62450200; Angiomed, Bard) was pushed forward through the incision into the peritoneal cavity. A 0.035-inch flexible-tip guide-wire (Terumo Corporation) was then inserted into the peritoneal cavity through the lumen of the ureteral catheter. Guided by the flexible-tip guide-wire, the vesical hole was enlarged with a dilator of an ureteroscope sheath (Microvasive, Boston Scientific Corporation) enveloped by a flexible over tube (equipment designed by the authors: 25 cm length, 5.5 mm internal diameter and 1 mm wall thickness). An ureteroscope was introduced into the peritoneal cavity through the over tube and allowed the creation of a pressure controlled CO_2 pneumoperitoneum up to 12 mmHg (Olympus Insufflator UHI-3 A90120A). Upper abdomen exploration and careful inspection of the diaphragm was performed using the ureteroscope.

The site of transdiaphragmatic approach was carefully chosen on the *muscular pars* of the left diaphragmatic dome. Peritoneal incision was made with a scissor (Olympus A2576) and the muscle fibers dissected until reaching the parietal pleura. Finally, we created a small hole in the parietal pleura and the ureteroscope was advanced into the thoracic cavity (Figure 1). In the thorax, CO_2 was insufflated up to 6 mmHg and the pleural cavity and lung surface were inspected. Under direct endoscopic control, lung biopsies were obtained from the lower left lung lobe using biopsy forceps (Olympus A2423). The ureteroscope was withdrawn from the thoracic cavity after CO_2 removal and expansion of the left lung. The peritoneal cavity was then decompressed through the over tube. At the end of the operation, a 14 Fr Foley catheter was inserted into the bladder and the balloon was inflated with 10 cm^3 of saline.

In this study, oral feeding was started within the following 24 hours. Pigs were evaluated daily and followed for 15 days. Bladder catheter was removed four days after surgery. Necropsy examination was then performed with particular attention to the site of vesical and diaphragmatic incision.

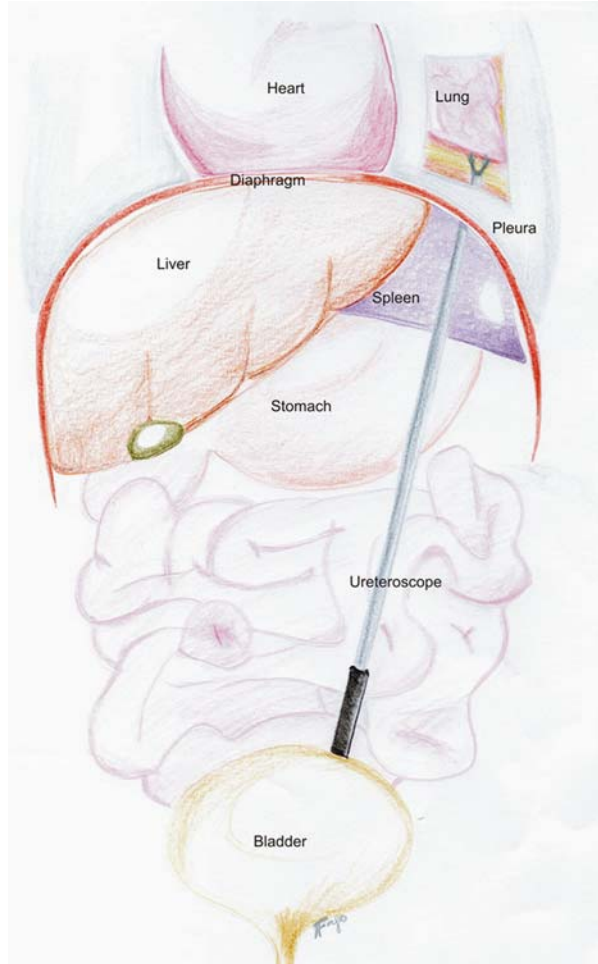

Fig. 1. Schematic drawing of transvesical and transdiaphragmatic approach.

Results

Transvesical and transdiaphragmatic endoscopic thoracoscopy with lung biopsy was performed on six pigs. As we have previously described, all procedures involved in the creation of the vesical hole (cystoscopy, bladder mucosal incision, vesicotomy, transvesical overtube passage) were performed without complications. The ureteroscope was introduced into the peritoneal cavity and the diaphragm was easily identified. The length of the ureteroscope allowed us to cross through the diaphragm (small incision in the parietal peritoneum, dissection of muscle fibers and incision of the parietal pleura) in all animals without difficulty (Figure 2). The ureteroscope working-channel allowed creating a pressure-controlled CO_2-pneumothorax up to 6 mmHg. In the thorax, the visualization provided by the ureteroscope was limited to the lower half-cavity but allowed us easily to perform lower lobe lung biopsy (Figure 3). At the end of the procedure, it was easy to expand the lung and the ureteroscope showed signs of contraction of the small hole created in the diaphragm. The operative time from bladder-wall incision to completion of the surgery varied between 10 and 15 minutes.

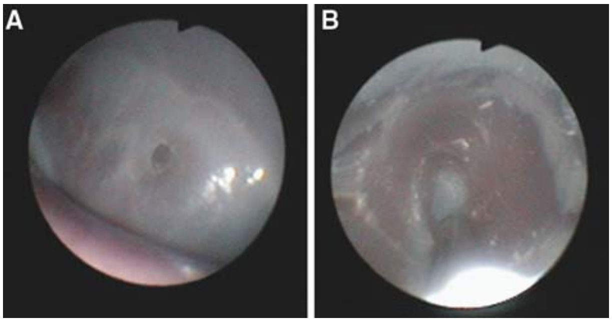

Fig. 2. Endoscopic views of a small hole on the *muscular pars* of left diaphragmatic dome. **A** Incision in diaphragmatic peritoneum. **B** Muscular hole being constructed in diaphragm *pars muscularis*.

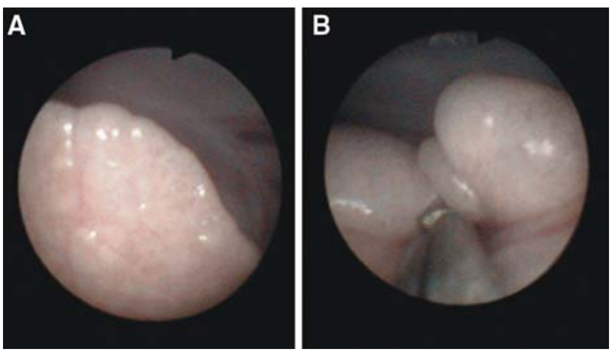

Fig. 3. Representative endoscopic views of lung biopsy. **A** Edge of left lower lung lobe; **B** lung biopsy being performed.

After recovery of anesthesia, the pigs tolerated a regular diet started the morning after surgery and they ambulated freely, exhibiting normal behavior. No adverse event occurred during the survival period. Until day 4 post-operative, pigs tolerated well the bladder catheter. After its removal, pigs began to void normally.

The postmortem examination 15 days after surgery revealed complete healing of the vesical and diaphragmatic incision (Figure 4). At necropsy, the lung biopsies were completely healed. There were no signs of infection or adhesions in both thoracic and peritoneal cavities.

Discussion

The widespread acceptance of minimally invasive techniques has revolutionized the practice of surgery including thoracic surgery. Within a short period of time, video-assisted thoracic surgery has become an acceptable approach with multiple studies confirming the advantages of thoracoscopy when compared to open procedure, which include shorter hospital stay, rapid recovery and return to physical activity, and excellent cosmetic results [1, 18, 21]. Recently, innovative natural orifices endoscopic techniques using per-oral transgastric surgery appear to further minimize surgical aggression in what has been designated as third generation surgery [10, 16]. In fact, several studies have confirmed the technical feasibility of transgastric diagnostic and therapeutic peritoneoscopy, including liver biopsy, tubal ligation, gastrojejunostomy, cholecystectomy, splenectomy, oophorectomy and partial hysterectomy [7–9, 11–14, 19–20]. In this regard, we showed for the first time that transvesical endoscopic approach to the peritoneal cavity is also feasible and particularly useful to inspect diaphragm and upper abdominal organs [10, 16]. Moreover, this approach revealed particularly useful to complement transgastric port, becoming cholecystectomy by natural orifices a reliable procedure, at least in the porcine model [16]. The feasibility and usefulness of transvesical endoscopic peritoneoscopy for upper abdominal procedures raised the rationale to extend its application to the thoracic cavity.

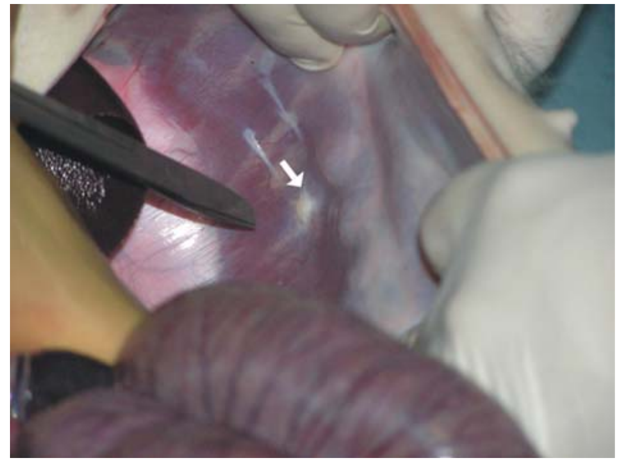

Fig. 4. Postmortem examination of diaphragm. Please note the small scar in the diaphragm *pars muscularis* (arrow).

The aim of this study was to determine the technical feasibility and the safety of the transvesical approach to the thoracic cavity with lung biopsy in a porcine model in a long-term survival study. These experiments demonstrate that a transdiaphragmatic hole can be performed safely without injuring the lung or pericardium. The transdiaphragmatic incision could be made using the rigid ureteroscope and the scissors introduced through the working-channel. Interestingly, with our approach, we could easily identify the whole diaphragm and select the precise site of the incision. We could not reach the entire thoracic cavity mainly due to limitations of current instruments (rigid and not long enough). Anyway, Lower lobe lung biopsies were also performed without any complications.

This study provides the first successful evidence that the thoracic cavity might also be reached through NOTES. We anticipate some theoretical advantages to a transvesical-diaphragmatic approach to the thoracic cavity such as less pain and certainly a better cosmetic effect than open or thoracoscopic procedures. We predict less pain because, according to pain physiology, visceral wall has much less nervous terminal endings than skin, fascia and muscles. Transbronchic procedures might also share from these advantages but they are available only for peri-hilar lesions. In fact, although our approach might have some limitations (the risk of abdominal infection or malignant cell spillage from the thoracic cavity), there is a vast number of interstitial pulmonary diseases where bronchoscopy with transbronchic biopsy is unviable. For these conditions, we could predict that transvesical-diaphragmatic approach might have a potential role. Similarly, with the appropriate instruments, pleural interventions like thoracic sympathectomy for the treatment of palmar hyperhidrosis and Raynauds disease might also appear feasible with transvesical-diaphragmatic approach avoiding thoracic incisions [3]. Another potential application of transvesical approach to the thoracic cavity is the implantation of phrenic nerve pacing electrodes for diaphragm stimulation [4], or just diaphragm pacing as recently described by transgastric approach [12]. Recently, Fritscher-Ravens et al. reported the feasibility and safety of a variety of interventional trans-esophageal cardiac procedures using endoscopic ultrasound in live porcine model. In those experiments, the procedures studied included needle biopsies, contrast medium injections into atrium and coronary arteries, direct intracardiac recording of ECG, cardiac conductive tissue ablation and direct cardiac pacing [5]. However, the superb view of the pericardium and the proximity of cardiac structures by transvesical approach might allow a variety of transdiaphragmatic interventional procedures to be performed under direct control or under endoscopic ultrasound control without the risks of trans-esophageal approach such as infection or absence of direct control. Moreover, the transvesical approach could be useful in the treatment of pericardial effusion and tamponade, especially those with malignant effusions. In fact, in these cases, the creation of a pericardioperitoneal window seems to be the most effective method of drainage [15].

In our experiments, we did not place any pleural drain at the end of the examination and no complications were reported, namely pneumothorax. In fact, we avoid this complication because: (i) we created a pressure-controlled CO_2-pneumothorax only up to 6 mmHg; (ii) we promoted re-expansion of the lung during the withdrawing of the ureteroscope; (iii) of the small size of lung biopsy. The vesical 5 mm hole has been well tested in our previous survival porcine study and had also no problems of closure [10]. In fact, we did not observe any side effects or complications over a two-week follow-up period. All pigs thrived after surgery and postmortem examination did not reveal any signs of infection or adhesions in the thoracic cavity.

This preliminary study was only designed to assess the technical feasibility of transvesical and transdiaphragmatic thoracoscopy. The ultimate implications for humans can only be assessed with the development of endoscopes with some flexibility and length to reach overall thoracic cavity. However, our current study clearly demonstrates that the transvesical and transdiaphragmatic approach to the thoracic cavity is feasible and safe in a porcine model with long-term survival assessment.

Conclusions

This study demonstrates that endoscopic transvesical-diaphragmatic thoracoscopy with lung biopsies is technically feasible in a porcine model. However, although this study extends the potential applications of NOTES to the thoracic cavity, new instruments and much work are needed to provide evidence that this could be translated for humans with advantages for patients.

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References

1. Ayed AK, Raghunathan R (2000) Thoracoscopy versus open lung biopsy in the diagnosis of interstitial lung disease: a randomised controlled trial. J R Coll Surg Edinb 45: 159–163
2. Blanc FX, Atassi K, Bignon J, Housset B (2002) Diagnostic value of medical thoracoscopy in pleural disease. A 6-year retrospective study. Chest 121: 1677–1683
3. Dewey TM, Herbert MA, Hill SL, Prince SL, Mack MJ (2006) One-year follow-up after thoracoscopic sympathectomy for hyperhidrosis: outcomes and consequences. Ann Thorac Surg 81: 1227–1232
4. DiMarco AF (2005) Restoration of respiratory muscle function following spinal cord injury. Review of electrical and magnetic stimulation techniques. Respir Physiol Neurobiol 147: 273–287
5. Fritcher-Ravens A (2006) EUS – experimental and evolving techniques. Endoscopy 38: 95–99
6. Hazelrigg SR, Landreneau RJ, Mack M, Acuff T, Seifert PE, Auer JE, Magee M (1993) Thoracoscopic staped resection for spontaneous pneumothorax. J Thorac Cardiovasc Surg 105: 389–393
7. Jagannath SB, Kantsevoy SV, Vaughn CA, Chung SSC, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Scorpio DG, Magee CA, Pipitone LJ, Kalloo AN (2005) Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model. Gastrointest Endosc 61: 449–453
8. Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevoy SV (2004) Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 60: 114–117
9. Kantsevoy SV, Hu B, Jagannath SB, Vaughn CA, Beitler DM, Chung SSC, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Pipitone LL, Talamini MA, Kalloo AN (2006) Transgastric endoscopic splenectomy. Is it possible? Surg Endosc 20: 522–525
10. Lima E, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL, Correia-Pinto J (2006) Transvesical endoscopic peritoneoscopy: A novel 5 mm-port for intra-abdominal scarless surgery. J Urol 176: 802–805
11. Merrifield BF, Wagh MS, Thompson CC (2006) Peroral transgastric organ resection in the abdomen: feasibility study in pigs. Gastrointest Endosc 63: 693–697
12. Onders R, McGee MF, Marks J, Chak A, Schilz R, Rosen MJ, Ignagni A, Faulx A, Elmo MJ, Schomisch S, Ponsky J (2006) Diaphragm pacing with natural orifice transluminal endoscopic surgery: potential for difficult-to-wean intensive care unit patients. Surg Endosc 21: 475–479
13. Pai RD, Fong DG, Bundga ME, Odze RD, Rattner DW, Thompson CC (2006) Transcolonic endoscopic cholecystectomy: a NOTES survival study in a porcine model (with video). Gastrointest Endosc 64: 428–434
14. Park PO, Bergstrom M, Ikeda K, Fritscher-Ravens A, Swain P (2005) Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 61: 601–606
15. Rodriguez MI, Ash K, Foley RW, Liston W (1999) Pericardio peritoneal window:aparoscopic approach. Surg Endosc 13: 409–411

16. Rolanda C, Lima E, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL, Correia-Pinto J (2007) Third Generation Cholecystectomy by Natural Orifices: Transgastric and Transvesical Combined Approach. Gastrointest Endosc 65: 111–117
17. Roviaro GE, Varoli F, Vergani C, Maciocco M (2002) State of the art in thoracoscopic surgery. A personal experience of 2000 videothoracoscopic procedures and an overview of the literature. Surg Endosc 16: 881–892
18. Santambrogio L, Nosotti M, Bellavit N, Mezzetti M (1995) Videothoracoscopy versus thoracotomy for diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 59: 868–870
19. Wagh MS, Merrifield BF, Thompson CC (2005) Endoscopic Transgastric Abdominal Exploration and Organ Resection: Initial Experience in a Porcine Model. Clin Gastroenterol and Hepatol 3: 892–896
20. Wagh MS, Merrifield BF, Thompson CC (2006) Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. Gastrointest Endosc 63: 473–478
21. Waller DA, Forty J, Morritt GN (1994) Video-assisted thoracoscopic surgery versus thoracotomy for spontaneous pneumothorax. Ann Thorac Surg 58: 372–476

Chapter 4

Nephrectomy by transvesical and transgastric ports

Lima E, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Osório L, Moreira I, Carvalho JL, Correia-Pinto J. Third-generation nephrectomy by natural orifice transluminal endoscopic surgery. *J Urol*; 178: 2648-2654, 2007.

Third-Generation Nephrectomy by Natural Orifice Transluminal Endoscopic Surgery

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Purpose: Recently there has been increasing enthusiasm for performing simple abdominal procedures by transgastric surgery. We previously reported the usefulness of a combined transgastric and transvesical approach to cholecystectomy. In this study we assessed the feasibility of combined transgastric and transvesical approach for performing a more complex surgical procedure, such as nephrectomy, in a porcine model.

Materials and Methods: In a nonsurvival study combined transgastric and transvesical approaches were established in 6 female pigs. Under ureteroscope guidance we installed a transvesical 5 mm over tube into the peritoneal cavity and a flexible gastroscope was passed orally into the peritoneal cavity by a gastrotomy. We performed right or left nephrectomy with instruments introduced by the 2 devices that worked in the renal hilum, alternating device intervention for dissection and retraction procedures.

Results: Four right and 2 left nephrectomies were performed. There were no complications during the creation of transvesical and transgastric access. In all animals we visualized the 2 kidneys. The renal vessels and ureter were reasonably individualized and ligated separately with ultrasonic scissors, which were introduced through the transvesical port. In 2 early cases mild hemorrhage occurred after ultrasonic ligation. To overcome this complication we applied clips successfully before ultrasonic ligation in the remaining animals. Thus, complete renal release and mobilization to the stomach were achieved in all animals.

Conclusions: Nephrectomy by natural orifices using the combined transgastric and transvesical approach is technically feasible, although to our knowledge there is no reliable method for removing the specimen with current instruments.

Key Words: kidney; swine; nephrectomy; endoscopy; surgical procedures, minimally invasive

Renal surgery has its origin some 400 years B.C.E. with the drainage of abscesses and the removal of calculi from renal fistulas. In the early 19th century kidneys were sometimes removed inadvertently during attempted ovarian surgery with the observation that the remaining kidney continued to produce normal amounts of urine. However, it was not until 1869 that Simon performed the first planned nephrectomy.[1] During the last century there was progressive development of the surgical technique, aiming mainly at organ resection without apprehension and associated morbidity.

With the first laparoscopic nephrectomy in 1990 performed by Clayman et al a revolution began with the implementation of laparoscopic techniques that had become accepted by the urological community worldwide, initially for benign and more recently for malignant renal disease.[2] The main reasons that minimally invasive surgery increased in popularity were the many proven advantages over traditional open procedures, such as minimal scarring, decreased pain and more rapid patient recovery.[3]

Currently NOTES is being studied as a potentially less invasive alternative to conventional laparoscopy for intra-abdominal surgery. In fact, there is increasing hope that we will be able to perform the most common abdominal procedures in humans using this revolutionary technique that seems to be third-generation surgery. After the development of transvaginal peritoneal access, mainly for specimen extraction,[4] Gettman et al used this approach to perform nephrectomy.[5] More recently transgastric access to the peritoneal cavity was described with unexpected success.[6] Subsequently we had the opportunity to test the feasibility and safety of a transvesical port to the peritoneal and thoracic cavities.[7,8] This port was revealed to be particularly important because some procedures that appeared hazardous and not viable using an isolated transgastric port become feasible and safe when performed by a combined transgastric and transvesical approach, as we recently described for cholecystectomy.[9]

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Study received approval from ethical review boards at Minho University, Braga, Portugal.

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Before translation in humans additional preclinical studies are still needed to increase our confidence with these techniques in high risk procedures such as nephrectomy.[10] We report the feasibility of the combined transgastric and transvesical approach for performing scarless natural orifice nephrectomy in a porcine model.

MATERIALS AND METHODS

This study was approved by ethical review boards at Minho University, Braga, Portugal. After a surgical learning curve of 4 animals (data not shown) right or left nephrectomy was performed in 6 consecutive anesthetized female pigs (Sus scrofus domesticus) weighing 25 to 30 kg. After the surgical procedures the animals were immediately sacrificed and necropsy was performed.

Pig Preparation

The animals were fed liquids for 3 days and then were denied food for 24 hours and water for 6 before surgical intervention. All procedures were performed using general anesthesia, as described previously.[7]

Surgical Technique and Instruments

The technique of performing nephrectomy by NOTES was begun using a transvesical port and subsequently a transgastric port (fig. 1). Through the transvesical port we used a rigid Olympus® A2942A ureteroscope, LCSC5L UltraCision® Harmonic Scalpel® Long Shears ultrasonic scissors or an EL5ML Ligamax™5 clip applicator. Through the transgastric port an adult, forward viewing, double channel Olympus GIF-2T160 endoscope was introduced. Through the working channels of the 2 endoscopes we used certain instruments, including 1) ureteroscope instruments (Olympus A2574 grasping forceps and Olympus A2576 scissors) and 2) gastroscope instruments (an Olympus KD-11Q-1 needle knife, a Microvasive® 5156-01 guidewire, a Microvasive 5837 through the scope balloon, Olympus FG-6L-1 and FG-47L-1 grasping forceps, a KD-16Q-1 papillotomy knife and a Sensation™ M00562650 endoscopic snare). For cautery we used standard Olympus PSD 20 electrocautery equipment.

Transvesical Access

A transvesical port was established, as previously described by our group.[7] Briefly, a ureteroscope was introduced into the bladder with CO_2 distention. After making a small mucosal incision on the bladder dome we used a 5Fr open end 62450200 Selectip™ ureteral catheter to perform cystotomy. Guided by a 0.035-inch flexible tip RF*GA35153M Terumo® guidewire the vesical hole was enlarged with the dilator of a 250-105 Microvasive ureteroscope sheath, which was enveloped with a 5.5 mm over tube. A rigid ureteroscope was introduced into the peritoneal cavity within the over tube, allowing the creation of pressure controlled CO_2 pneumoperitoneum as necessary. The peritoneal cavity was thoroughly examined.

Transgastric Access

As previously described,[9] we introduced the gastroscope into the peritoneal cavity through a gastrotomy established on the anterior stomach wall. The gastric wall incision was made by a needle knife with cautery and it was then increased using a papillotomy knife. All procedures were monitored using the view provided by the ureteroscope introduced through the transvesical port.

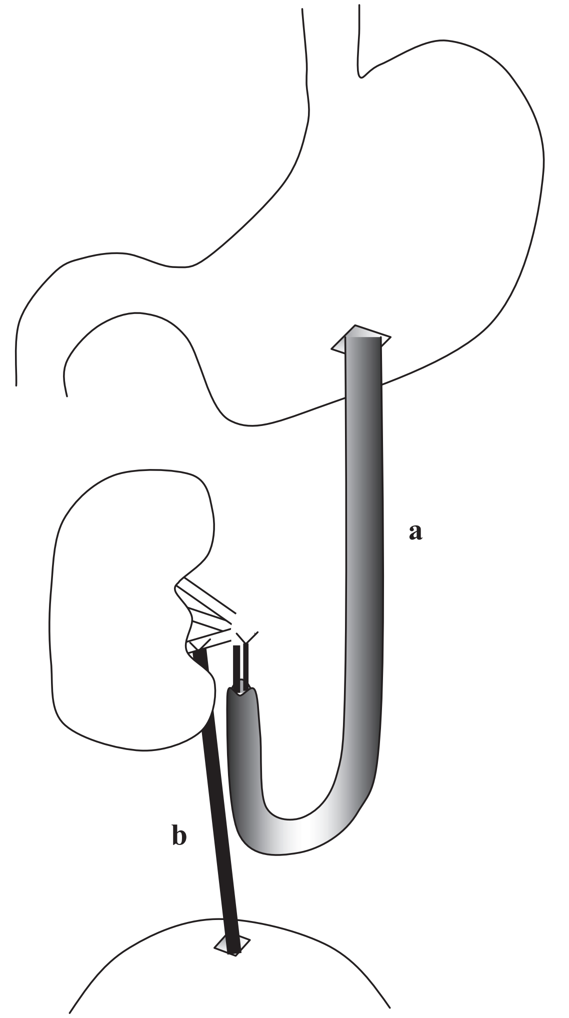

FIG. 1. Instrument positioning for nephrectomy by combined transgastric and transvesical approach. *a*, gastroscope in retroflexion approaching renal hilus. *b*, ureteroscope.

Nephrectomy Procedure

The animals were placed in the lateral decubitus position at the beginning of the procedure to expose the contralateral kidney. Subsequently the selected kidney and respective hilum were immediately identified by the 2 endoscopes. We then mobilized the lower kidney pole by opening the parietal peritoneum with cautery using the needle knife introduced by the gastroscope. This procedure was helped by suspending the peritoneum using grasping forceps introduced through the working channel of the ureteroscope. Subsequently the peritoneum was reflected off the kidney hilum by serial combined actions of the grasping forceps and a needle knife introduced through the ureteroscope and gastroscope, respectively. This maneuver exposed the hilar elements, such as the renal vein, renal artery and urinary excretory structure. The renal vessels were then individualized and completely dissected from the surrounding tissues using instruments introduced through the 2 endoscopes, which worked in coordinated fashion.

After the renal artery and vein were completely dissected and circumferentially individualized the ureteroscope was removed from the peritoneal cavity. Subsequently 5 mm ultrasonic scissors were introduced into the peritoneal cavity through the transvesical over tube and guided to the renal hilum using the gastroscopic image. The artery was positioned between the blades of the ultrasonic scissors and divided using level 1 for maximum coagulation. The renal vein was divided in a similar procedure. In 2 pigs the renal vessels were clipped before division by the ultrasonic scissors. It is worth mention that the renal vessels were divided using 5 mm transvesical instruments, which were used under gastroscope guidance. When the renal hilum was completely free, we completed kidney dissection by isolating and mobilizing the upper pole using transvesical ultrasonic scissors or the needle knife, always under gastroscope guidance. Finally, we divided the ureter by half of its trajectory and the kidney was dragged from its bed in the direction of the stomach, held by an endoscopic snare. However, the kidney was left in the animal since we were not able to extract it with the current instruments.

After removing the organ the hilar renal area was washed and inspected for bleeding. Adjacent organs were evaluated for evidence of laceration and perforation.

RESULTS

Nephrectomy by the combined transgastric and transvesical approach was done in 6 pigs. The procedures involved in the creation of the vesical hole (cystoscopy, bladder mucosal incision, cystotomy and transvesical over tube passage) were performed easily and rapidly, and without complications in all animals. The ureteroscope was introduced in straightforward fashion into the peritoneal cavity and CO_2 insufflation was performed without incident. The ureteroscopic image was particularly valuable for helping the gastroscope operator select the most appropriate point for gastrotomy on the anterior gastric wall (fig. 2). Additionally, the external view of the gastric wall provided by the ureteroscope allowed us to create the gastrotomy while preventing damage to the major gastric vessels and adjacent structures (fig. 2, *B*). In fact, beginning access to the peritoneal cavity through the transvesical approach resulted in no complications during gastric incision and gastroscope entrance into the peritoneal cavity.

From the transgastric and transvesical ports it was possible to easily find the selected kidney for nephrectomy (fig. 3). It should be stressed that the gastroscope was used most of the time in retroflexion. In fact, the kidney was more easily visualized by the gastroscope in the retroflexion position, directing its tip toward the upper quadrant. This allowed us to work with the gastroscope in a stable position.

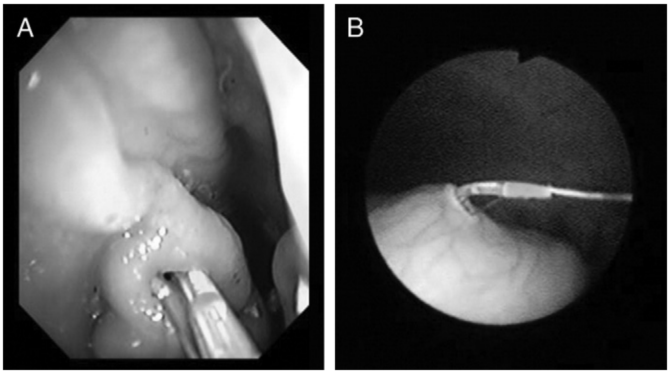

FIG. 2. Gastrotomy creation with papillotomy knife. *A*, gastroscopic image shows internal view. *B*, ureteroscopic image shows external view.

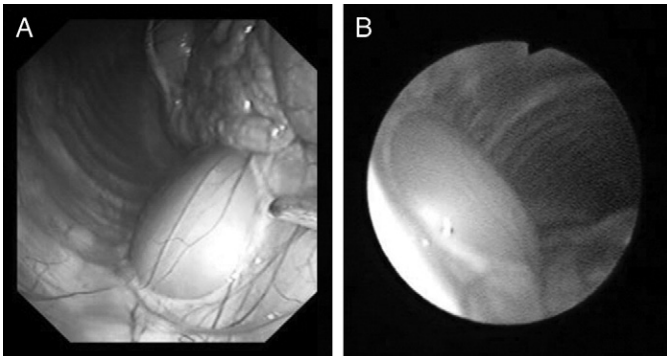

FIG. 3. Renal identification before starting dissection. *A*, gastroscopic image. *B*, ureteroscopic image.

Further procedures in the performance of nephrectomy were done using coordinated movements of the gastroscope and ureteroscope operators, which increased during the experimental protocol. Creation of a peritoneal window in the lower pole of the kidney and subsequent dissection to expose the renal hilum were accomplished in all animals in a rapid and safe way (fig. 4). These procedures were done most of the time by the gastroscope operator, whereas the ureteroscope operator grasped the peritoneum. Maneuvers to dissect and isolate the hilar vessels were done using gastroscope or ureteroscope instruments, always in coordinated movements (fig. 5). Although it was time-consuming, vessel isolation was reasonably accomplished without hemorrhage in all animals.

To promote renal vessel ligation we always used the same sequence, characterized by removal of the ureteroscope and followed by the introduction of ultrasonic scissors into the peritoneal cavity through the transvesical over tube. Transvesical instrument exchange was always guided by the gastroscopic image (fig. 6). In the first 2 animals ligation of the artery and vein with the ultrasonic scissors was efficient with no evidence of hemorrhage (figs. 7 and 8). In animals 3 and 4 ultrasonic ligation of the renal artery was insufficient, causing mild hemorrhage that significantly blurred the view of renal hilar structures. Although in these cases hemorrhage could be safely controlled with gastroscope instru-

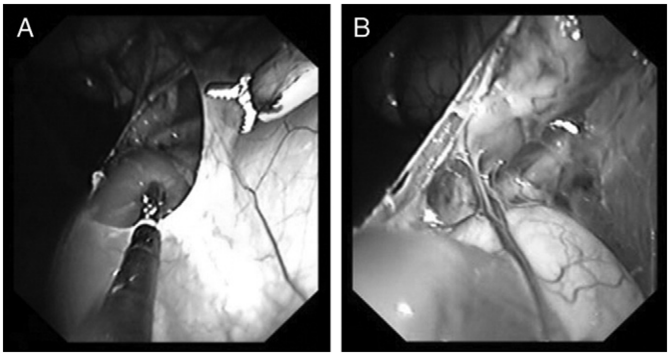

FIG. 4. Creation of peritoneal window for hilar approach. *A*, opening peritoneum. *B*, visualizing hilar elements.

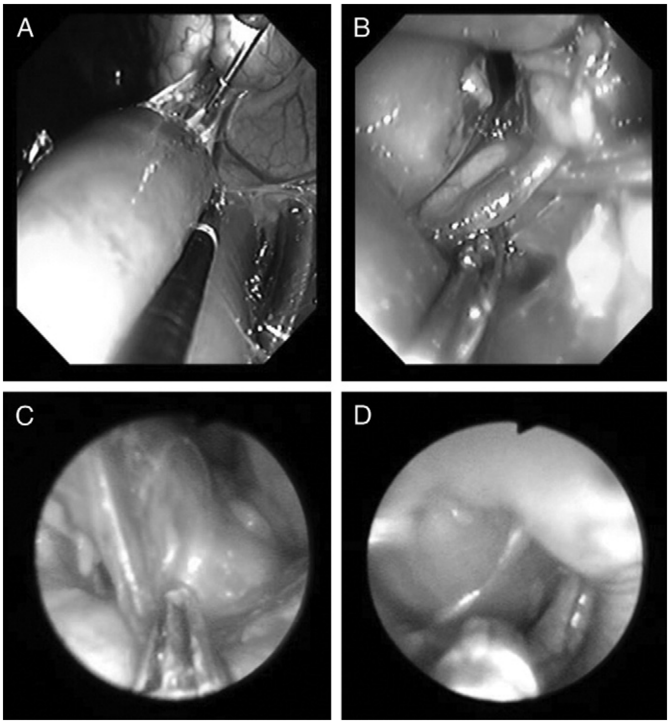

FIG. 5. Renal vessel dissection. *A*, gastroscopic view of renal vein. *B*, gastroscopic view of renal artery. *C*, ureteroscopic view of renal artery. *D*, ureteroscopic view of renal vein.

ments, such as grasping forceps followed by ultrasonic cautery reapplication, in the last 2 animals we successfully applied endoscopy clips before ultrasonic ligation to increase the safety of vessel ligation. Clip application was easy and

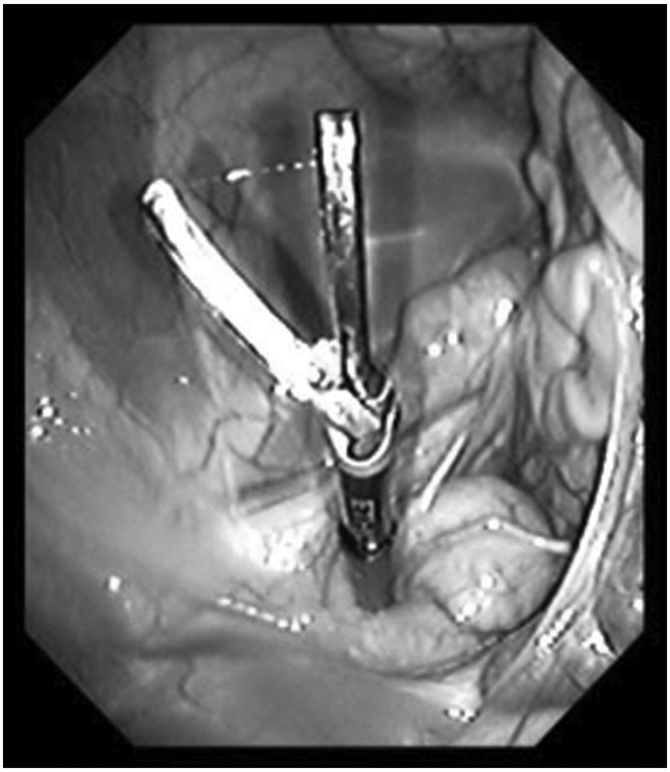

FIG. 6. Gastroscopic view of entrance of ultrasonic scissors into abdomen by transvesical port.

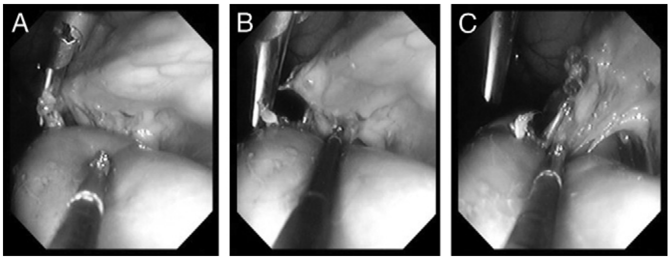

FIG. 7. Gastroscopic image reveals renal artery ultrasonic ligation. *A*, starting ligation. *B*, finishing ligation. *C*, completed ligation.

this approach was particularly successful with hemorrhage in none of these cases.

After vessel ligation ureteral dissection and section were easily accomplished in all animals (fig. 9). The kidney was easily released by sectioning the peritoneum from the upper renal pole and posterior perirenal tissue. For these procedures we used gastroscope cautery or transvesical ultrasonic scissors. The kidney was then mobilized from the renal bed, held with a gastroscopic snare and pulled to the stomach (fig. 10).

Nephrectomy was performed under pressure controlled CO_2 pneumoperitoneum. However, it should be emphasized that most of the time the surgical procedure was performed under a low CO_2 pressure of around 3 mm Hg. In fact, pneumoperitoneal pressure was increased up to 12 mm Hg only during gastric perforation and exchange of the transvesical surgical instrument.

Median time for the overall procedure, including establishment of the transvesical and transgastric port, was around 120 minutes (range 90 to 150). Procedure time decreased with experience.

All animals were sacrificed at the end of the nephrectomy procedure, immediately after surgery. Necropsy did not reveal any damage to the abdominal viscera that was related to transgastric and transvesical access to the peritoneal cavity. It was possible to confirm nephrectomy and perfect ligation of the renal vessels.

DISCUSSION

The current study confirms that nephrectomy is feasible exclusively by NOTES. Moreover, the combined transgastric and transvesical approach was particularly useful for complete renal manipulation. Thus, renal intervention might be included in the list of potential clinical indications for NOTES.

This study describes a revolutionary surgical approach that is being used for an increasing number of procedures, such as

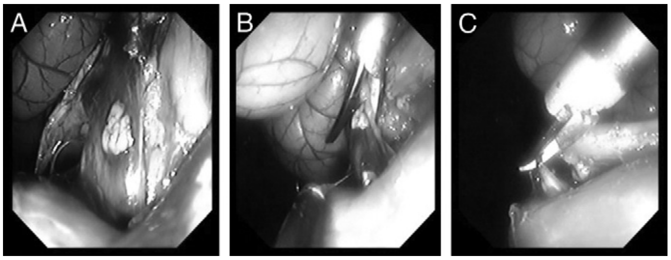

FIG. 8. Gastroscopic image demonstrates renal vein ultrasonic ligation. *A*, dissected vein. *B*, starting ligation. *C*, finishing ligation.

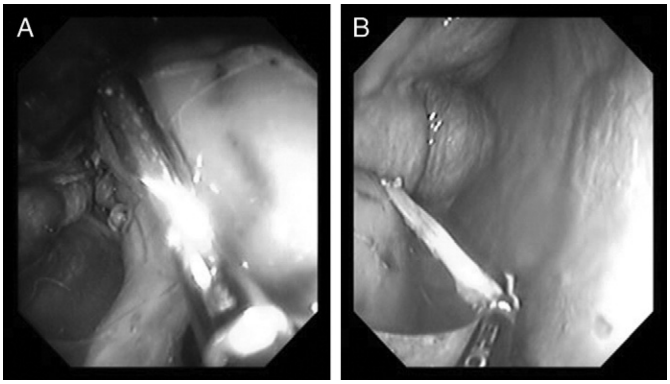

FIG. 9. *A*, individualized ureter. *B*, ureteral ligation

fallopian tube ligation, cholecystectomy, gastrojejunostomy, partial hysterectomy, oophorectomy and splenectomy essentially via the transgastric route.[11–17] In fact, there are several theoretical advantages to NOTES. 1) There are no abdominal incisions and, therefore, abdominal wound infections and incisional hernias are avoided, possibly resulting in less pain and certainly in a better cosmetic effect. 2) There may be potential advantages of a more rapid recovery, fewer adhesions and less postoperative ileus. 3) The natural orifice approach to the peritoneal cavity may be the ideal route in morbidly obese patients.[10]

Believing in the potential benefits of natural orifices approach to abdominal surgery, to our knowledge we were the first group to use a combined transgastric and transvesical approach to perform cholecystectomy, aiming to overcome many limitations that were previously described for the isolated transgastric approach related to anatomy exposure, organ retraction, grasping and limited triangulation.[9] Interestingly the combination of transgastric and transvesical ports was also particularly useful for approaching the kidney, making nephrectomy feasible by NOTES. We used the transvesical port because it is diametrically opposed to the transgastric port and seems to offer additional advantages over transvaginal and transcolonic ports.[18] In fact, although the transvesical port does not support as large instruments as transvaginal and transcolonic ports, it is sterile, available in the 2 genders and seems particularly safe, at least in a porcine model, even when left unclosed. Moreover, the bladder dome offers the most anterior position in the lower abdomen, allowing the introduction of surgical instruments above the bowel loops.[7,19] As proven by Gettman et al,[5] the great advantage of the transvaginal approach is its availability to remove the specimen.

Regarding the surgical technique, after a short learning curve we could open the renal peritoneum and dissect the renal vessels and ureter in a safe way. To open the peritoneum and dissect the hilum the coordination of the gastroscope and ureteroscope operators was vital. In fact, the 2 operators were constantly alternating their intervention on dissection vs retraction procedures. Whereas the ureteroscope had the advantage of being rigid, it had a significant limitation in width and image resolution as well as its fragile instruments. In contrast, the gastroscope had an enormous advantage in width and image quality but its flexibility and unstable platform frequently compromised its intervention. The gastroscope operator dealt with this limitation, working frequently in retroflexion with the gastroscope loop supported on the abdominal walls. With this approach we could dissect the right or left kidney in a similar way. However, it might be emphasized that in pigs the 2 kidneys are not hidden by the colon. In fact, predicting translation into humans, we should not neglect that the colon loop might complicate any renal approach by NOTES.

Regarding vessel ligation, we refused the idea of using an endoscopic loop to ligate the renal vein and artery simultaneously, as others described for splenectomy.[17] We chose to individualize each vessel, which we reasonably accomplished in the majority of cases, ligating them individually with ultrasonic scissors. Ultrasonic ligation was sufficient for most vessels but in 2 animals we observed mild hemorrhage after ultrasonic ligation. In this sequence we successfully applied surgical clips in some animals before ultrasonic ligation. The ureter was also easily dissected and ligated in all cases. After complete kidney release we used an endoscopic snare to hold up the organ and pull it out to the stomach.

During our experiments we realized that most of the time we could work safely with a low CO_2 pressure of approximately 3 mm Hg. We have 2 major explanations for this finding. 1) The entrance of the instruments into the abdomen is parallel to the abdominal wall. Thus, we do not need significant pneumoperitoneum because the instruments use the abdominal wall as a fulcrum when mobilized. 2) The close-up properties of endoscopic instruments, particularly the gastroscope, might be particularly relevant because, if confirmed in posterior experiments, it could mean that the surgical stress of NOTES procedures might be significantly decreased compared with that of laparoscopy. In fact, most surgical laparoscopic stress is related to CO_2 pressure.[20]

A major limitation of the current technique is related to our inability to safely close the gastrotomy. In fact, a critical element of any transgastric procedure is the ability to securely close the gastrotomy site that is required for endoscope passage and specimen removal. It is generally considered that an appreciable increase in patient morbidity from postoperative gastric leaks would expunge any patient advantage of the transgastric approach. For NOTES to achieve widespread adoption gastrotomy closure must be completely reliable. In this regard there are currently several endoscopic suturing devices in development.[21] Because we do not have available at our laboratory a reliable device to close the gastrotomy, we did not enlarge the gastrotomy to pull the specimen into the stomach. To promote its extraction we

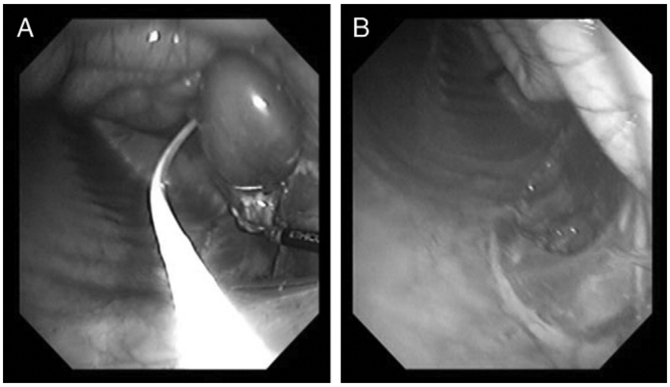

FIG. 10. Completed nephrectomy. *A*, gastroscopic snare drags released kidney. *B*, renal bed after kidney removal.

predicted that it would be removed after its division or morcellation. Thus, we decided to sacrifice all animals after nephrectomy and necropsy revealed that the renal vessels were completely sealed.

A common drawback of the NOTES approach is its limited capability to deal with perioperative complications. Although we were able to control mild hemorrhage with current commercial instruments, we believe that new instruments and devices are needed to increase our confidence in NOTES to perform complex intra-abdominal surgical procedures. Current ureteroscopes are highly developed for diagnostic and limited therapeutic tasks in the urinary tract but they are far from the ideal design to be used in NOTES. They have several limitations that limit their capabilities. 1) The image quality of the ureteroscope is not similar to that of the gastroscope or laparoscope and light intensity is also sometimes inadequate. 2) Ureteroscopes usually have a diameter of between 3.3 and 4.3 mm with 1 or 2 working channels of 4.2 Fr and 6.6 Fr, respectively, which limits the size of instruments. The endoscope shaft should be 5 mm and it should contain a larger channel to introduce other instruments with better efficiency. 3) Although the current rigid ureteroscope has some advantage for NOTES, such as allowing vigorous organ retraction for exposure, its rigidity might be a limitation to achieve retroperitoneum and other organs that are not in the axis of the bladder dome. Moreover, the tip of the ureteroscope should have flexibility and the ability to maneuver in all planes, allowing better tissue manipulation. The ideal device should allow complete rigidity for insertion and positioning with subsequent rigidity of the shaft, allowing traction/counter traction and continued flexibility of the tip, which should free the surgeon hands to manipulate different organs and tissues. 4) We should emphasize that the ultrasonic shears and even the clips that we used in this study for hilar ligation are not consensually approved for human purposes.

Although these concepts of NOTES could seem futuristic, we believe that guidelines for NOTES have already been established. Moreover, robotics and magnetic positioning technology can provide additional input for NOTES.[22] The feasibility of nephrectomy by NOTES appears in our understanding as the extreme of a large spectrum of renal procedures that can potentially be done by NOTES in the near future. However, we might consider that much study is still needed to refine techniques, verify safety and document efficacy before translation into humans to minimize unexpected complications.

CONCLUSIONS

Right and left nephrectomy using NOTES was feasible in a porcine model. Our study also demonstrates the limitations of the standard devices since we could not reliably achieve gastrotomy closure and remove the specimen. This study provides encouragement to further innovative programs to create devices designed to advance the safety of NOTES.

ACKNOWLEDGMENTS

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Abbreviations and Acronyms

NOTES = natural orifice transluminal endoscopic surgery

REFERENCES

1. Moll F and Rathert P: The surgeon and his intention: Gustav Simon (1824–1876), his first planned nephrectomy and further contributions to urology. World J Urol 1999; **17:** 162.
2. Clayman RV, Kavoussi LR, Soper NJ, Dierks SM, Meretyk S, Darcy MD et al: Laparoscopic nephrectomy: initial case report. J Urol 1991; **146:** 278.
3. Harrell AG and Heniford T: Minimally invasive abdominal surgery: lux et veritas past, present, and future. Am J Surg 2005; **190:** 239.
4. Gill IS, Cherullo EE, Meraney AM, Borsuk F, Murphy DP and Falcone T: Vaginal extraction of the intact specimen following laparoscopic radical nephrectomy. J Urol 2002; **167:** 238.
5. Gettman MT, Lotan Y, Napper CA and Cadeddu JA: Transvaginal laparoscopic nephrectomy: development and feasibility in the porcine model. Urology 2002; **59:** 446.
6. Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA et al: Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 2004; **60:** 114.
7. Lima E, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL et al: Transvesical endoscopic peritoneoscopy: a novel 5 mm-port for intra-abdominal scarless surgery. J Urol 2006; **176:** 802.
8. Lima E, Henriques-Coelho T, Rolanda C, Pego JM, Silva D, Carvalho JL et al: Transvesical thoracoscopy: a natural orifice transluminal endoscopic approach for thoracic surgery. Surg Endosc 2007; **21:** 854.
9. Rolanda C, Lima E, Pego JM, Henriques-Coelho T, Silva D, Carvalho JL et al: Third generation cholecystectomy by natural orifices: transgastric and transvesical combined approach (with video). Gastrointest Endosc 2007; **65:** 111.
10. Rattner D and Kalloo A: ASGE/SAGES Working Group on natural orifice transluminal endoscopic surgery. SAGES/ASGE Working Group on NOTES. Surg Endosc 2006; **20:** 329.
11. Jagannath SB, Kantsevoy SV, Vaughn CA, Chung SSC, Cotton PB, Gostout CJ et al: Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model. Gastrointest Endosc 2005; **61:** 449.
12. Park PO, Bergstrom M, Ikeda K, Fritscher-Ravens A and Swain P: Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 2005; **61:** 601.
13. Kantsevoy SV, Jagannath SB, Niiyama H, Chung SSC, Cotton PB, Gostout CJ et al: Endoscopic gastrojejunostomy with survival in a porcine model. Gastrointest Endosc 2005; **62:** 287.
14. Bergstrom M, Ikeda K, Swain P and Park PO: Transgastric anastomosis by using flexible endoscopy in a porcine model. Gastrointest Endosc 2006; **63:** 307.
15. Wagh MS, Merrifield BF and Thompson CC: Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. Gastrointest Endosc 2006; **63:** 473.
16. Merrifield BF, Wagh MS and Thompson CC: Peroral transgastric organ resection in the Abdomen: feasibility study in pigs. Gastrointest Endosc 2006; **63:** 693.
17. Kantsevoy SV, Hu B, Jagannath SB, Vaughn CA, Beitler DM, Chung SSC et al: Transgastric endoscopic splenectomy. Is it possible? Surg Endosc 2006; **20:** 522.

18. Fong DG, Pai RD and Thompson CC: Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. Gastrointest Endosc 2007; **65:** 312.
19. Rolanda C, Lima E and Correia-Pinto J: Searching the best approach for third-generation cholecystectomy. Gastrointest Endosc 2007; **65:** 354.
20. Neudecker J, Sauerland S, Neugebauer E, Bargamaschi R, Bonjer HJ, Cuschieri A et al: European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. Surg Endosc 2002; **16:** 1121.
21. Sclabas GM, Swain P and Swanstrom LL: Endoluminal methods for gastrotomy closure in natural orifice transenteric surgery (NOTES). Surg Innov 2006; **13:** 23.
22. Park S, Bergs RA, Eberhart R, Baker L, Fernandez R and Cadeddu JA: Trocar-less instrumentation for laparoscopy: magnetic positioning of intra-abdominal camera and retractor. Ann Surg 2007; **245:** 379.

Chapter 5

Endoscopic closure of transvesical port

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Endoscopic Closure of Transmural Bladder Wall Perforations

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Abstract

Background: Traditionally, intraperitoneal bladder perforations caused by trauma or iatrogenic interventions have been treated by open or laparoscopic surgery. Additionally, transvesical access to the peritoneal cavity has been reported to be feasible and useful for natural orifice translumenal endoscopic surgery (NOTES) but would be enhanced by a reliable method of closing the vesicotomy.

Objective: To assess the feasibility and safety of an endoscopic closure method for vesical perforations using a flexible, small-diameter endoscopic suturing kit in a survival porcine model.

Design, setting, and participants: This pilot study was performed at the University of Minho, Braga, Portugal, using six anesthetized female pigs.

Interventions: Closure of a full-thickness longitudinal incision in the bladder dome (up to 10 mm in four animals and up to 20 mm in two animals) with the endoscopic suturing kit using one to three absorbable stitches.

Measurements: The acute quality of sealing was immediately tested by distending the bladder with methylene-blue dye under laparoscopic control (in two animals). Without a bladder catheter, the animals were monitored daily for 2 wk, and a necropsy examination was performed to check for the signs of peritonitis, wound dehiscence, and quality of healing.

Results and limitations: Endoscopic closure of bladder perforation was carried out easily and quickly in all animals. The laparoscopic view revealed no acute leak of methylene-blue dye after distension of the bladder. After recovery from anaesthesia, the pigs began to void normally, and no adverse event occurred. Postmortem examination revealed complete healing of vesical incision with no signs of infection or adhesions in the peritoneal cavity. No limitations have yet been studied clinically.

Conclusions: This study demonstrates the feasibility and the safety of endoscopic closure of vesical perforations with an endoscopic suturing kit in a survival porcine model. This study provides support for further studies using endoscopic closure of the bladder which may lead to a new era in management of bladder rupture and adoption of the transvesical port in NOTES procedures.

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1. Introduction

Intraperitoneal bladder rupture may be caused by trauma (blunt or penetrating) or by iatrogenic interventions, particularly after resection following bladder-tumour removal [1]. Traditionally, these intraperitoneal perforations have been treated by open surgery or recently by laparoscopy, and the results of the prompt repair of the perforation site have been highly desirable, although others have proposed a conservative approach, consisting of either simple bladder drainage or bladder drainage with percutaneous drainage of the peritoneum, which also yields good results [2–4]. But for the majority of authors, urgent surgical closure remains the primary standard treatment for acute intraperitoneal perforation [1,5]. However, surgical closure, whether accomplished by laparotomy or by laparoscopy, is accompanied by risks of slow recovery from surgery because of ileuses and other sequelae, especially in patients who undergo closure of a perforation after laparotomy. Endoscopic closure of iatrogenic or traumatic vesical perforations might have the potential advantage of avoiding major additional trauma associated with laparotomy for surgical closure, with quicker recovery and shorter hospitalization.

Recently, a transvesical approach to the peritoneal cavity has been described by Lima et al [6] as a potential way to perform natural orifice transluminal surgery (NOTES). In experimental studies in pigs it was demonstrated that closure of a 5-mm bladder hole is not absolutely necessary if bladder drainage is assured. However, the development of an effective closure device might enable the widespread adoption of the transvesical port in NOTES.

The aim of this study was to evaluate the feasibility and the safety of endoscopic closure of vesical perforations with an endoscopic suturing kit in a porcine model.

2. Methods

The ethical review board of Minho University (Braga, Portugal) approved this study. Survival studies of endoscopic closure of transmural bladder-wall perforations using endoscopic suturing kit were performed in six consecutive 20–30-kg female pigs (*Sus scrofus domesticus*).

2.1. *Pig preparation*

The animals were restrained from food and water for 6 h before the surgical procedure. As previously described in detail [6], all procedures were performed under general anaesthesia, with 6.0-mm endotracheal intubation (Super Safety clear tracheal tube, Ruschelit, Rüsch, Kernen, Germany) and mechanical ventilation.

2.2. *Endoscopic suturing*

Paul Swain et al [7,8] developed a new device that has proven to be versatile and reliable in a variety of applications. It consists of three components (Fig. 1): (1) 3-0 thread attached to a metal T-tag; (2) a 19-gauge needle catheter, a long hollow needle enclosed in a plastic outer sheath, with a stylet to dislodge the T-tag (Cook Endoscopy, Winston-Salem, NC, USA); and (3) a thread lock-and-cut device for the thread (Davol, CR Bard, Murray Hill, NJ, USA).

A metal tag with a 3-0 Monocryl thread (Ethicon, Somerville, NJ) was loaded into the needle, and the needle point was

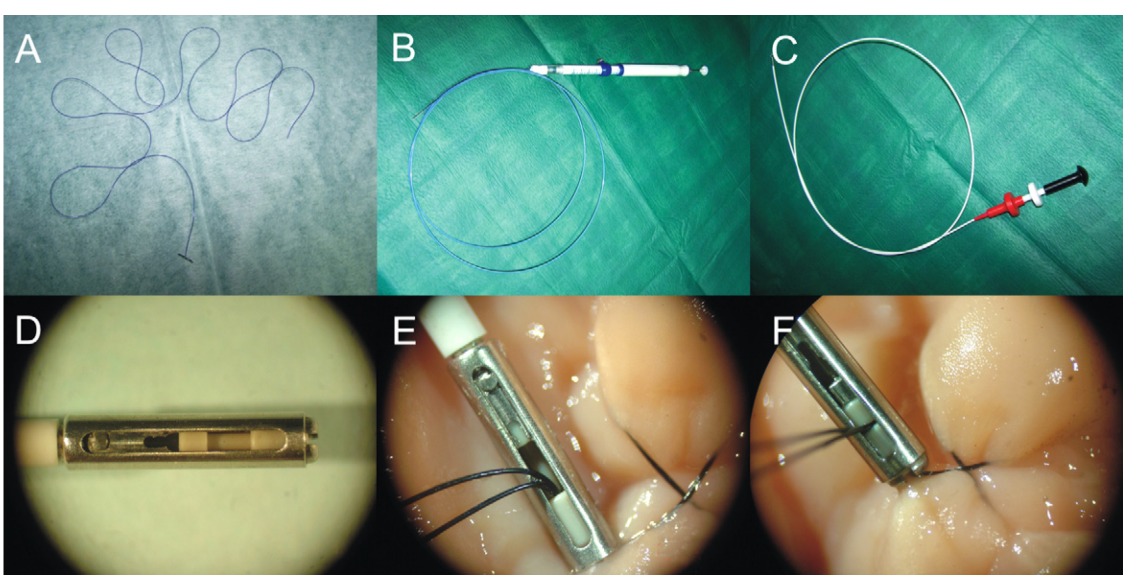

Fig. 1 – Endoscopic suturing kit. (A) The violet Monocryl holding the metallic T-tag; (B) endoscopic needle; (C) locker device; (D–F) sequence of macroimages of the locking mechanism.

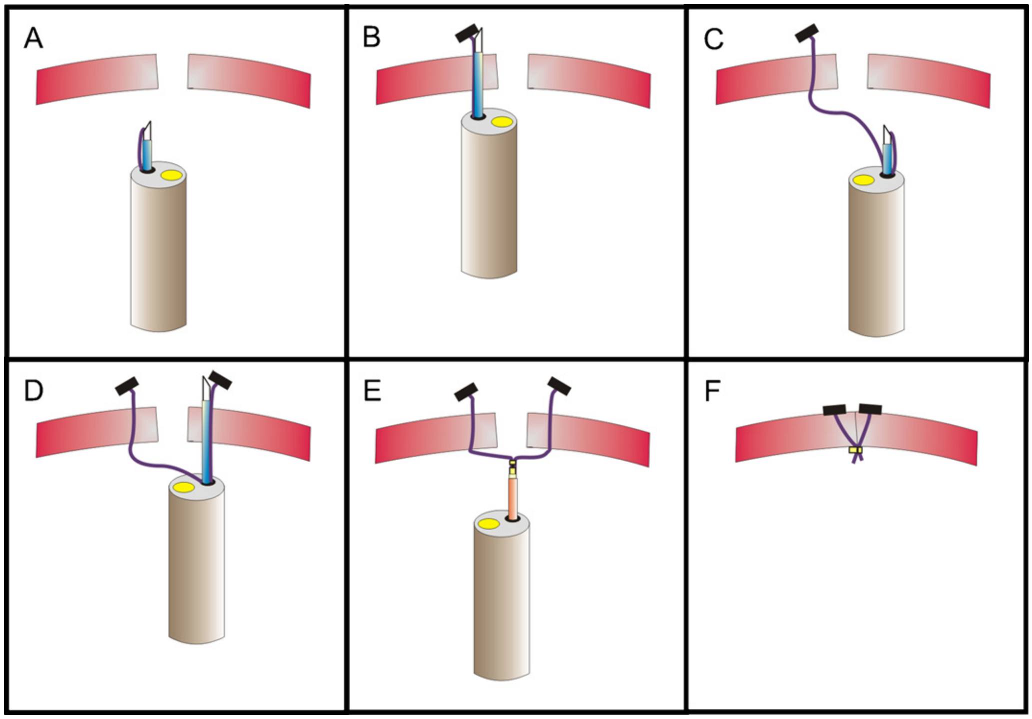

Fig. 2 – Diagram of the T-tags appliance and locking in the bladder wall. (A) Endoscopic needle approaching the edge of vesicotomy; (B) release of the first T-tag; (C) endoscopic needle approaching of the other edge of the vesicotomy; (D) release of the second T-tag; (E) lock advancement; (F) lock release.

withdrawn into the protective sheath. The needle, loaded with the tag and the thread, was passed through the working channel of a cystoscope, and the needle tip was advanced by a distance that penetrated through the bladder tissue into the peritoneum parietal surface. The depth of suture placement was controlled by extending the needle by a fixed distance in its sheath, which in the current experiments was fixed at 10 mm. The sheath acted as a stop, so that the distance penetrated by the needle could be controlled with some precision. This protective sheath was used to act as a stop to prevent the needle from passing too deeply. Once each pair of stitches had been placed, the threads were locked together. Subsequently, a combination device to lock and cut the thread was used (Fig. 1D–E). First, the threads were passed through holes in a cylinder with thread locks from a Bard (Davol) EndoCinch kit (Bard Billerica, Boston, MA, USA) and advanced until the lock was positioned snugly against the bladder wall. The lock was closed by pushing a pin into a cylinder compressing the two threads. The lock-and-cut device then forced the threads against an edge, which caused the threads to be cut. The suturing components were small enough to fit through the working channel of a cystoscope.

2.3. *Surgical technique*

A continuous-flow rigid cystoscope (Olympus A20933A with telescope A1931A) was introduced through the urogenital sinus and urethra into the bladder with CO_2 distension. Before any further intervention, the bladder was emptied of urine and refilled with CO_2. Then a full-thickness longitudinal incision of 10 mm (four animals) or 20 mm (two animals) at the bladder dome was created with endoscopic scissors (Karl Storz 26168A) introduced through the working channel of the cystoscope. Subsequently, the cystoscope was introduced into the peritoneal cavity to confirm a full-thickness incision of the bladder wall. All of the animals developed pneumoperitoneum, which was controlled with the insertion of a Veress needle into the peritoneal cavity.

Three steps were involved in the endoscopic closure of the perforation (Fig. 2): (1) With the animals in Trendelenburg position, the needle punctured on the edge of the perforation. (The 19-gauge needle was loaded with the metal T-tag attached to a 3-0 violet Monocryl thread 90 cm in length was advanced through the working channel of the cystoscope and placed through the full thickness of one the edges of the bladder wall.) By advancing the stylet, the T-tag and thread were released from the needle and left in the exterior part of the bladder. (2) Needle puncture of the opposite edge of the perforation, followed by release of T-tag, was performed in a similar way. (3) Knot tying was then accomplished, followed by suture cutting with a lock-and-cut device which was advanced to tie the threads together. The defect was closed by pulling the threads on either side of the incision together until they were snug against the lock and then closing the lock and subsequently cutting the threads with the lock-and-cut device and suture-cutting device. This resulted in a secure closure of the perforation. The adequacy of immediate closure was checked by performing a methylene-blue leak test under

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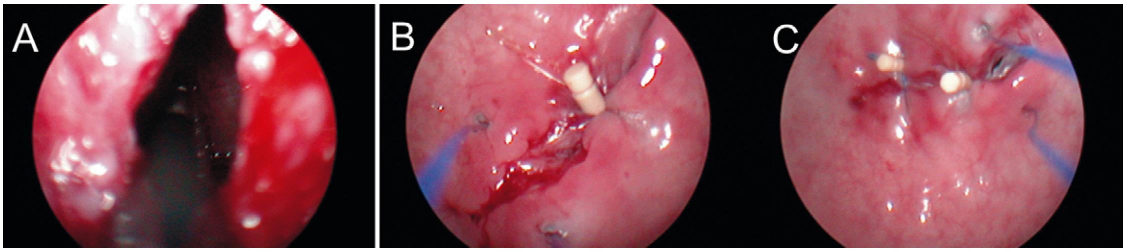

Fig. 3 – Inside bladder view during T-tag application in a 20-mm vesicotomy. (A) Open vesicotomy; (B) One lock applied and the positioning of an additional pair of threads (violet Monocryl) for a subsequent locking; (C) ending endoscopic suture of the 20-mm vesicotomy closure (third pair of T-tags being applied).

laparoscopic control in two animals. In this procedure the bladder was insuflatted with a hydrostatic column of up to 50 cm H_2O.

All animals were allowed to recover from anaesthesia. No catheter was left in the bladder. Oral feeding was started within 24 h. All animals were evaluated daily for 15 d. Necropsy examination was then performed with particular attention to the site of vesical perforation.

3. Results

Six bladder perforations of 10 mm to 20 mm in length were performed on six female pigs. All procedures involved in the creation of the vesical hole (cystoscopy, bladder full-thickness incision, and introduction of stitches) were performed without complication. We confirmed the presence of the perforation when we felt the pneumoperitoneum increase and saw the bowel loops inside the peritoneal cavity with the cystoscope.

The needle loaded with the T-tag punctured the bladder wall 5 mm to 10 mm from the edge of the perforation, and this component of the procedure was easy, accurate, and reliable. After application of each pair of threads, the margins of the perforations were closed by pulling smoothly on the threads which were positioned outside the cystoscope. Then each pair of threads was held by applying the cylindrical locks (Fig. 3). The application of the lock and its release was easy and quick in all animals. We were able to close all of the perforations effectively using one pair of threads in perforations $\leq$10 mm or three pairs in perforations between 10 mm and 20 mm. From the technical point of view, the endoluminal closure of the bladder perforation using the endoscopic suturing kit was fairly simple and straightforward. By controlling the pneumoperitoneum pressure with intermittent switching, opening or closing the Veress needle introduced into the peritoneal cavity transabdominally, we did not experience any difficulty in maintaining patency of the bladder lumen. The mean operative time from bladder-wall incision to completion of the closure was around 15 min.

In two animals the entire procedure (perforation, application of T-tags, and locking) was monitored by laparoscopy. In these animals we were able to fill the bladder with saline solution or solution coloured with methylene-blue dye until the bladders were fully distended and no leaks were observed laparoscopically (Fig. 4).

After the surgical procedure no catheters were left in the bladders, and the animals were allowed to recover from anaesthesia. After this, the pigs began to void urine normally and tolerated a regular diet which started the morning after surgery. They ambulated freely, exhibiting normal behaviour for 15 d, and no adverse event occurred during this survival period.

The postmortem examination 15 d after surgery revealed complete healing of the bladder wall incision. In the locale of vesical perforation, the sutures and locks were detected, and signs of healing without any evidence of transmural dehiscence were observed in all pigs (Fig. 5). There were

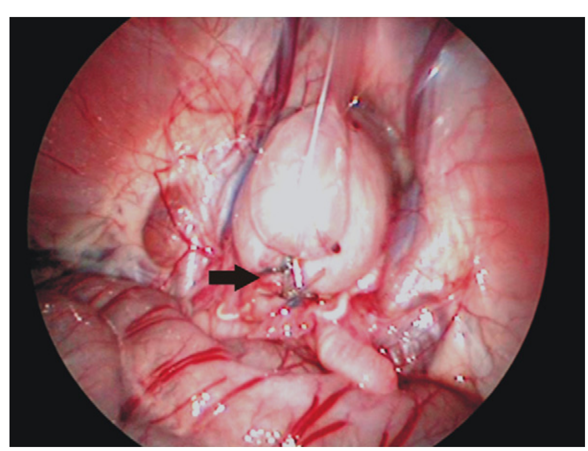

Fig. 4 – Laparoscopic view after T-tag application and distention of the bladder with saline. Twenty-millimeter vesicotomy closure after application of six metallic T-tags (arrow), which allowed three separated stitches.

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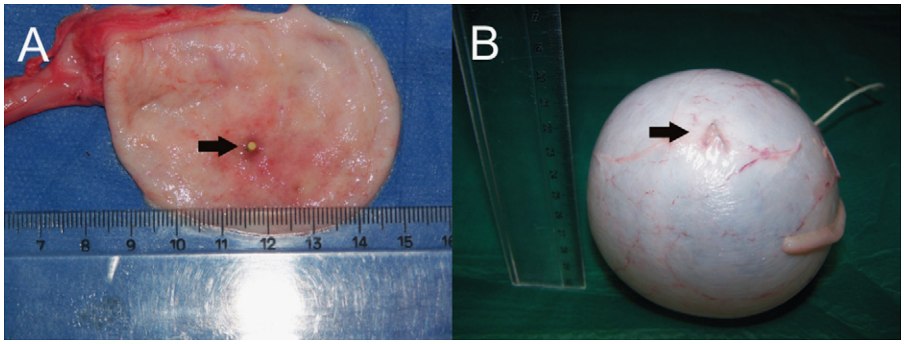

Fig. 5 – Necropsy images from the bladder after closure of a 10-mm vesicotomy. (A) Inside view showing the lock (arrow); (B) outside view showing metallic T-tags (arrow).

no signs of infection, visible leakage, or adhesions in the peritoneal cavity of any of the animals.

4. Discussion

This study describes a successful method for endoscopic closure of bladder perforations using the endoscopic suturing kit (T-fasteners with a locking cinch). Using a cystoscope with a regular 7F working channel, this method was feasible, easy, and safe in a survival porcine model.

Bladder perforation is a relatively common finding during the clinical activity of a urologist. In fact, several causes can result in bladder perforation, such as iatrogenic damage during transurethral resection of bladder lesions, blunt or penetrating abdomen-pelvic trauma [1,5], and more recently the planned vesicotomy described for NOTES procedures [6,9,10]. Until now, if we discovered a bladder rupture after transurethral bladder resection; we needed to convert from endoluminal to laparoscopy or even laparotomy in order to repair the perforation safely [1,5]. For small ruptures, bladder drainage might have been enough, but we commonly needed to leave the bladder catheterized for several days. Also, for small perforations following resections after removal of malignancies, bladder catheterization might have been be contraindicated in order to avoid intraperitoneal spillage of malignant cells. This happened because, until now, urologists have been unable to develop a reliable method for closing these perforations endoluminally.

Interestingly, if we look for endoscopic methods for closing perforations from other viscera like the gastrointestinal tract, it is possible to find many methods and devices designed for this purpose. In fact, one of the most highlighted challenges in surgery and gastroenterology is the endoscopic suturing of intestinal perforations caused by disease, inadvertent injury during endoscopy and endosurgery, and more recently, intentional perforations created for NOTES purposes. Currently, three types of full-thickness suture devices are under evaluation for perforation closure of stomach and colon: two through-the-endoscope devices such as the endoscopic suturing kit (T-fasteners with a locking cinch) and the gProx (USGI Medical, San Clemente, CA, USA), and one over-the-endoscope device, the Eagle Claw Suturing Device (Apollo Group and the Olympus Medical Systems, Tokyo, Japan) [11]. The endoscopic suturing kit has been used successfully in different gastrointestinal procedures (perforations after endoluminal gastric or colon resections, transgastric gastrojejunostomy and pyloroplasty, closure of perforated gastric ulcer) both in animals and humans [12–17]. Because this method uses equipment that works through a 2.8-mm channel of a standard gastroscope, we hypothesized that we could apply it through a 7F working channel of a cystoscope.

In this study, we applied the endoscopic suturing kit (T-fasteners with a locking cinch) method to closure vesicotomies from 10 mm to 20 mm in length, leaving the animals to survive without any bladder catheter. The method to apply the T-tags was easy, quick, and reliable to close a vesicotomy independent of its dimensions. In fact, we could apply one to three T-tags without difficulty in a mean time of ~15 min.

This method uses a full-thickness stitch that was easily applied in the bladder and does not require complex technology. All animals survived without any problems. A potential concern of closure with a full-thickness, needle-puncture technique is the risk of injury to adjacent intra-abdominal viscera. To avoid this, the depth of suture placement needs to be controlled precisely by extending the needle by a fixed distance in its sheath according the bladder-wall thickness that, in pigs, we found to be 10 mm.

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Additionally, such complications can also be avoided using the Trendelenburg position and the pneumoperitoneum that is generated after bladder perforation, since we use CO_2 during cystoscopy. These components of the procedure are important in order to avoid inadvertent placement of T-tags into a contiguous bowel loop and may be the reasons that we did not experience any of these complications in the postoperative period.

Regarding the appliance of T-tags in the bladder, it should be emphasized that for us, it seemed even easier than in the stomach or the colon because the instruments involved in the T-tag application and locking worked inside a rigid device (cystoscope) and the puncture was always done perpendicular to the bladder wall. Moreover, we would highlight that this method allowed application of each stitch precisely in place and always under good visual control.

Based on our previous experience with the transvesical approach to the peritoneal cavity using an over-tube (NOTES techniques) that easily allowed control of the pneumoperitoneum, we know that a major concern during the planning of these studies is the potential risk of a massive air leak through the bladder perforation into the peritoneal cavity causing tension on the pneumoperitoneum, resulting in cardiorespiratory compromise. To avoid this, we inserted percutaneously a Veress needle to relieve pneumoperitoneal hypertension. By using this decompression technique immediately after the development of the pneumoperitoneum, none of the animals developed cardiorespiratory compromise, and the visibility of the perforation was maintained for successful closure. Moreover, in practice, we did not observe problems with bladder deflation, even in the pigs that had measured evidence of a pneumoperitoneum before the introduction of Veress needle. Indeed, small, full-thickness, flexible endoscopic incisions in the bladder do not usually collapse the bladder completely. Another advantage of percutaneous insertion of a Veress needle into the peritoneal cavity is the possibility of emptying the peritoneal cavity of CO_2 after bladder-wall closure.

A potential limitation of this method that leaves a foreign body in the bladder (the locks) might be the lithogenic stimulus that it can promote. It is well known that any nonabsorbable material left in bladder can start a lithogenic process, and in fact, the locks are made of PEEK (polyetheretherketone), a nonabsorbable material. However, in our experiments we used for the first time T-tags held in place by an absorbable stitch using a 3-0 Monocryl thread. Therefore, we can predict that after 4–6 wk the absorption of the thread releases the lock into the bladder cavity that, because of its small dimensions ($3\ mm \times 1.5\ mm$), can be easily voided in the urine through the urethra. The application of T-tags with an absorbable suture is an innovative aspect of this study.

Regarding the potential benefits of this method to close iatrogenic bladder perforations endoscopically, we predict that it may be possible to avoid the additional trauma associated with laparotomy for surgical closure, with consequent quicker recovery and shorter hospitalization. The ability to close a perforation immediately within 10 min to 15 min after recognition during, for instance, a bladder resection limits the inevitable delay in treatment and may minimize the morbidity associated with surgical trauma. Moreover, it has the additional advantage of avoiding the risk of adhesions that may develop from peritoneal incision and dissection often involved with laparotomy and even laparoscopy. The duration of hospitalization may be shortened by eliminating the risk of ileus that frequently complicates laparotomy. Patients with serious comorbid conditions may not tolerate general anaesthesia and additional trauma associated with the open surgery. This method can be completed with the patient under raquianaesthesia, thereby eliminating the need for general anaesthesia and risks associated with it. Lastly, we predict that the cost-effectiveness of this method when compared with open or laparoscopic methods might constitute an additional advantage for its clinical application. However, although the suturing kit already has FDA (Food and Drug Administration [USA]) and CE (Conformité Européenne [Europe]) approval, it does not yet have a commercially defined price.

Although this study appears to provide enough support for human application, further studies might be useful to define the role of endoluminal closure of bladder perforations in terms of size (small vs large perforations), underlying bladder pathology (normal bladder vs inflamed bladder), and comparison with surgical closure. In contrast to our experiments, where we studied the closure of longitudinal perforations, rupture after trauma or iatrogenic are often not linear but irregular. Although the authors believe that this is not critical or a limitation for the application of T-tags, testing T-tags in these circumstances may be warranted.

Finally, despite the obvious utility of this method in iatrogenic and traumatic bladder rupture, this study strongly encourages application of the transvesical port in the emerging field of NOTES, which in

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general aims to minimize surgically associated abdominal stress. In fact, after the description of the transvesical port and its usefulness to perform several intra-abdominal procedures (ie, cholecystectomy and nephrectomy), it would be advantageous to develop a reliable closure method for vesicotomy which avoids bladder catheterization [18,19]. We believe the observations presented here might be relevant to transluminal procedures performed during NOTES procedures using the transvesical approach.

5. Conclusions

This study demonstrates the feasibility and the safety of endoscopic closure of vesical perforations using an endoscopic suturing kit (T-fasteners with a locking cinch) in a survival porcine model. This study provides support for further studies which assess the usefulness of clinical application of T-fasteners in this novel endoscopic method to close perforations in the bladder. This development may open a new era in management bladder rupture and transvesical port in NOTES procedures.

Author contributions: Jorge Correia-Pinto had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Lima, Correia-Pinto.
Acquisition of data: Lima, Osório, Pêgo, Silva, Henriques-Coelho, Mosse.
Analysis and interpretation of data: Lima, Correia-Pinto.
Drafting of the manuscript: Lima, Correia-Pinto.
Critical revision of the manuscript for important intellectual content: Bergström, Park, Mosse, Swain.
Statistical analysis: None.
Obtaining funding: Lima, Rolanda, Carvalho, Correia-Pinto.
Administrative, technical, or material support: Osório, Silva, Henriques-Coelho.
Supervision: Correia-Pinto.
Other (specify): None.

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References

[1] Gomez RG, Ceballos L, Coburn M, et al. Consensus statement on bladder injuries. BJU Int 2004;94:27–32.
[2] Figueiredo AA, Tostes JG, Jacob MV. Laparoscopic treatment of traumatic intraperitoneal bladder rupture. Int Braz J Urol 2007;33:380–2.
[3] Yee DS, Kalisvaart JF, Borin JF. Preoperative cystoscopy is beneficial in selection of patients for laparoscopic repair of intraperitoneal bladder rupture. J Endourol 2007;21: 1145–8.
[4] Pansadoro A, Franco B, Laurenti C, Pansadoro V. Conservative treatment of intraperitoneal bladder perforation during transurethral resection of bladder tumor. Urology 2002;60:682–4.
[5] Lynch TH, Martínez-Piñeiro L, Plas E, et al. EAU guidelines on urological trauma. Eur Urol 2005;47:1–15.
[6] Lima E, Rolanda C, Pêgo JM, et al. Transvesical endoscopic peritoneoscopy: a novel 5-mm port for intra-abdominal scarless surgery. J Urol 2006;176:802–5.
[7] Swain P, Park PO. Endoscopic suturing. Best Pract Res Clin Gastroenterol 2004;18:37–47.
[8] Swain P. Endoscopic suturing: now and incoming. Gastrointest Endosc Clin N Am 2007;17:505–20.
[9] Lima E, Rolanda C, Pêgo JM, et al. Transvesical thoracoscopy: a natural orifice translumenal endoscopic approach for thoracic surgery. Surg Endosc 2007;21:854–8.
[10] Gettman MT, Blute ML. Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice translumenal endoscopic surgery. Mayo Clin Proc 2007;82:843–5.
[11] Sclabas GM, Swain P, Swanström LL. Endoluminal methods for gastrotomy closure in natural orifice transenteric surgery (NOTES). Surg Innov 2006;13:23–30.
[12] Ikeda K, Mosse CA, Park PO, et al. Endoscopic full-thickness resection: circumferential cutting method. Gastrointest Endosc 2006;64:82–9.
[13] Ikeda K, Fritscher-Ravens A, Mosse CA, et al. Endoscopic full-thickness resection with sutured closure in a porcine model. Gastrointest Endosc 2005;62:122–9.
[14] Park PO, Bergström M, Ikeda K, et al. Endoscopic pyloroplasty with full-thickness transgastric and transduodenal myotomy with sutured closure. Gastrointest Endosc 2007;66:116–20.
[15] Bergström M, Ikeda K, Swain P, Park PO. Transgastric anastomosis by using flexible endoscopy in a porcine model (with video). Gastrointest Endosc 2006;63:307–12.
[16] Raju GS, Shibukawa G, Ahmed I, et al. Endoluminal suturing may overcome the limitations of clip closure of a gaping wide colon perforation (with videos). Gastrointest Endosc 2007;65:906–11.
[17] Pham BV, Raju GS, Ahmed I, et al. Immediate endoscopic closure of colon perforation by using a prototype

endoscopic suturing device: feasibility and outcome in a porcine model (with video). Gastrointest Endosc 2006;64: 113–9.
[18] Rolanda C, Lima E, Pêgo JM, et al. Third generation cholecystectomy by natural orifices: transgastric and transvesical combined approach. Gastrointest Endosc 2007; 65:111–7.
[19] Lima E, Rolanda C, Pêgo JM, et al. Third generation nephrectomy by natural orifices translumenal endoscopic surgery. J Urol 2007;178:2648–54.

Editorial Comment on: Endoscopic Closure of Transmural Bladder Wall Perforations

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Lima and coworkers present a well-conducted safety and feasibility pilot study that was performed using a novel endoscopic kit for the management of bladder wall perforations in a porcine model [1]. The results are of potential relevance as they are presented by authors with robust experience in the transvesical approach to the peritoneal cavity during natural orifice transluminal endoscopic surgery (NOTES). The thrust behind this paper seems to confirm the current trend of the surgical world and, in particular, of urology to find new, minimally invasive, alternative approaches for many surgical procedures [2,3].

As pointed out by the authors [1], the clinical usefulness of this endoscopic kit can be found in the apparently safe achievement of a water-tight bladder closure at the end of surgery; however, striving toward minimally invasive surgery must not distract the clinician from accurate and standard clinical management. In this case, the feeling is that the endoscopic closure of the bladder should be reserved for cases in which a targeted perforation is performed and any other extravesical problem has been previously assessed. When tackling abdominal trauma, for example, a laparoscopic abdominal inspection can be a better investigational tool. Anyhow, this study can indeed lead the way in suggesting an alternative when performing a novel and apparently valid method in a potentially catheter-free setting. As in most cases of uncomplicated bladder perforation, however, simple catheterization can be sufficient for healing. The question of when to use the device remains unanswered. Many points raised by this paper need to be further assessed, such as the cost–benefit ratio, the safety of the procedure, and the rationale and the correct indications for its use [4].

References

[1] Lima E, Rolanda C, Osório L, et al. Endoscopic closure of transmural bladder wall perforations. Eur Urol. In press. doi:10.1016/j.eururo.2008.06.010.
[2] Branco AW, Branco Filho AJ, Kondo W, et al. Hybrid transvaginal nephrectomy. Eur Urol 2008;53:1290–4.
[3] Box GN, Lee HJ, Santos RJ, et al. Rapid communication: Robot-assisted NOTES nephrectomy: initial report. J Endourol 2008;22:503–6.
[4] Gettman MT, Box G, Averch T, et al. Consensus statement on natural orifice transluminal endoscopic surgery and single-incision laparoscopic surgery: heralding a new era in urology? Eur Urol 2008;53:1117–20.

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Editorial Comment on: Endoscopic Closure of Transmural Bladder Wall Perforations

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NOTES (natural orifice transluminal endoscopic surgery) is gaining worldwide attention among the public [1] and interventional doctors [2]. Development of the instruments for this approach are a limiting factor; thus, Lima et al [3] should be congratulated for performing this feasibility study using a novel NOTES endoscopic suturing and cutting instrument (shown in Fig. 1 of their article) following intraperitoneal bladder rupture. This elegant system would appear to have a short learning curve and to be useful in clinical practice; however, as with any novel device, a few caveats need to be addressed.

Assuming a human model is used, there will on occasion be intraperitoneal corruption of varying degrees, including surgery, perforation of the bowel, inflammatory disease, or systemic illness. Although transvesical intraperiteonoscopy has been shown to be feasible in humans [4], the above examples would all cause adhesions, making blind entry or manipulation in this area unsafe.

In these situations, when performing laparoscopic surgery, we would advocate a retroperitoneal approach to avoid the corrupted areas [5]. If the surgeon were unfamiliar with this approach, an open technique (Hasson) would be used to safely enter the intraperitoneal space, followed by laparoscopic adhesiolysis.

Another issue would be the blind passing of the needle and thread with clips into the peritoneal cavity, which would increase the risk of bowel injury and potentiate the formation of an enterovesical fistula or bowel leak (see Fig. 1 in MacRae [1]). The clips to hold the suture and the suture itself are foreign bodies, so the risk of stone formation is an issue; however, this future risk is relatively small compared to performing an emergency laparotomy for the perforation.

Finally, if planning on performing this procedure, peritoneal inspection must be performed to reliably inspect the entire length of bowel. A flexible camera could overcome this issue and allow an adequate inspection. Any bowel injury would need suturing. The system described could oversew any areas with diathermy injury or formal enterotomy, but the bowel would need steadying to complete the repair. Currently, the described system cannot perform the latter.

If using this instrument in clinical practice, I would suggest that the patient be placed in steep Trendelenburg, followed by intraperitoneal pneumoinsufflation to further delineate the bladder perforation from any organs, placement of a 5-mm umbilical camera to inspect the bowel in detail, and direct observation of the instrument suturing the perforation. If bowel is affected, two additional 5-mm ports would suffice to safely repair any enterotomies (and if needed, repair the bladder).

I hope to see further development of these instruments as we move forward into the new era of NOTES.

References

[1] MacRae F. Surgeons remove man's appendix through his mouth in world first operation. Mail Online. April 19, 2008. Available at www.dailymail.co.uk/news/article-560021/Surgeons-remove-mans-appendix-mouth-world-operation.html.

[2] Gettman MT, Box G, Averch T, et al. Consensus statement on natural orifice transluminal endoscopic surgery and single-incision laparoscopic surgery: heralding a new era in urology? Eur Urol 2008;53:1117–20.

[3] Lima E, Rolanda C, Osório L, et al. Endoscopic closure of transmural bladder wall perforations. Eur Urol. In press. doi:10.1016/j.eururo.2008.06.010.

[4] Gettman MT, Blute ML. Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice translumenal endoscopic surgery. Mayo Clin Proc 2007;82:843–5.

[5] Joseph JV, Patel HR. Extraperitoneal laparoscopy and robotic surgery. New York: Springer. In press.

DOI: 10.1016/j.eururo.2008.06.012

DOI of original article: 10.1016/j.eururo.2008.06.010

Chapter 6

Discussion

Since the introduction of laparoscopic surgery that has been shown that reduction of surgical incisions reduces post-operative pain and recovery time. Envisioning evolution Reddy and Rao from India performed a very controversial procedure: Human transgastric appendectomy (Rattner and Kalloo, 2006). Recognizing the potential benefits of this procedure, Kalloo and collaborators in 2004 pursued this idea performing in a very well structured way testing in pigs the feasibility and limitations of abdominal surgery without scars through a transgastric port (Kalloo et al., 2004). This was the birth of *Natural Orifice Translumenal Endoscopic Surgery* (NOTES). This approach was envisioned with several advantages once it would avoid the abdominal incisions and all the consequences of them, such as incisional hernias and infections of surgical wounds. Moreover, it has the theoretical potential to reduce even more the postoperative pain and recovery time when compared with laparoscopy. This makes sense because the factors that cause visceral pain are different from those that cause somatic pain. In fact, it is well-known for several years that cutting the gut and viscera rarely elicit pain.

Fascinated by this approach and predicting the emergence of what we saw as the '*Third Generation Surgery*', we started with this venture project in 2005. At that time there was a terrific debate about the potential benefits from transgastric access and the several challenges that it was causing regarding the several limitations that were being identified by the scarce groups that were testing the transgastric port experimentally. In fact, there was a consensus that the transgastric access was not totally sterile and the difficulties in its endoscopic closure could be cause of serious complications in abdominal surgery. Despite the aggressive criticisms from the most conservative surgeons and endoscopists, the possibility to perform scarless surgery nursed an increasing number of dreamers and believers in NOTES. Thus, a joint effort from key persons from the *American Society for Gastrointestinal Endoscopy* (ASGE) and *Society of American Gastrointestinal Endoscopic Surgeons* (SAGES) collected the preliminary data and summarized in a white paper the most important limitations and some potential strategies to overcome them (Rattner and Kalloo, 2006). Interestingly, these strategies were mainly based on increasing the size and complexity of gastroscopes with more working-channels, tools and capabilities.

In this sequence, and believing in the rationale of NOTES, we also tried to identify what would be the major limitations and what strategies we could launch with our limited technological resources to solve those limitations. In our point of view, the major limitations of isolated transgastric port were related with the nature of the gastroscope instruments (flexible and parallel), which made the surgeons to loose some important principles from classical and laparoscopic surgery during transgastric procedures, such as: i) absence of triangulation; ii) poor retraction capability; iii) the necessity to work frequently in retroflexion with an inverted image.

Thus, we hypothesized that the development of a lower abdominal port for introduction of rigid instruments would be a simple and easy way to overcome most of those limitations of the isolated transgastric port. Using current urologic instruments, we planned an atraumatic method to create a transvesical port. In a preliminary surviving experimental study, we demonstrated that the transvesical endoscopic approach to the peritoneal cavity was feasible and easy to create without any further complications in a porcine model even we left the vesicotomy open just with a bladder catheter (chapter 2) (Lima et al., 2006).

The transvesical port revealed properties to become an excellent access to the abdominal cavity. In fact, this access is naturally sterile, anatomically is the most anterior lower abdominal port providing instrument access to the peritoneal cavity above the bowel loops. Moreover, it allowed the introduction of rigid instruments into the peritoneal cavity enhancing the possibility to retract structures in an easy way. The only disadvantage was due to the diameter of the urethra limiting specimen retrieval and the size of the instruments used by this approach (chapter 2) (Lima et al., 2006).

Given the unexpected good results from our first study, we felt encouraged to test the possibility to reach even the thoracic cavity, what we could perform after surpass the diaphragm. In this study, although we had been able to perform only limited thoracoscopy and lung biopsies, it definitively extended the intervention field of NOTES from peritoneal to thoracic cavity as well (chapter 3) (Lima et al, 2007).

Subsequently, other group from Harvard University developed the transcolonic access as concurrent with the transvesical approach. This study confirmed the benefits of a lower abdominal access namely the possibility to introduce rigid instruments and direct image from the upper abdominal organs, what pushed them to perform transcolonic cholecystectomy (Pai et al., 2006; Fong et al., 2007). However, the transcolonic port retained many of the limitations previously described for the transgastric port, because it is not sterile requiring a reliable and effective closure device that was not available even at this moment.

Given the ongoing difficulties in finding safe devices for endoscopic closure, several investigators tried to re-discovery the transvaginal access (posterior colpotomy), which was being used for many years by the gynecologists to perform pelvic interventions. This access provided the same benefits as the transvesical and transcolonic accesses and revealed safe because it is easily closed without an endoscopic device since its closure is possible with current surgical stitches from outside. In fact, the transvaginal port allows introduction of rigid instruments and organ retrieval even of large dimensions. These characteristics gave confidence to the Mareascaux group from IRCAD; Strasbourg in France to perform the first totally NOTES transvaginal cholecystectomy in Humans in 2007 (Marescaux et al., 2007), a procedure that easily became popular and widespread worldwide. However, this approach still has a serious constrain as it is only available in females.

Table 1. Clinical comparison of gastric and lower abdominal accesses.

	Stomach	**Bladder**	**Vagina**	**Colon**
Rigid instruments	No	Yes	Yes	Yes
Available in both genders	Yes	Yes	No	Yes
Sterility	No	Yes	No	No
Size	Wide	Narrow	Wide	Wide
Closure	In study	Yes	Yes	In study
Specimen retrieval	Yes	No	Yes	Yes

After the description of all lower abdominal accesses several conclusions come out, such as the lower abdominal ports are better for upper abdominal procedures and useful as accessory ports for transgastric access. The comparison of all abdominal ports (table 1) seems to select the transvaginal port as the most reliable for Human application at this moment. In fact, the transvaginal access is the most commonly used in Human field so far. However, it has a serious limitation since it is available only in females and can raise serious psychological concerns that we are still far a way to fully know the impact. Taking this into account, we believe that the transvesical port is likely the most universal access from lower abdomen. However, the transvesical access had faced some reluctance from Medical community since we did not describe a way to close it in our first description. Thus, we checked all current methods to close visceral holes endoscopically and we tested the usefulness of T-fasteners with a locking cinch system. In this study, we could demonstrate the feasibility and the safety of endoscopic closure of vesical perforations with an endoscopic suturing kit (T-fasteners with a locking cinch) in a survival porcine model. These findings provide immediate support for clinical application of this method to close bladder perforations both in management bladder rupture and transvesical port in NOTES procedures (Chapter 5) (Lima et al., 2008).

Confirming our initial hypothesis that the transvesical approach would overcome some limitations of isolated transgastric access, we demonstrated that adding the transvesical to the transgastric port provided the surgical team of a better surgical triangulation and effective retraction. In fact, with this strategy we reported for the first time the third generation nephrectomy by pure NOTES combined accesses (transgastric and transvesical ports) launching the concept of combined or multiple ports for NOTES (Chapter 4) (Lima et al., 2007).

Regarding the potential applications of the transvesical port in Humans given its anatomic and physiological properties, we predict that the transvesical port can have several types of application in Humans, such as: i) isolated port for both urological and non-urologic procedures as deeply scrutinized in manuscripts from annexes 1 and 2; ii) as an accessory port for combining with other ports as developed in manuscript from annex 2; iii) in hybrid procedures with abdominal ports, namely with the single-port access as advanced in manuscript from annexes 2 and 3 (Lima et al., 2008; Lima et al., 2008; Gettman et al., 2008).

In conclusion, the thesis fully characterized experimentally the rationale, method for creation, usefulness, limitations, and closure method of the transvesical port for potential clinical application in NOTES. Moreover, the closure method can have other applications in Humans namely as a reliable way to close endoscopically traumatic or iatrogenic bladder ruptures.

Future Directions

Most criticism against NOTES ecoes what was said against those who were pioneering laparoscopic surgery in the late 1980s. Laparoscopic surgery has now become a gold standard in the treatment of many abdominal diseases. We should have learned the lesson and look at new coming techniques with a good attitude.

Currently available instruments are designed to function inside the urinary and gastrointestinal tract and have some limitations when used inside the peritoneal cavity. Certainly the birth of NOTES is pushing researchs and surgeons to design a new generation of instruments and equipment. Hybrid instruments that combine patterns typical of rigid and flexible endoscopy will be the next genation technology to be used in our future surgical rooms.

Advanced endoscopic skills are of paramout importance to perform NOTES. If NOTES is to be adapted in humans the structure of training programs in Urology and Surgery must change. Introducing and advanced tier of training in NOTES will probably be a necessity.

The transvesical access to the peritoneal cavity was demonstrated to be feasible, safe and useful for many intrabdominal procedures in a porcine model. The next logical step is to get institutional review boards (IRB) approval for Human application of the transvesical port. The first clinical trials should combine the transvesical port and laparoscopy. This will provide a margin of confort in prenting and dealing with complications as we progress to pure transvesical procedures.

Annex 1

The transvesical endoscopic port for NOTES

Lima E, Rolanda C, Correia-Pinto J. Transvesical endoscopic peritoneoscopy: intra-abdominal scarless surgery for urologic applications. *Curr Urol Rep*; 9: 50-54, 2008.

Transvesical Endoscopic Peritoneoscopy: Intra-abdominal Scarless Surgery for Urologic Applications

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For many abdominal procedures, advantages such as minimal scarring, reduced pain, and faster recovery have made laparoscopy the favored approach over traditional open surgery. The most recent minimally invasive approach is natural orifice transluminal endoscopic surgery (NOTES), which limits morbidity because this surgery does not require incision. This article reviews the history, development, and current and future applications of NOTES in the field of urology.

Introduction

The introduction of laparoscopic surgery at the end of the 20th century revolutionized modern surgical practice, significantly changing surgical considerations, techniques, and all other aspects of modern surgical patient care [1]. Simultaneously, endoscopy evolved from simple diagnostic to progressively invasive therapeutic procedures [2]. Historically, endoscopy has avoided gastrointestinal lumen perforation; although this principle mostly persists, recent anecdotal reports have described safe endoscopic procedures beyond the visceral wall, such as transgastric drainage of pancreatic pseudocyst [3]. Reddy and Rao [4], for example, performed transgastric appendectomy in humans cases, while Kalloo et al. [5••] demonstrated the feasibility and surgical utility of transgastric access to the peritoneal cavity in a porcine model.

These developments marked a new era in minimally invasive abdominal surgery, compelling novel, previously audacious goals, such as avoidance of incisions and pain. With the visceral wall no longer a barrier to endoscopic intervention, various authors described novel, complex abdominal procedures [6–16]. In 2006, such reports motivated researchers in this emerging field to organize the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR), a joint initiative supported by the American Society for Gastrointestinal Endoscopy (AGES) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES). Proceedings were reported in the Natural Orifice Transluminal Endoscopic Surgery (NOTES) white paper [17••]. European researchers also formed the European Association of Transluminal Surgery (http://www.eats.fr) and the EURO-NOTES Foundation (http://www.euro-notes.eu) to ease cooperation between the European Association for Endoscopic Surgery (EAES) and the European Society of Gastrointestinal Endoscopy (ESGE), which focuses on NOTES-related activities. As a result, an increasing number of researchers are committed to NOTES, publishing experimental reports and attending industry-supported, international conferences where specialists confirm the approach's feasibility and efficacy for abdominal surgery.

The use of natural orifices for abdominal surgery entrance ports subsequently lead to transvesical access, resulting in unexpected success for abdominal urologic and nonurologic procedures [18••].

This article reviews the current status of NOTES, focusing on new challenges and potential clinical applications in urology.

Current Status of NOTES

Rationale and potential benefits

NOTES is a revolutionary peritoneal cavity intervention; a natural convergence of intraluminal (endoscopy) and extraluminal (laparoscopy) endoscopic techniques [19]; a third-generation surgery after open surgery (first generation) and laparoscopy (second generation) [16,18••,20] that requires new equipment, special training, and often interdisciplinary collaboration. Advantages over other approaches include no scarring, less anesthesia and postoperative pain, no abdominal wound infection or incisional hernia, fewer adhesions and postoperative ileus, and more rapid recovery [17••]. However, no studies have demonstrated advantages beyond cosmetic appearance. Studies need to compare the efficacy of NOTES and laparoscopy in terms of surgical stress prevention and morbidity. Impact on immune system also needs to be determined. Until these issues are addressed, potential benefits remain theoretical.

Experimental studies

Natural orifice surgery began in 1928 when Decker [21] performed the first culdoscopy. In 2002, Gettman et al. [22] reported a transvaginal laparoscopic nephrectomy in five female pigs using a single 5-mm abdominal trocar; however, limitations related to the porcine model and instrumentation made the procedure cumbersome. Kalloo et al. [5••] reported the first natural orifice endoscopic surgery using a transgastric approach in a porcine model in which they orally introduced a flexible endoscope into the peritoneal cavity to perform peritoneoscopy and liver biopsies. At procedure's end, researchers closed the gastric wall with endoscopic clips. In five experiments, all pigs recovered and gained weight.

Several studies have since used the transgastric port for intraperitoneal abdominal procedures, such as fallopian tube ligation, cholecystectomy, gastrojejunostomy, lymphadenectomy, oophorectomy, partial hysterectomy, splenectomy, appendectomy, and diaphragmatic pacing [6–15,23]. Following the initial enthusiasm, however, abdominal procedures through isolated transgastric routes raised limitations that jeopardized application in humans. Potential barriers to clinical practice included safe access to peritoneal cavity; gastric closure; infection prevention; spatial orientation; stable multitasking platform to obtain adequate anatomy exposure, organ retraction, secure grasping, and triangulation; difficulty in controlling the pneumoperitoneum; and management of iatrogenic intraperitoneal complications. These limitations are primarily related to the isolated transgastric approach and the characteristics of endoscopes such as flexibility [17••].

Lima et al. [18••] hypothesized that a port enabling rigid instrument use would be advantageous, and subsequently assessed the feasibility and safety of a 5-mm transvesical port for abdominal cavity access. This approach was feasible and safely performed in a survival porcine model [18••]. Recently, the same researchers used the transvesical port to perform thoracoscopy with lung biopsies through the diaphragm in a survival porcine model study [24]. A transcolonic port approach has also been reported involving several complications related to the nonsterile nature of the colon [25].

Cholecystectomy is the most challenging isolated transgastric approach. Using two endoscopes, or a single endoscope conjugated with a transabdominal trocar, Park et al. [7] and Swanstrom et al. [26] experienced significant difficulties performing cholecystectomy using shape-lock technology. Rolanda et al. [20] introduced a combined transgastric and transvesical approach to effectively perform moderately complex upper-abdominal procedures such as cholecystectomy. More recently, Lima et al. [16] used the same combined approach to perform nephrectomy. In fact, this was the first group to combine distinct natural orifices approaches to perform complex abdominal surgery.

Human studies

Reddy and Rao [4] proved the transgastric approach feasibility by performing a NOTES appendectomy in humans [4]. Recently, Marescaux et al. [27] performed a transvaginal cholecystectomy using a single abdominal 2-mm trocar. Although unpublished, Brazilian researchers claim to have performed cholecystectomy by a hybrid transvaginal and transabdominal trocar approach. More recently, the first human cases of transgastric cholecystectomy have been presented using a single transabdominal trocar. Further, initial clinical evaluation of the bladder as a NOTES port has already been successfully attempted in humans [28].

Current limitations

NOTES is still in an investigational, developmental stage. Several limitations need to be addressed before these procedures are safe and reliable. NOSCAR has established taxonomy, delineated the current limitations of NOTES, and instigated a unified plan of research to propel NOTES into human practice. Challenges include creating a safe, transmural access point; maintaining sterility of peritoneal cavity despite peroral instrument use; creating a pneumoperitoneum to distend the peritoneal cavity and allow adequate visualization; ensuring availability of endoscopes and equipment for therapeutic procedures; and developing an entirely reliable means of securely closing the transmural access point [17••]. Of these barriers to clinical practice, gastrostomy closure is the most crucial to solve; various devices are being developed to aid closure [29]. Fast, simple, and effective endoscopic suturing devices will be important for anastomosis, closure of access incisions, and treatment of complications such as bleeding. Examples of endoscopic suturing devices include the prototype known as the Eagle Claw (Olympus America, Center Valley, PA); the novel endoscopic incision and closure device called the Stringer Device (LSI Solutions, Victor, NY); the g-Prox (USGI Medical, San Clemente, CA), which combines an aggressive grasper with a needle delivery device that delivers expandable baskets connected by permanent suture; and a prototype device that combines the well-known technology of T-fasteners with a locking cinch device (Johnson and Johnson, New Brunswick, NJ) [29,30]. Currently, endoclips are the most commonly used method for gastrostomy closure [5••]. However, endoclips are designed for hemostasis and are not sited for approximating gastrostomy edges for incision closure.

Unless safe and simple devices with proven efficacy for endoscopic closure are available, NOTES will remain in the research field due to an unacceptable complication risk in general practice. Availability of a safe and simple gastrostomy closure device is therefore essential for widespread adoption.

The Role of Urology in NOTES

Bladder as natural orifice

As with the transgastric port innovation, the transvesical approach surpassed a classical urologic barrier, the urinary tract wall. Bladder wall perforation was considered a potential complication of urologic procedures. However, with success similar to that of transgastric port, the bladder is an attractive port for NOTES procedures once sterilized because it allows passage of rigid instruments and it is the most anterior access (above bowel loops) from the lower abdomen [18••].

Technique

Until recently, experimental and human preliminary studies reported that the transvesical port was easy to install, even with instruments for urologic purposes, using a technique based on the Seldinger principle. We use a ureteroscope introduced through the urethra into the bladder with pneumodistension, emptying urine from the bladder and distending it with CO_2. The vesicotomy site is carefully selected on the bladder dome. A mucosal incision is made with scissors introduced through the working channel of the ureteroscope. Subsequently, a 5 Fr open-ended ureteral catheter is pushed through the incision into the peritoneal cavity. A 0.035-inch flexible-tip guidewire is inserted into the peritoneal cavity through the ureteral catheter lumen. Guided by the flexible-tip guide-wire, a ureteroscope sheath dilator enlarges the vesical port with a flexible 5.5–mm overtube enveloping it. Introduction of a ureteroscope via overtube into the peritoneal cavity establishes a pressure-controlled CO_2 pneumoperitoneum. The ureteroscope is ultimately withdrawn from the abdominal cavity after CO_2 removal and a Foley catheter is inserted into the bladder for 3 to 4 days [18••,24].

Advantages and limitations

Lower abdominal access points, including the transvesical, transvaginal, and transcolonic ports, can be used as an isolated or complementary transgastric port. Several researchers who performed complex abdominal procedures via an isolated transgastric pathway have encountered problems with decreased triangulation and retroflexion [26]. Lower abdominal ports, however, may overcome some of these limitations, with added advantage in complex operations. Although lower abdominal ports provide frontal access to upper abdominal organs and enable improved instrument access, the transvesical port offers sterility and the anatomical advantage of the most anterior lower abdominal access. Further, the transvesical port enables rigid instrument introduction and does not necessarily require closure [31].

Accessing the peritoneal cavity through a natural orifice risks damaging adjacent organs during visceral wall incision. Among natural orifice ports, transvesical port creation with a Seldinger-like technique may be the safest approach because bowel loops that contact the bladder wall are unrestricted in the abdomen, which make them run away from bladder instruments. Further, in procedures involving two natural orifices, such as transgastric and transvesical, the transvesical image can easily monitor the transgastric creation.

The transvesical port procedure involves a significant challenge related to instrument size, limiting organ retrieval through this port. Another concern related to transvesical port use is the necessity of bladder closure. Vesical perforation involves potential complications, such as peritoneal urine leakage with secondary infection (peritonitis), that commonly occur as delayed complications of undiagnosed traumatic vesical perforation or pathological bladder conditions, such as neoplasms. Experiments in pigs demonstrated that 5 mm bladder hole closure is not absolutely necessary if bladder drainage is assured [18••,24]. However, development of a closure device or method is imperative for the widespread adoption of transvesical port option in NOTES.

Applications in urology

NOTES' urologic application may not be immediately apparent, considering the current acceptance of laparoscopic surgery. However, several groups are using natural orifices to perform complex procedures such as nephrectomy.

Gettman et al. [22] first performed a complete transvaginal laparoscopic dissection and nephrectomy in a porcine model using a single, 5-mm abdominal trocar for visualization. A completely transvaginal laparoscopic nephrectomy was performed once, but limitations imposed by porcine anatomy and available instrumentation hindered the procedure [22]. More recently, Clayman et al. [32] performed a porcine nephrectomy with a single 12-mm trocar placed in the midline and the transvaginal introduction of a TransPort Multi-Lumen Operating Platform (USGI Medical, San Clemente, CA). This flexible device has four working channels and can be locked into position, creating a rigid multitasking platform that enables two-handed tissue manipulation [32]. Further, Lima et al. [16] demonstrated the feasibility of NOTES nephrectomy. In a nonsurvival study, combined transgastric and transvesical approaches were established in six female pigs. Under ureteroscope visualization through a 5-mm transvesical port, researchers controlled the orally introduced flexible gastroscope by the gastrotomy into the peritoneal cavity. Right or left nephrectomy were performed using instruments introduced by devices that worked in the renal hilum, alternating intervention on dissection or retraction procedures. In all animals, both kidneys were visualized, and the renal vessels and ureter were reasonably individualized and ligated separately with ultrasonic scissors introduced through the transvesical port [16].

Nephrectomy most likely will be one of the final renal procedures potentially performed by NOTES in the near future. However, much research is needed to minimize unexpected complications before NOTES can be applied in humans. Robotics and magnetically anchored instrumentation used to perform single trocar laparoscopic nephrectomy may be logical steps in the development of scarless abdominal surgery by NOTES [33].

Beyond renal procedures, other potential human applications of NOTES in urology include varicocelectomy, investigation of nonpalpable testis, and treatment of urachus remnants using transgastric or transvesical ports.

Involvement of urologists in other abdominal procedures

NOTES may present a tremendous challenge for urologists in terms of technical demands. It may also involve multidisciplinary teams to deal with nonurologic clinical situations, considering the simplicity of accessing and viewing the upper abdominal organs via the transvesical port [15,24].

In animal and human settings, the transvesical port enables feasible and useful peritoneoscopy of all intra-abdominal viscera, mainly the upper abdominal organs [18••,24,28]. Further, the transvesical port is gaining a place in NOTES as a unique port associated with the transgastric port [16,20]. Rolanda et al. [20] demonstrated the utility of a combined transgastric and transvesical approach, performing a reliable, feasible, exclusive NOTES cholecystectomy. This study emphasized the transvesical port's ability to overcome limitations reported in a cholecystectomy performed exclusively through a transgastric port [20].

Although possibly difficult to accept clinically, the transvesical port provides exceptional access to the upper abdominal organs and may enable a transdiaphragmatic endoscopic approach to the thoracic cavity in a long-term survival study in a porcine model [21].

Most of these studies are preliminary and only represent the birth of NOTES in urology; however, they demonstrate a need for new instruments and further research that provides evidence that experimental successes may advantageously translate to clinical practice in humans.

Conclusions

In many areas of medicine, divisions between specialties are blurring. For example, stent placement for carotid stenosis is now performed by neuroradiologists, interventional radiologists, vascular surgeons, and cardiologists. Similar reports commonly occur in other clinical areas. Currently, NOTES procedures and research are primarily performed by gastroenterologists and surgeons. However, because the mouth and colon are not the only access points, urologists and gynecologists have approached the peritoneum through the bladder and vagina. Further, NOTES has enabled transvaginal nephrectomy, transgastric adrenalectomy (unpublished data), peritoneoscopy, and thoracoscopy using a transvesical approach, and cholecystectomy and nephrectomy using a combined transvesical and transgastric approach [16,18••,20,22,24, 28,32]. These procedures have mostly been performed in animal models, but human application is pending.

Urologists have been encouraged in this developing field to meet an especially great demand should NOTES develop as some investigators have proposed. Further, the future may require the development of new NOTES training programs to address specific demands.

Disclosures

No potential conflict of interest relevant to this article was reported.

References and Recommended Reading

Papers of particular interest, published recently, have been highlighted as:

- • Of importance
- •• Of major importance

1. Harrell AG, Heniford BT: **Minimally invasive abdominal surgery: lux et veritas past, present, and future.** *Am J Surg* 2005, **190:**239–243.
2. Liu R, Chand B, Ponsky J: **The future of surgical endoscopy.** *Endoscopy* 2005, **37:**38–41.
3. Vitale GC, Lawhon JC, Larson GM, et al.: **Endoscopic drainage of the pancreatic pseudocyst.** *Surgery* 1999, **26:**616–623.
4. Richards WO, Rattner DW: **Endoluminal and transluminal surgery: no longer if, but when.** *Surg Endosc* 2005, **19:**461–463.
5.•• Kalloo AN, Singh VK, Jagannath SB, et al.: **Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity.** *Gastrointest Endosc* 2004, **60:**114–117.

The first description of transgastric surgery. This manuscript marks the birth of NOTES.

6. Jagannath SB, Kantsevoy SV, Vaughn CA, et al.: **Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model.** *Gastrointest Endosc* 2005, **61:**449–453.
7. Park PO, Bergström M, Ikeda K, et al.: **Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos).** *Gastrointest Endosc* 2005, **61:**601–606.
8. Kantsevoy SV, Jagannath SB, Niiyama H, et al.: **Endoscopic gastrojejunostomy with survival in a porcine model.** *Gastrointest Endosc* 2005, **62:**287–292.
9. Bergström M, Ikeda K, Swain P, Park PO: **Transgastric anastomosis by using flexible endoscopy in a porcine model.** *Gastrointest Endosc* 2006, **63:**307–312.
10. Fritscher-Ravens A, Mosse CA, Ikeda K, Swain P: **Endoscopic transgastric lymphadenectomy by using EUS for selection and guidance.** *Gastrointest Endosc* 2006, **63:**302–306.
11. Wagh MS, Merrifield BF, Thompson CC: **Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model.** *Gastrointest Endosc* 2006, **63:**473–478.

12. Merrifield BF, Wagh MS, Thompson CC: **Peroral transgastric organ resection: a feasibility study in pigs.** *Gastrointest Endosc* 2006, **63:**693–697.
13. Kantsevoy SV, Hu B, Jagannath SB, et al.: **Transgastric endoscopic splenectomy: is it possible?** *Surg Endosc* 2006, **20:**522–525.
14. Sumiyama K, Gostout CJ, Rajan E, et al.: **Pilot study of the porcine uterine horn as an in vivo appendicitis model for development of endoscopic transgastric appendectomy.** *Gastrointest Endosc* 2006, **64:**808–812.
15. Onders R, McGee MF, Marks J, et al.: **Diaphragm pacing with natural orifice transluminal endoscopic surgery: potential for difficult-to-wean intensive care unit patients.** *Surg Endosc* 2007, **21:**475–479.
16. Lima E, Rolanda C, Pêgo JM, et al.: **Third generation nephrectomy by natural orifices translumenal endoscopic surgery.** *J Urol* 2007, In press.
17.•• Rattner D, Kalloo A, and SAGES/ASGE working group on NOTES. **ASGE/SAGES working group on natural orifice translumenal endoscopic surgery.** *Surg Endosc* 2006, **20:**329–333.
This interdisciplinary manuscript established the fundamental challenges to the safe introduction of NOTES.
18.•• Lima E, Rolanda C, Pêgo JM, et al.: **Transvesical endoscopic peritoneoscopy: A novel 5 mm port for intra-abdominal scarless surgery.** *J Urol* 2006, **176:**802–805.
Includes the first description of the transvesical port approach and represents the beginning of the urology commitment to NOTES.
19. Malik A, Mellinger JD, Hazey JW, et al.: **Endoluminal and transluminal surgery: Current status and future possibilities.** *Surg Endosc* 2006, **20:**1179–1192.
20. Rolanda C, Lima E, Pêgo JM, et al.: **Third-generation cholecystectomy by natural orifices: transgastric and transvesical combined approach (with video).** *Gastrointest Endosc* 2007, **65:**111–117.
21. Decker A: **Culdoscopy: a method for visual diagnosis of gynecologic disease.** *Clin Symp* 1952, **4:**201–210.
22. Gettman MT, Lotan Y, Napper CA, Cadeddu JA: **Transvaginal laparoscopic nephrectomy: development and feasibility in the porcine model.** *Urology* 2002, **59:**446–450.
23. Sumiyama K, Gostout CJ, Rajan E, et al.: **Transgastric cholecystectomy: transgastric accessibility to the gallbladder improved with the SEMF method and a novel multibending therapeutic endoscope.** *Gastrointes Endosc* 2007, **65:**1028–1034.
24. Lima E, Henriques-Coelho T, Rolanda C, et al.: **Transvesical thoracoscopy: a natural orifice translumenal endoscopic approach for thoracic surgery.** *Surg Endosc* 2007, **21:**854–858.
25. Fong DG, Pai RD, Thompson CC: **Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model.** *Gastrointest Endosc* 2007, **65:**312–318.
26. Swanstrom LL, Kozarek R, Pasricha PJ, et al.: **Development of a new access device for transgastric surgery.** *J Gastrointest Surg* 2005, **9:**1129–1137.
27. Marescaux J. **Operation Anubis: A new step in NOTES history!** Available at http://www.websurg.com/notes. Accessed on September 13, 2007.
28. Gettman MT, Blute ML: **Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice translumenal endoscopic surgery.** *Mayo Clin Proc* 2007, **82:**843–845.
29. Sclabas GM, Swain P, Swanstrom LL: **Endoluminal methods for gastrotomy closure in natural orifice transenteric surgery (NOTES).** *Surg Innov* 2006, **13:**23–30.
30. Ryou M, Pai RD, Sauer JS, et al.: **Evaluating an optimal gastric closure method for transgastric surgery.** *Surg Endosc* 2007, **21:**677–680.
31. Rolanda C, Lima E, Correia-Pinto J: **Searching the best approach for third-generation cholecystectomy.** *Gastrointest Endosc* 2007, **65:**354–355.
32. Clayman RV, Box GN, Abraham JB, et al.: **Rapid communication: transvaginal single-port NOTES nephrectomy: initial laboratory experience.** *J Endourol* 2007, **21:**640–644.
33. Zeltser IS, Bergs R, Fernandez R, et al.: **Single trocar laparoscopic nephrectomy using magnetic anchoring and guidance system in the porcine model.** *J Urol* 2007, **178:**288–291.

Annex 2

Transvesical and other ports for N.O.T.E.S.

Lima E, Rolanda C, Correia-Pinto J. NOTES performed using multiple ports of entry: current experience and potential implications for urologic applications. *J Endourol* 2008 (in press)

ABSTRACT

Background and purpose: Isolated transgastric port raises serious limitations in performing natural orifice translumenal endoscopic surgery (NOTES) complex procedures in urology field. Attempting to overcome these limitations several solutions has been advanced, such as the hybrid approach (adding a single abdominal port access) or the pure NOTES combined approach (joining multiple natural orifice ports). This article reviews the current state of experimental and clinical results of multiple ports in NOTES.

Patients and Methods: A literature search of PubMed was performed, seeking publications from January 2002-to-2008 on NOTES. Additionally, we looked at pertinent abstracts of annual meetings of the American Urological Association, the European Association of Urology, and the World Congress of Endourology from 2007.

Results: In urology, multiple ports of entry seem to be necessary mainly for moderate complex procedures. Thus, we could find studies using the hybrid approach (combination of transgastric or transvaginal access with a single transabdominal port), or using the pure NOTES combined approach (transgastric and transvesical, transvaginal and transcolonic, or transgastric and transvaginal). Anyway there is still limited experience in Humans using these approaches and no comparative studies exist so far. Meanwhile, we are waiting for new equipments and instruments more appropriate for these novel techniques.

Conclusions: In urology, it is predictable that for moderate complex procedures we will need multiple ports being the most appealing approach the transvaginaltransabdominal (hybrid approach), whereas in a pure NOTES perspective the transgastric-transvesical approach seems to be the preferred approach.

Key Words: *endoscopy; NOTES; transgastric surgery; transvesical surgery*

INTRODUCTION

Minimally Invasive Surgery (MIS) is rapidly becoming the standard for surgical care. In fact, refinements in laparoscopic surgery have progressed to the point that complex surgical procedures can now be performed in a minimally invasive fashion.[1] Recently, natural orifice translumenal endoscopic surgery (NOTES) has emerged as a potential exciting evolution of minimally invasive surgical care. This new approach was firstly used by Reddy and Rao that carried out in a few humans cases appendectomy by a transgastric access followed by Kalloo et al that demonstrated in a structured study the feasibility and potential surgical usefulness of transgastric access to the peritoneal cavity in a porcine model.[2] Subsequently, others authors described more complex intraabdominal procedures using isolated transgastric route.[3-14] Following the initial enthusiasm, the possibility to carry out abdominal procedures through isolated transgastric route faced several limitations (White Paper. Surg Endosc 2006).[15]

Believing in the potential benefits of natural orifices approach for abdominal surgery, Lima et al hypothesized that other ports would be advantageous. In this sequence, they assessed the feasibility and safety of creating a transvesical port for the abdominal cavity.[16] As occurred with transgastric port, the transvesical approach also broke a classical sanctuary of urology: the wall of urinary tract. In fact, the idea to perforate the bladder wall was always feared as potential complication of urological procedures.

Following the unexpected success of transgastric port, the bladder comes out as an attractive port for NOTES procedures once it is sterile, allows passage of rigid instruments and appears anatomically as the most anterior lower abdominal access.[16,17]

RATIONALE FOR MULTIPLE PORT NOTES

Current laparoscopic surgery is using rigid instruments introduced at strategic anatomic points through the abdominal wall. The positioning of the trocars is an important issue since it can determine the feasibility of the procedure. This occurs because the correct positioning of the trocars is essential for triangulation and many times for grasping and efficient traction. In NOTES, the initial steps were carried out with common gastroscopes and flexible instruments introduced through its parallel working channels. Thus, after description of the first intra-abdominal moderate complex procedures (ie. cholecystectomy) serious limitations related with absence of using rigid instruments and lack of triangulation come out. For instances, Park et al conducted the first pilot study in pigs applying NOTES to perform transgastric cholecystectomy. Using two endoscopes or a single endoscope conjugated with a transabdominal trocar, cholecystectomy was feasible, but important limitations were identified such as difficulty in controlling the pneumoperitoneum, in obtaining a stable platform and adequate anatomy exposure, organ retraction, secure grasping and triangulation of instruments.[4] Swanström et al attempted to overcome these limitations providing some rigidity to the gastroscope using shapelock technology as a new over tube for transgastric surgery. However, even with this equipment, isolated transgastric approach for gallbladder manipulation remained a challenge with a success rate around 33%.[18]

In fact, most of these limitations namely the lack of triangulation, effective grasping and traction, and the working difficulties in retroflexion were closely related with the use of an isolated transgastric approach due to the characteristics of the gastroscopes such as its flexibility. Attempting to overcome these limitations several solutions has been advanced, such as the construction of more rigid transgastric platforms,[19] the combination of the transgastric access with a transabdominal port (hybrid approach using for instances the umbilicus)[20-21] or with a lower abdominal access (pure NOTES combined approach) (fig. 1).[22-24]

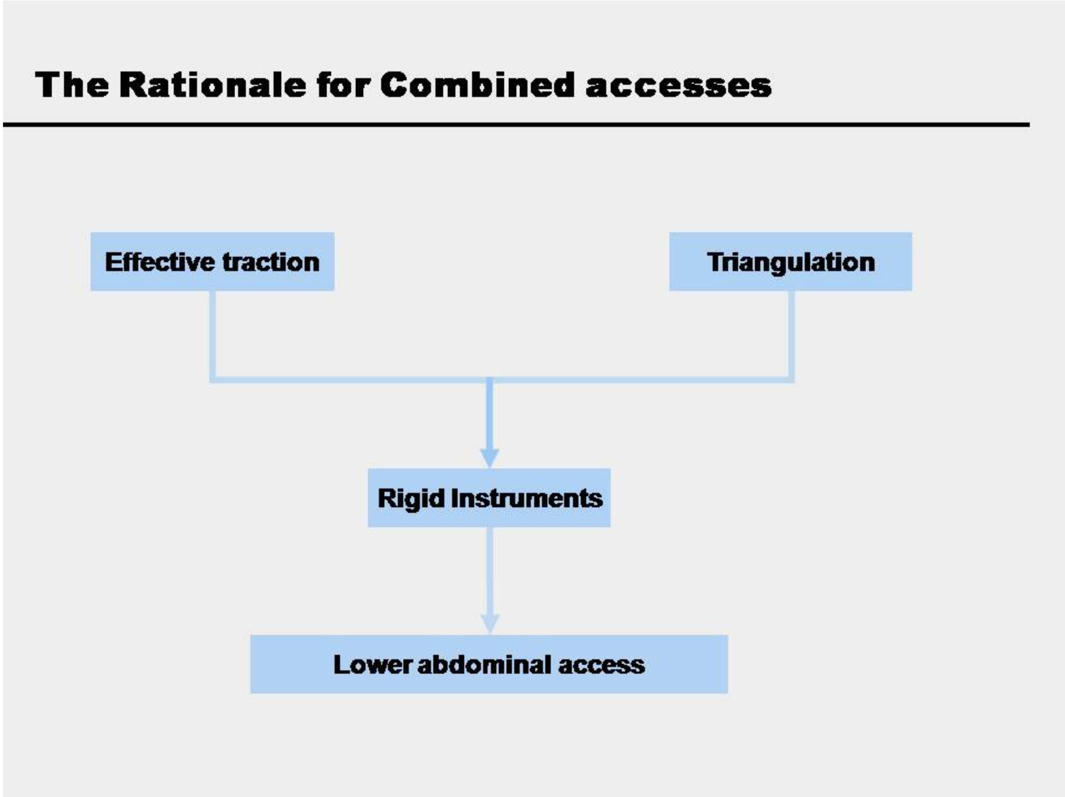

Figure 1 – The rationale for combined accesses for pure NOTES.

THE TRANSVESICAL PORT AMONGST THE LOWER ABDOMINAL PORTS

For lower abdominal access several options exists. In fact, after the old description of the transvaginal port in forties,[25] the transvesical[16] and the transcolonic approaches[26] were recently described (Fig. 2). Despite these accesses share the possibility to introduce rigid instruments into the abdomen, the transvesical port appears at the most anterior positioning in the sagital plan and for this reason with less risk to damage viscera. Moreover, introducing the surgical instruments from the bladder dome gives the possibility to work above bowel loops, instead through among them.

Additionally, the transvesical port is the unique lower abdominal access that is naturally sterile, and available in both genders in contrast to the transvaginal access. Unfortunately, the transvesical port does not allow specimen retrieval as transvaginal and transcolonic approaches (Table 1). For all these reasons, always it is needed the combination of a lower abdominal access to the transgastric port, the transvesical port seems quite attractive.

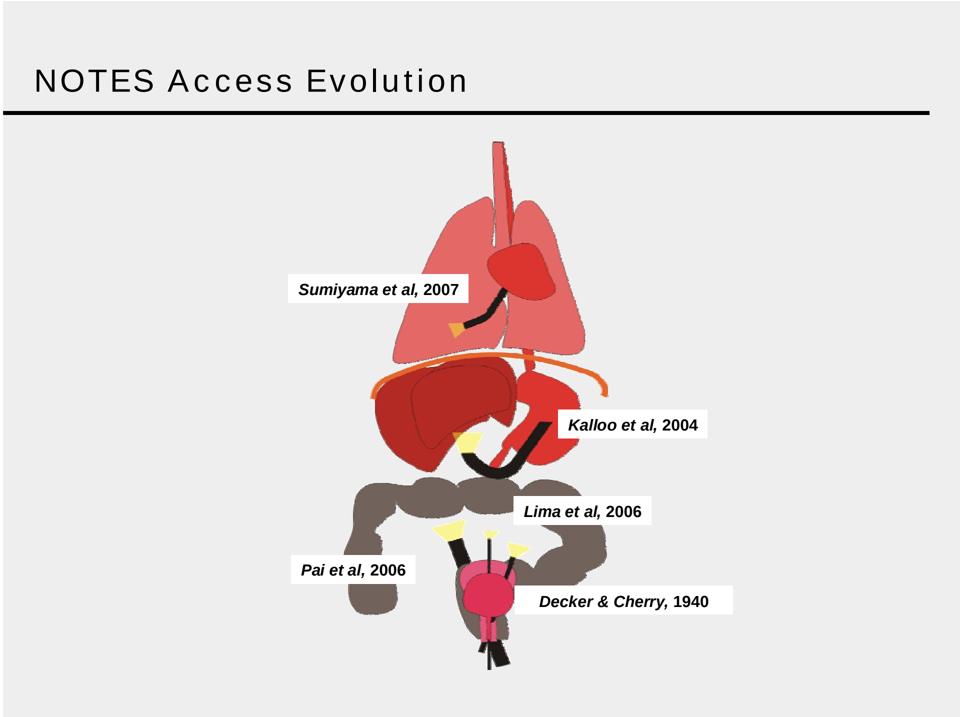

Figure 2 – Drawing with NOTES accesses.

Comparison of Lower Abdominal Accesses

	Bladder	Vagina	Colon
Rigid instruments	Yes	Yes	Yes
Available in both sexs	Yes	No	Yes
Sterility	Yes	No	Colon preparation needed
Abdominal positional access	Anterior		Posterior
Size	Up to 6 mm	Wide	Wide
Closure	Bladder catheter	Easy	equipment needed
Specimen retrieval	No	Yes	Yes

Table 1 - Comparison of lower abdominal accesses.

EXPERIMENTAL AND CLINICAL WORK-PROCEDURAL

The efficiency of the concept of combining transgastric (using flexible instruments) and transvesical (using rigid instruments) ports was tested performing two moderately complex procedures such as cholecystectomy and nephrectomy by pure NOTES approach.[22,24] Believing in the potential benefits of NOTES approach for abdominal surgery, Rolanda et al and Lima et al used a transgastric and transvesical combined approach to perform cholecystectomy and nephrectomy, respectively, aiming to overcome many limitations previously described for isolated transgastric approach related with anatomy exposure, organ retraction, grasping and limited triangulation.

This group used the transvesical port because it is diametrically opposed to the transgastric port and seems to offer additional advantages over transvaginal and transcolonic ports for the reasons cited above. However, recently there is a report of a nephrectomy using the combination of transgastric and transvaginal approach.[27] In this study the transgastric port was introduced first followed by the gastroscope that guided the introduction of a second transvaginal endoscope through a novel laparoscopic trocar/endoscopic over tube device. The advantage of this approach was the possibility to removal of the specimen through the vagina.[27]

In a reverse thinking, many authors are using the transvaginal approach for dissection, replacing the transgastric by the transvaginal port for dissection and specimen retrieval. Those that are using flexible instruments through vagina still need to use a rigid instrument to provide effective retraction. In these studies, commonly the rigid instrument(s) is (are) being introduced transabdominally. Anyway, this strategy allowed performing safe transvaginal nephrectomy[28,29] and cholecystectomy[30] in the porcine model[22-23] and even the firsts Human cholecystectomies[31-33] and nephrectomy.[34]

In the same way of thinking, Meining et al, described the combination of transsigmoid approach using a specially designed trocar with a grasper introduced transabdominally to perform cholecystectomy in an acute porcine model study.[35] Recently, another group described the transcolonic approach associated with the transvaginal port to perform distal pancreatectomy in survival porcine model. In this study was used the combination of an endoscope advanced into peritoneal cavity through an anterior colotomy with a computer-assisted linear stapler introduced transvaginally.[36]

A alternative way is being developed by the University of Texas that use a magnetic anchoring and guidance system to perform in porcine model nephrectomy with a single transabdominal trocar and more recently cholecystectomy by pure NOTES through vagina.[37,38]

TECHNIQUES FOR GAINING ABDOMINAL ACCESS THROUGH NATURAL ORIFICES

As in laparoscopy we have discussion regarding the way to choose the first trocar to start the pneumoperitoneum and to monitor the placement of the other ports, accessing the peritoneal cavity through a natural orifice has always the risk of damaging the adjacent organs during creation of the hole in the visceral wall. In fact, accessing the peritoneal cavity in a blind way through the transgastric port can damage adjacent organs as reported by many authors.[15,39,40] Interestingly, the technique to establish the transvesical port was described using neither cutting instruments nor cattery. This makes the transvesical port as the safest port to start access to the peritoneal cavity and particularly useful in procedures involving multiple natural orifices, since the transvesical image can easily monitories the transgastric creation.

The placement of the transvesical port is based on the Seldinger principle.[16,17,41] Currently, Lima et al performed it using an ureteroscope introduced through the urethra into the bladder with pneumo-distension, the bladder is emptied from urine and distended with CO2. The vesicotomy site is carefully selected on the bladder dome. A mucosal incision is made with a scissors introduced through the working channel of the ureteroscope. Subsequently, a 5 Fr open-ended ureteral catheter is pushed forward through the incision into the peritoneal cavity. A 0.035-inch flexible-tip guide-wire is then inserted into the peritoneal cavity through the lumen of the ureteral catheter. Guided by the flexible-tip guide-wire, the vesical hole is enlarged with a dilator of an ureteroscope sheath enveloped by a flexible 5.5 mm over tube. An ureteroscope is introduced into the peritoneal cavity through the over tube and allows the creation of a pressure controlled CO2 pneumoperitoneum.[16-17]

To establish the transgastric port several variants had already been described.[2-14] Rolanda et al suggested to establish it under gastric outside view provided by a transvesical scope in order to avoid damage of gastric wall vessels or adjacent organs. The gastrotomy site is carefully chosen on the anterior wall. A gastric-wall incision is made by pushing forward a needle knife, followed by its sheath with cautery under a 12 mmHg CO2 pneumoperitoneum (induced through the transvesical port). The needleknife sheath is then used for positioning a guidewire. The puncture dilation is performed with an 18-mm through-the-scope balloon over the guidewire or by extending the gastrotomy with a sphincterotom. Then, the gastroscope is pushed forward and passed into the peritoneal cavity. All the procedures become safer if they are monitored by a scope positioned through a lower abdominal access or transabdominally. As an alternative method, a PEG-like transgastric approach to the peritoneal cavity appears technically simple and safe.[39]

The transcolonic port is also being developed. As it was described it is established using a sterile dual-channel endoscope was introduced through the anus and advanced 15 to 20 cm from the anal verge. A needle knife is used to make a subcentimeter linear incision. Once the incision is complete, the needle knife is retracted, and the catheter is advanced through the incision into the peritoneum and the endoscope is then advanced through the colonic wall into the peritoneal cavity.[26]

The transvaginal port was already described since the forties[25] and had already been used for several intra-abdominal procedures by gynecologists. Recently, there is a recrudescent enthusiasm with the transvaginal port for upper abdominal procedures since it does not have associated the risks of the transgastric port.[31-34] The method is easy to establish. Briefly, the peritoneal cavity is entered through an incision in the posterior vaginal cul-de-sac.

POTENTIAL RISKS AND BENEFITS TO USING MULTIPLE PORTALS

Until now the most tested associations are the hybrid methods (transvaginaltransabdominal,[33-33] transcolonic-transabdominal[35] and transgastric-transabdominal[20,21]) and the pure NOTES association transgastric-transvesical,[22,24] but other associations had also been reported as transvaginal-transcolonic36 and the transgastric-transvaginal.[27]

Always we establish a natural orifice port there are associated risks related with its creation as well as risks associated with delayed leaking of leaving an ‘-otomy’ not completely closed. Thus, it seems reasonably to expect that association of multiple portals causes more risks.

However, current use of multiple portals association has also unravelled several benefits. First of all, after creation of a port, it is possible to minimize the risk of the second port as the first port can allow monitoring the creation of the second port.

Moreover, it is even predictable that the use of associated portals can enhance to find better and more reliable methods to closure the '-otomies'. Anyway, the great advantage to use multiple portals is related with the enhanced ability to increase triangulation, grasping and retraction manoeuvres and consequent enhanced dissection.
Finally, the establishment of multiple portals associations commonly requires multidisciplinary team involvement. This can be looked as a limitation or an advantage. In our point of view, this constitutes an advantage once it brings for the some 'battle field' resources and expertises from different interventional environments, what for sure will help to achieve easier solutions and new methods and ideas.

OPINION REGARDING BENEFITS FOR UROLOGIC SPECIFIC NOTES (POTENTIAL USES)

The appeal of NOTES in urology may not be immediately apparent, considering the more or less mainstream acceptance of laparoscopic surgery. On the other hand, several groups are using natural orifices to carry out complex procedures such as nephrectomy.
The first attempt was made by Gettman et al that performed complete transvaginal laparoscopic dissection and nephrectomy in the porcine model using a single, 5-mm abdominal trocar for visualization. A completely transvaginal laparoscopic nephrectomy was performed once, but limitations imposed by the porcine anatomy and by the currently available instrumentation made the procedure very cumbersome at that time.[28]
More recently, Clayman et al recovered this idea and carried out a porcine nephrectomy recurring to a single 12-mm trocar placed in the midline and the new TransPort Multi-Lumen Operating Platform (USGI Medical, San Clemente, CA) passed transvaginally. This flexible device has four working channels and can be locked into position, thereby creating a rigid multitasking platform that allows two-handed tissue manipulation.[29]
Stretching the limits, Lima et al demonstrated the feasibility of pure NOTES nephrectomy. In a non-survival study, transgastric and transvesical combined approaches were established in 6 female pigs. Under ureteroscope control, passed through a 5 mm transvesical port, a flexible gastroscope was passed per-orally into peritoneal cavity by a gastrotomy. Either right or left nephrectomy were carried out using instruments introduced by both devices that worked in the renal hilum alternating their intervention either on dissection or retraction procedures. In all animals, both kidneys were visualized, and the renal vessels and ureter were reasonably

individualized, clipped and then ligated separately with ultrasonic scissors, which was introduced through the transvesical port.[24]

The feasibility of nephrectomy by NOTES appears as the extreme of a large spectrum of renal procedures that can potentially be done by NOTES in the near future. However, we might take into account that much work is still needed to refine techniques, verify safety, and document efficacy before Human translation in order to minimize unexpected complications. For instances, magnetically anchored instrumentation as suggested by Zeltser et al and Scott et al might be a good application and may be the next logical step toward the development of truly scarless abdominal surgery by NOTES.[37,38]

NOTES might appears as a tremendous challenge for the urologists. In addition to technical demands to perform urological NOTES, urologists might be called to become involved in multidisciplinary teams dealing with extra-urological clinical situations. This might occur since the extraordinary simplicity to install the transvesical port and the excellent view of upper abdominal organs that it provides.

Both in animals and human settings, the transvesical port revealed feasible and useful to perform peritoneoscopy of all intra-abdominal viscera, mainly the upper abdominal organs. Moreover, the transvesical port is gaining a place in NOTES as a unique port to associate with the transgastric port in both genders.[22,23] Although more hardly to accept clinically, the exceptional opportunity that the transvesical port provides to view the upper abdominal organs, it was even suggested that the transvesical port would make possible transdiaphragmatic endoscopic approach to the thoracic cavity in a long-term survival study in a porcine model.[17]

Most of these studies are still preliminary and embody the birth of NOTES. NOTES is still in development and no well-established criteria are already defined. Anyway, we predict that with the current concept of flexible scopes, always we advance for a surgical procedure that in laparoscopy uses up to 3 trocars, in NOTES it will be feasible through an isolated natural orifice (fig. 3); whereas always we are dealing with a surgical procedure that use more than 3 trocars in laparoscopy, we predict that association of multiple portals will be necessary (fig. 4). Always association is needed the most appealing approaches are the transvaginal-transabdominal or in a pure NOTES perspective the transgastric-transvesical approach.

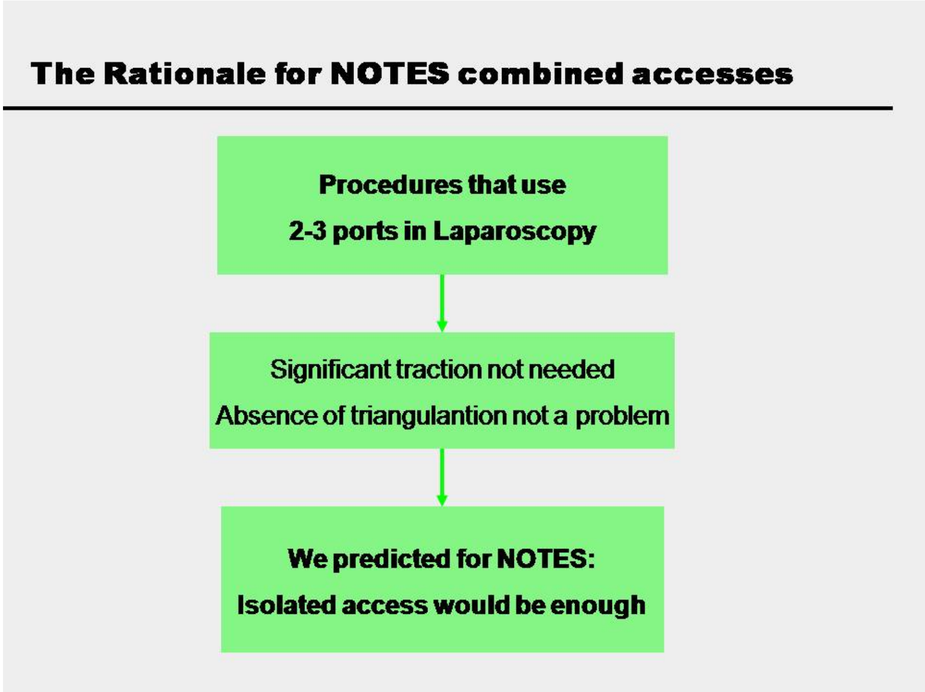

Figure 3 – Rationale for isolated port in NOTES.

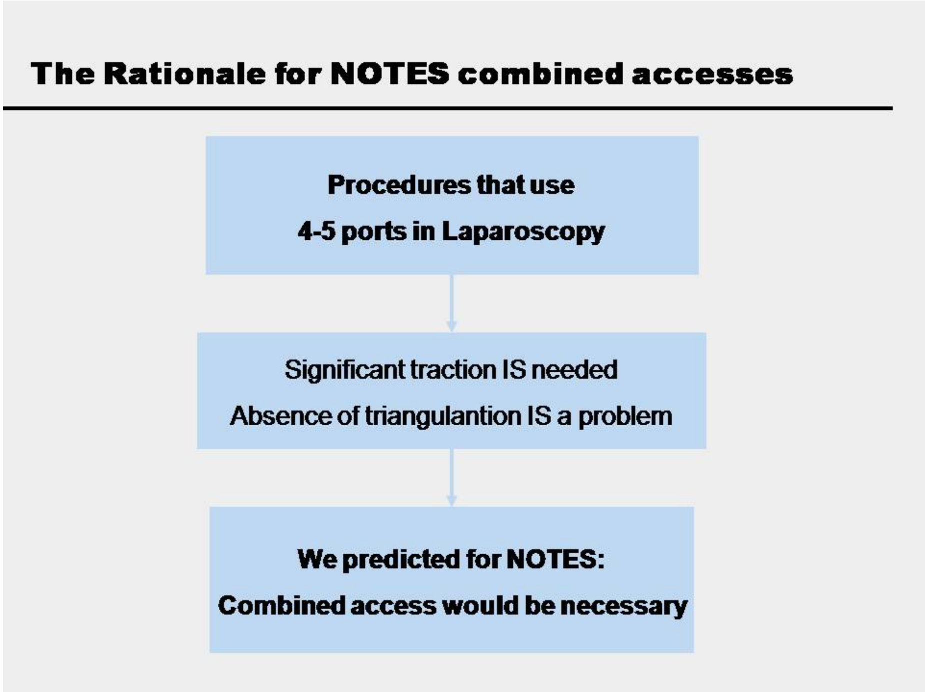

Figure 4 – Rationale for multiple ports in NOTES.

CONCLUSION

In urology, it is predictable that for moderate complex procedures we will need multiple ports being the most appealing approach the transvaginal-transabdominal (hybrid approach), whereas in a pure NOTES perspective the transgastric-transvesical approach seems to be the preferred approach.

REFERENCES

1.Harrell AG Harrell AG, Heniford T: Minimally invasive abdominal surgery: Lux et veritas past, present, and future. Am J Surg 2005; 190: 239.

2.Kalloo AN, Singh VK, Jagannath SB, et al: Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 2004; 60: 114.

3.Jagannath SB, Kantsevoy SV, Vaughn CA, et al: Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model. Gastrointest Endosc 2005; 61: 449.

4.Park PO, Bergstrom M, Ikeda K, et al: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 2005; 61: 601.

5.Kantsevoy SV, Jagannath SB, Niiyama H, et al: Endoscopic gastrojejunostomy with survival in a porcine model. Gastrointest Endosc 2005; 62: 287.

6.Bergstrom M, Ikeda K, Swain P, et al: Transgastric anastomosis by using flexible endoscopy in a porcine model. Gastrointest Endosc 2006; 63: 307.

7.Wagh MS, Merrifield BF, Thompson CC: Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. Gastrointest Endosc 2006; 63: 473.

8.Merrifield BF, Wagh MS, Thompson CC: Peroral transgastric organ resection in the Abdomen: feasibility study in pigs. Gastrointest Endosc 2006; 63: 693.

9.Kantsevoy SV, Hu B, Jagannath SB, et al: Transgastric endoscopic splenectomy. Is it possible? Surg Endosc 2006; 20: 522.

10.Fritscher-Ravens A, Mosse CA, Ikeda K, et al: Endoscopic transgastric lymphadenectomy by using EUS for selection and guidance. Gastrointest Endosc. 2006; 63: 302.

11. Sumiyama K, Gostout CJ, Rajan E, et al: Pilot study of the porcine uterine horn as an in vivo appendicitis model for development of endoscopic transgastric appendectomy. Gastrointest Endosc 2006; 64: 808.

12.Onders R, McGee MF, Marks J, et al: Diaphragm pacing with natural orifice transluminal endoscopic surgery: potential for difficult-to-wean intensive care unit patients. Surg Endosc 2007; 21: 475.

13.Hu B, Kalloo AN, Chung SS, et al: Peroral transgastric endoscopic primary repair of a ventral hernia in a porcine model. Endoscopy 2007; 39: 390-393.

14.Perretta S, Dallemagne B, Coumaros D, et al: Natural Orifice Transluminal Endoscopic Surgery. Transgastric Cholecystectomy in a survival porcine model. Surg Endosc 2007; 11; [Epub ahead of print]

15.Rattner D, Kalloo A, and SAGES/ASGE working group on NOTES: ASGE/SAGES Working group on natural orifice translumenal endoscopic surgery. Surg Endosc 2006; 20: 329.

16.Lima E, Rolanda C, Pêgo JM, et al: Transvesical endoscopic peritoneoscopy: A novel 5 mm-port for intra-abdominal scarless surgery. J Urol 2006;176: 802.

17.Lima E, Henriques-Coelho T, Rolanda C, et al: Transvesical thoracoscopy: A natural orifice translumenal endoscopic approach for thoracic surgery. Surg Endosc 2007; 21: 854.

18.Swanstrom LL, Kozarek R, Pasricha PF, et al: Development of a new access device for transgastric surgery. J Gastrointest Surg 2005; 9: 1129.

19.Bardaro JS, Swanstrom L. Development of advanced endoscopes for natural orifice translumenal endoscopic surgery (NOTES). Minimally invasive Therapy 2006; 15: 378.

20.Shih SP, Kantsevoy SV, kalloo AN, et al: Hybrid minimally invasive surgery-a bridge between laparoscopic and translumenal surgery. Surg Endosc 2007; 21: 1450.

21.Mintz Y, Horgan S, Cullen J, et al: NOTES: the hybrid technique. J Laparoendosc Adv Surg Tech A 2007; 17: 402.

22.Rolanda C, Lima E, Pêgo JM, et al: Third Generation Cholecystectomy by Natural Orifices: Transgastric and Transvesical Combined Approach. Gastrointest Endosc 2007; 65: 111.

23.Rolanda C, Lima E, Correia-Pinto J: Searching the best approach for third-generation cholecystectomy. Gastrointest Endosc 2007; 65: 354.

24.Lima E, Rolanda C, Pêgo JM, et al: Third generation nephrectomy by natural orifice translumenal endoscopic surgery. J Urol 2007; 178: 2648.

25.Decker A: Culdoscopy: A method for visual diagnosis of gynecologic disease. Clin Symp 1954; 6: 210.

26.Fong DG, Pai RD, Thompson CC: Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. Gastrointest Endosc 2007; 65: 312.

27.Ponsky L, Isariyawongse J, McGee M, et al: Pure natural orifice translumenal endoscopic surgery (NOTES) nephrectomy using standard laparoscopic instruments in the porcine model. J Endourol 2007; 21: A91.

28.Gettman MT, Lotan Y, Napper CA, et al: Transvaginal laparoscopic nephrectomy: Development and feasibility in the porcine model. Urology 2002; 59: 446.

29.Clayman RV, Box GN, Abraham JB, et al: Rapid communication: transvaginal single-port NOTES nephrectomy: initial laboratory experience. J Endourol 2007; 21: 640.

30.Zornig C, Emmermann A, Von Waldenfels HA, et al: Laparoscopic cholecystectomy without visible scar: combined transvaginal and transumbilical approach. Endoscopy 2007; 39: 913.

31.Bessler M, Stevens PD, Milone L, et al: Transvaginal laparoscopically assisted endoscopic cholecystectomy: a hybrid approach to natural orifice surgery. Gastrointest Endosc 2007; 66: 1243.

32.Marescaux J, Dallemagne B, Perretta S, et al: Surgery without scars. Report of transluminal cholecystectomy in a human being. Arch Surg 2007; 142: 823.

33.Zorron R, Maggioni LC, Pombo L, et al: NOTES transvaginal cholecystectomy: preliminary clinical application. Surg Endosc 2007; 20; [Epub ahead of print]

34.Branco AW, Filho AJ, Kondo W, et al: Hybrid Transvaginal Nephrectomy. Eur Urol 2007; 5; [Epub ahead of print]

35.Meining A, Wilhelm D, Burian M, et al: Development, standardization, and evaluation of NOTES cholecystectomy using a transsigmoid approach in the porcine model: an acute feasibility study. Endoscopy 2007; 39: 860.

36.Ryou M, Fong DG, Pai RD, et al: Dual-port distal pancreatectomy using a prototype endoscope and endoscopic stapler: a natural orifice transluminal endoscopic surgery (NOTES) survival study in a porcine model. Endoscopy 2007; 39: 881.

37.Scott DJ, Tang SJ, Fernandez R, et al: Completely transvaginal NOTES cholecystectomy using magnetically anchored instruments. Surg Endosc 2007; 21: 2308.

38.Zeltser IS, Bergs R, Fernandez R, et al: Single trocar laparoscopic nephrectomy using magnetic anchosing and guidance system in the porcine model. J Urol 2007; 178: 288.
39.Kantsevoy SV, Jagannath SB, Niiyama H, et al: A novel safe approach to the peritoneal cavity for per-oral transgastric endoscopic procedures. Gastrointest Endosc 2007; 65: 497.
40.Ko CW, Shin EJ, Buscaglia JM, et al: Preliminary pneumoperitoneum facilitates transgastric access into the peritoneal cavity for natural orifice transluminal endoscopic surgery: a pilot study in a live porcine model. Endoscopy 2007; 39: 849.
41.Gettman MT, Blute ML: Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice translumenal endoscopic surgery. Mayo Clin Proc 2007; 82:843.

Annex 3

Consensus statement on N.O.T.E.S. in Urology

Gettman MT, Box G, Averch T, Cadeddu JA, Cherullo E, Clayman RV, Desai M, Frank I, Gill I, Gupta M, Haber GP, Humphreys M, Kaouk J, Landman J, Lima E, Ponsky L. Consensus Statement on Natural Orifice Transluminal Endoscopic Surgery and Single-Incision Laparoscopic Surgery: Heralding a New Era in Urology? *Eur Urol*; 53: 1117-1120, 2008.

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Editorial

Consensus Statement on Natural Orifice Transluminal Endoscopic Surgery and Single-Incision Laparoscopic Surgery: Heralding a New Era in Urology?

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For decades, urologists have implemented technologies that provide effective treatment while limiting morbidity. In many instances, this has been achieved by operating via natural body openings (eg, cystoscopy, transurethral resection, and ureteroscopy) [1,2]. Urologists have also pioneered novel techniques to address clinical situations where access through natural body openings was impossible, such as percutaneous stone surgery, laparoscopy, and robotics [3–5].

In the last 5 yr, exponential development of therapeutic endoscopy has been realized. There is interest now in developing surgical procedures that enter the peritoneum or retroperitoneum through hollow viscera that can be assessed via natural body openings precluding skin incisions [6,7]. The new approaches, coined natural orifice transluminal endoscopic surgery (NOTES), aim to further limit treatment morbidity, but studies addressing these approaches have yet to be initiated because the clinical techniques for these approaches are being developed [6]. NOTES can be performed as a pure procedure involving one portal of entry or as a combined procedure involving use of multiple body openings. NOTES can also be performed as hybrid procedures in conjunction with conventional transabdominal ports. Closely related to NOTES is development of procedures performed through a solitary small transabdominal incision. These procedures have been referred to as single-port access, single- port laparoscopy, or single-incision laparoscopy; consensus on the most appropriate name for the approach has not been achieved. More importantly, the ‘‘it's new, but is it better'' question again has yet to be addressed for these procedures, because they remain in their nascent forms.

Urology is favorably positioned for development of NOTES technology and introduction of new

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surgical approaches given our training in open surgical, endoscopic, and image-guided techniques. Urologists' long history and experience with these minimally invasive technologies give us an enormous advantage as we further develop and evaluate NOTES and single-incision procedures. In contrast to urology, other specialties are experiencing blurring of traditional procedural boundaries as new approaches are introduced. Specialties preferentially interested in diagnostic procedures are now interested in therapeutic interventions. On the other hand, specialties previously interested in predominantly open therapeutic interventions are now interested in diagnostic techniques or minimally invasive therapies.

Experimentally, urologists have been at the forefront of NOTES and procedures performed through solitary small abdominal incisions. The clinical event prompting experimental evaluation of urologic NOTES was the description of vaginal extraction of an intact surgical specimen following laparoscopic radical nephrectomy [8,9]. In 2002, Gettman et al described the first experimental application of natural orifice surgery when transvaginal nephrectomy was successfully performed in the porcine model [10]. Indeed, this work predated the acronym NOTES as well as the first recognized NOTES report by Kalloo et al in the gastroenterology literature, which was not reported until 2004 [11]. Likewise, the bladder was successfully used by Lima et al as a NOTES portal in experimental models [12]. Combined NOTES approaches involving transgastric and transvesical access have also been reported experimentally by the same group for nephrectomy and cholecystectomy [13,14] as well as thoracoscopy [15]. In addition, another combined NOTES nephrectomy technique was recently described by Ponsky et al using combined transgastric and transvaginal access [16]. NOTES operative platforms have also been engendered and evaluated by urologists. The magnetic anchoring and guidance system (MAGS) was introduced for active camera and instrument control. With MAGS, transvaginal nephrectomies and cholecystectomies have been performed experimentally [17,18] A TransPort multilumen operating platform (USGI Medical, San Clemente, CA) has also been successfully used by Clayman et al for hybrid transvaginal NOTES nephrectomy in the porcine model [19]. In addition, transvaginal hybrid NOTES nephrectomy has been performed experimentally with the da VinciS robot (Intuitive Surgical, Sunnyvale, CA) [20].

The new NOTES surgical techniques are also gaining momentum clinically. Branco et al described hybrid NOTES transvaginal nephrectomy involving vaginal placement of an endoscope and two 5-mm abdominal trocars to remove a nonfunctioning right kidney. Operative time was 170 min and no complications occurred [21]. Using novel instrumentation, single-incision laparoscopic surgery has emerged as another important clinical development. The pioneering work in urology was first described at the University of Texas Southwestern Medical Center and soon after at Cleveland Clinic [22–24]. The first single-incision transumbilical three-port nephrectomy was performed at the University of Texas Southwestern Medical Center. The first single-port transumbilical nephrectomy was performed at Cleveland Clinic. To date, researchers have routinely used this approach clinically for pyeloplasty and nephrectomy, and also prostatectomy and ileal ureter substitution, and donor nephrectomy (pers. comm., J. Kauok, Cleveland, OH, USA). At Case Western Reserve University, urologists have performed single-access site laparoscopic radical nephrectomy, whereby all instrumentation was placed through one 7-cm incision [25]. In 2007, Gettman and Blute also reported the initial clinical NOTES experience in urology with transvesical peritoneoscopy used to evaluate suprapubic tube placement in conjunction with robotic prostatectomy [7].

The opportunity for the new NOTES approaches is enormous, yet the technology is still very much in evolution and methods themselves must be carefully implemented and then scientifically evaluated. Active participation by urologists is mandatory in this regard. To discuss the emerging roles in urology for NOTES and procedures performed through solitary small abdominal incisions, 16 members of the Endourological Society met in Cancun, Mexico on November 1, 2007 during the 25th World Congress of Endourology. This was simply an ad hoc group of interested individuals not necessarily including all thought leaders in the field. In fact, the group welcomes additional participants at future meetings. Topics relevant to development of urologic NOTES were discussed and a working group named the Urology Working Group on NOTES was formed. Stated working group goals are to:

- Increase awareness of NOTES in urology
- Provide an outlet to share discoveries related to urologic NOTES
- Guide scientific evaluation and implementation of urologic NOTES
- Facilitate learning opportunities with urologic NOTES
- Define nomenclature of urologic NOTES

The vision of the working group is to safely and systematically implement NOTES in urology. We are well aware of the often cited statement: ‘‘everything good was once new, but everything new is not necessarily good.’’ The group remains firmly committed to evaluating the new approach once it has gone through formative technological and learning curve stages.

The working group will formally meet during major urologic meetings sponsored by the Endourological Society, American Urological Association, and the European Association of Urology. During these meeting, both didactic and research forums will be held. Didactic sessions will be open to all conference participants; however, formal inclusion in the working group will mandate that one has published or presented experimental or clinical work related to NOTES. Members are expected to actively participate in the research forum by providing brief summaries of their most recent NOTES activities. The first meeting of this nature has been scheduled through the auspices of the Endourological Society and will take place at the American Urological Association meeting on Saturday May 17, 2008.

At the initial meeting it was critical to the working group that urologic NOTES procedures must be performed by urologists, regardless of the portals of entry, because urologists are experts of diseases involving the urinary tract. Teams of surgeons are recommended for combined or hybrid urologic procedures involving non-urologic portals of entry, but the urologist should be the primary surgeon; however, if a transgastric portal was used, then the gastroenterologist would work with the urologist to open and close the portal. Similarly, for combined, pure, or hybrid NOTES procedures involving bladder access portals but non-urologic indications, urologists should also be the primary surgeon for access and closure of the bladder.

At the initial working group meeting, all participants agreed that pure NOTES (ie, transgastric, transcolonic, transvaginal, or transvesical) should be further developed as a research topic in urology before widespread clinical implementation. The rationale was simply that more barriers exist with pure NOTES than the other single small incision techniques. In addition, any NOTES clinical research at this time should be done under approval of an institutional review board. The group identifies lack of purpose-built endoscopes, instrumentation, and training as the most significant limitations presently for pure NOTES implementation; however, the group is actively addressing these concerns and developing solutions to these problems.

Based on the current state of the art, the working group concluded that procedures performed through solitary small abdominal incisions are immediately available for clinical implementation. The group recommends that outcomes be reported as part of a multi-institutional clinical study. Since the vision of the working group is that new technologies should be safely and systematically implemented, outcomes must be carefully tracked. To this end, a clinical registry and database are in the process of being established as a requisite for NOTES working group members.

As a premise it is also thought that the new urologic NOTES techniques including the single small abdominal incision techniques must match or exceed the efficacy and safety of other accepted minimally invasive techniques for the emerging approaches to be justified. The realist in the mix will rightfully question the value of these new approaches; each must prove itself to be equal or better than current laparoscopic approaches in the realms of efficiency, effectiveness, economy, and equanimity (ie, patient convalescence, morbidity, pain, and cosmesis). It is conceivable that such may not be the case and that NOTES and single small abdominal incision techniques may prove to be a blip rather than a staple in surgical evolution. The working group sees it as their responsibility to accurately report and assess these techniques as applied to each procedure such that what is of value can be identified and taught and what is of no proven benefit can be discarded.

Enthusiasm for the single small abdominal incision techniques in urology is high given the similarities to traditional laparoscopic surgery. For instance, urologists are already familiar with access and closure methodologies at the umbilicus as well as management of complications related to conventional laparoscopy and robotics. In addition, urologists are already trained in surgical techniques and surgical principles required for the new approach. However, whether one port proves to be preferable to four or five smaller ports remains to be proven.

In summary, NOTES and single small abdominal incision techniques are gaining momentum and may represent the next frontier in minimally invasive surgery. Although many unanswered questions persist, it is also critically important that urologists maintain their pioneering spirit and evaluate these new approaches carefully and scientifically. Based predominantly on experimental results, pure NOTES should be actively pursued as a research topic. The single small abdominal incision techniques are immediately available for careful clinical implementation and as such require immediate inclusion in a clinical registry to determine their proper role in minimally invasive urologic surgery, lest they be promoted before they are tested and thus fall into the trap of other highly touted but poorly tested urologic procedures that subsequently took years to ‘‘unmask’’ and discard, much to the public’s detriment. Indeed, a transition from standard laparoscopy to NOTES-type approaches is predicted only if this transition is supported by patient safety and clinical benefit. At the very least, evaluation of new technologies targeted for NOTES may well advance other existing urologic technologies such as percutaneous renal surgery, ureteroscopy, laparoscopy, or robotics. Furthermore, the working group adamantly supports the concept that urologists are uniquely situated to best evaluate NOTES approaches given the breadth of urologic training in open, endoscopic (cystoscopic, ureteroscopic, laparoscopic, percutaneous, and robotic) and image-guided (ultrasound and fluoroscopic) surgery.

Conflicts of interest

The authors have nothing to disclose.

References

[1] Rassweiler J, Teber D, Kuntz R, Hofmann R. Complications of transurethral resection of the prostate (TURP)—incidence, management, and prevention. Eur Urol 2006;50:969–80.
[2] Geavlete P, Georgescu D, Mirciulescu V, Niţă G. Ureteroscopic laser approach in recurrent ureteropelvic junction stenosis. Eur Urol 2007;51:1542–8.
[3] Michel MS, Trojan L, Rassweiller JJ. Complications in percutaneous nephrolithotomy. Eur Urol 2007;51:899–906.
[4] Clayman RV, Kavoussi LR, Soper NJ, et al. Laparoscopic nephrectomy: initial case report. J Urol 1991;146:278–82.
[5] Menon M, Shrivastava A, Kaul S, et al. Vattikuti Institute prostatectomy: contemporary technique and analysis of results. Eur Urol 2007;51:648–58.
[6] Rattner D, Kalloo A, ASGE/SAGES Working Group. ASGE/SAGES working group on natural orifice transluminal endoscopic surgery. Surg Endosc 2006;20:329–33.
[7] Gettman MT, Blute ML. Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice transluminal endoscopic surgery. Mayo Clinic Proc 2007;82:843–5.
[8] Gill IS, Cherullo EE, Meraney AM, et al. Vaginal extraction of the intact specimen following laparoscopic radical nephrectomy. J Urol 2002;167:238–41.
[9] Breda G, Silvestre P, Giunta A, et al. Laparoscopic nephrectomy with vaginal delivery of the intact kidney. Eur Urol 1993;24:116–7.
[10] Gettman MT, Lotan Y, Napper CA, Cadeddu JA. Transvaginal laparoscopic nephrectomy: development and feasibility in the porcine model. Urology 2002;59:446–50.
[11] Kalloo AN, Singh VK, Jagannath SB, et al. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 2004;60:114–7.
[12] Lima E, Rolanda C, Pego J, et al. Transvesical endoscopic peritoneoscopy: a novel 5 mm port for intra-abdominal scarless surgery. J Urol 2006;176:802–5.
[13] Rolanda C, Lima E, Pego J, et al. Third-generation cholecystectomy by natural orifices: transgastric and transvesical combined approach. Gastrointest Endosc 2007;65:111–4.
[14] Lima E, Rolanda C, Pego J, et al. Third-generation nephrectomy by natural orifice transluminal endoscopic surgery. J Urol 2007;178:2648–54.
[15] Lima E, Henriques-Coelho T, Rolanda C, et al. Transvesical thoracoscopy: a natural orifice translumenal endoscopic approach for thoracic surgery. Surg Endosc 2007;21:854–8.
[16] Ponsky L, Isariyawongse J, McGee M, et al. Pure natural orifice transluminal endoscopic surgery (NOTES) nephrectomy using standard laparoscopic instruments in the porcine model. J Endourol 2007;21:A91.
[17] Zeltser IS, Bergs R, Fernandez R, et al. Single trocar laparoscopic nephrectomy using magnetic anchoring and guidance system in the porcine model. J Urol 2007;178:288–91.
[18] Scott DJ, Tang SJ, Fernandez R, et al. Completely transvaginal NOTES cholecystectomy using magnetically anchored instruments. Surg Endosc 2007;21:2308–16.
[19] Clayman RV, Box GN, Abraham JB, et al. Rapid communication: transvaginal single-port NOTES nephrectomy: initial laboratory experience. J Endourol 2007;21:640–4.
[20] Box GN, Lee HJ, Santo RJS, et al. Robot-assisted NOTES nephrectomy: initial report. J Endourol. In press.
[21] Branco AW, Branco Filho AJ, Kondo W, et al. Hybrid transvaginal nephrectomy. Eur Urol 2008;53:1290–4.
[22] Raman JD, Bensalah K, Bagrodia A, et al. Laboratory and clinical development of single keyhole umbilical nephrectomy. Urology 2007;70:1039–42.
[23] Desai MM, Rao PP, Aron M, et al. Scarless single port transumbilical nephrectomy and pyeloplasty: first clinical report. BJU Int 2008;101:83–8.
[24] Kaouk JH, Haber G-P, Goel R, et al. Single-port laparoscopic surgery in urology: initial experience. Urology 2007;71:3–6.
[25] Ponsky L, Cherullo E, Sawyer M, et al. Single access site laparoscopic radical nephrectomy: initial clinical experience. J Endourol. In press.

Bibliography

General Bibliography

Abbou CC, Salomon L, Hoznek A, Antiphon P, Cicco A, Saint F, Alame W, Bellot J, Chopin DK. Laparoscopic radical prostatectomy: preliminary results. Urology 2000;55:630-634.

Ayed AK, Raghunathan R. Thoracoscopy versus open lung biopsy in the diagnosis of interstitial lung disease: a randomised controlled trial. J R Coll Surg Edinb 2000;45:159-163.

Bardaro SJ, Swanstrom L. Development of advanced endoscopes for natural orifice translumenal endoscopic surgery (NOTES). Minim Invasive Ther Allied Technol. 2006;15:378-383.

Benton P, Hewlett JH. Surgery through the ages: a pictorial chronical. NY: Hastings House Pub.,1944;31.

Bergström M, Ikeda K, Swain P, Park PO. Transgastric anastomosis by using flexible endoscopy in a porcine model (with video). Gastrointest Endosc 2006;63:307-312.

Bernheim BM. Organoscopy: cystoscopy of the abdominal cavity. Ann Surg 1911;53: 764–767.

Bessler M, Stevens PD, Milone L, Parikh M, Fowler D. Transvaginal laparoscopically assisted endoscopic cholecystectomy: a hybrid approach to natural orifice surgery. Gastrointest Endosc 2007;66:1243-1245.

Blanc FX, Atassi K, Bignon J, Housset B. Diagnostic value of medical thoracoscopy in pleural disease. A 6-year retrospective study. Chest 2002;121:1677–1683.

Box GN, Lee HJ, Santos RJ, Abraham JB, Louie MK, Gamboa AJ, Alipanah R, Deane LA, McDougall EM, Clayman RV. Robot-assisted NOTES nephrectomy: initial report. J Endourol 2008;22:503-506.

Bozzini PH. Lichtleiter, eine Erfindung zur Anschauung innerer Teile und Krankheiten. J Prak Heilk 1806; & 24:107.

Branco AW, Filho AJ, Kondo W, Noda RW, Kawahara N, Camargo AA, Stunitz LC, Valente J, Rangel M. Hybrid Transvaginal Nephrectomy. Eur Urol 2007;5;[Epub ahead of print]

Breda G, Silvestre P, Giunta A, Xausa D, Tamai A, Gherardi L. Laparoscopic nephrectomy with vaginal delivery of the intact kidney. Eur Urol 1993;24:116-117.

Clayman RV, Box GN, Abraham JB, Lee HJ, Deane LA, Sargent ER, Nguyen NT, Chang K, Tan AK, Ponsky LE, McDougall EM. Rapid communication: transvaginal single-port NOTES nephrectomy: initial laboratory experience. J Endourol 2007;21:640-644.

Clayman RV, Kavoussi LR, Soper NJ, Dierks SM, Meretyk S, Darcy MD, Roemer FD, Pingleton ED, Thomson PG, Long SR. Laparoscopic nephrectomy: initial case report. J Urol 1991;146:278-282.

De Rocher B. Cystoscopie et catheterisme des uretes. Ann Mal Org Genito-Urin 1890;10:413.

Decker A. Culdoscopy: A method for visual diagnosis of gynecologic disease. Clin Symp 1952;6:201-210.

Desai MM, Rao PP, Aron M, Pascal-Haber G, Desai MR, Mishra S, Kaouk JH, Gill IS. Scarless single port transumbilical nephrectomy and pyeloplasty: first clinical report. BJU Int 2008;101:83-88.

Desormeaux AJ. The endoscope and its application to the diagnosis and treatment of affections of the genitourinary passages. Chicago Med J 1867;24:177–194.

Dewey TM, Herbert MA, Hill SL, Prince SL, Mack MJ. One-year follow-up after thoracoscopic sympathectomy for hyperhidrosis: outcomes and consequences. Ann Thorac Surg 2006;81:1227–1232.

DiMarco AF. Restoration of respiratory muscle function following spinal cord injury. Review of electrical and magnetic stimulation techniques. Respir Physiol Neurobiol 2005;147:273–287.

Dubois F, Icard P, Berthelot G, Levard H. Coelioscopic cholecystectomy. Ann Surg 1990;211:60–62.

Figueiredo AA, Tostes JG, Jacob MV. Laparoscopic treatment of traumatic intraperitoneal bladder rupture. Int Braz J Urol 2007;33:380-382.

Fong DG, Pai RD, Thompson CC. Transcolonic endoscopic abdominal exploration: a NOTES survival study in a porcine model. Gastrointest Endosc 2007;65:312-318.

Fritcher-Ravens A. EUS – experimental and evolving techniques. Endoscopy 2006;38:95–99.

Fritscher-Ravens A, Mosse CA, Ikeda K, Swain P. Endoscopic transgastric lymphadenectomy by using EUS for selection and guidance. Gastrointest Endosc. 2006;63:302-306.

Gagner M, Lacroix A, Bolté E. Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. N Engl J Med 1992;327:1033.

Gaskin TA, Ische JH, Matthews JL, Winchester SB, Smith RJ. Laparoscopy and the general surgeon. Surg Clin North Am 1991;71:1085–1097.

Gettman MT, Blute ML. Transvesical peritoneoscopy: initial clinical evaluation of the bladder as a portal for natural orifice translumenal endoscopic surgery. Mayo Clin Proc 2007;82:843-845.

Gettman MT, Box G, Averch T, Cadeddu JA, Cherullo E, Clayman RV, Desai M, Frank I, Gill I, Gupta M, Haber GP, Humphreys M, Kaouk J, Landman J, Lima E, Ponsky L. Consensus Statement on Natural Orifice Transluminal Endoscopic Surgery and Single-Incision Laparoscopic Surgery: Heralding a New Era in Urology? Eur Urol. 2008;53:1117-1120

Gettman MT, Lotan Y, Napper CA, Cadeddu JA. Transvaginal laparoscopic nephrectomy: development and feasibility in the porcine model. Urology 2002;59:446-450.

Gill IS, Cherullo EE, Meraney AM, Borsuk F, Murphy DP, Falcone T. Vaginal extraction of the intact specimen following laparoscopic radical nephrectomy. J Urol 2002;167:238-241.

Gill IS, Fergany A, Klein EA, Kaouk JH, Sung GT, Meraney AM, Savage SJ, Ulchaker JC, Novick AC. Laparoscopic radical cystoprostatectomy with ileal conduit performed completely intracorporeally: the initial 2 cases. Urology 2000;56:26-29.

Gomez RG, Ceballos L, Coburn M, Corriere JN Jr, Dixon CM, Lobel B, McAninch J. Consensus statement on bladder injuries. BJU Int 2004;94:27-32.

Gorden A. The history and development of endoscopic surgery. In Sutton C, Diamond MP eds, Endoscopic Surgery for Gynaecologists. London: WB Saunders,1993:3–7.

Guillonneau B, Cathelineau X, Barret E, Rozet F, Vallancien G. Laparoscopic radical prostatectomy: technical and early oncological assessment of 40 operations. Eur Urol 1999;36:14-20.

Gunning JE, Rosenzweig BA. Evolution of endoscopic surgery, In white RA, Klein SR (eds): Endoscopic Surgery. Boston: Mosby Year Book, Inc.,1991;1-9.

Harrell AG, Heniford T. Minimally invasive abdominal surgery: lux et veritas past, present, and future. Am J Surg 2005;190:239-243.

Hasson HM. A modified instrument and method for laparoscopy. Am J Obstet Gynecol 1971;110:886-887.

Haubrich WS. History of endoscopy. In: Sivak MV, ed. Gastroenterologic Endoscopy. Philadelphia, PA: WB Saunders Co.,1987;2-19.

Hausmann VH. Maximilian Nitze (1848–1906) Seine Bedeutung fiir die Entwicklung der Urologie. Z Urol Nephrol 1987; 80:539.

Hazelrigg SR, Landreneau RJ, Mack M, Acuff T, Seifert PE, Auer JE, Magee M. Thoracoscopic staped resection for spontaneous pneumothorax. J Thorac Cardiovasc Surg 1993;105:389–393.

Hochberger J, Lamade W. Transgastric surgery in the abdomen: the dawn of a new era? Gastrointest Endosc 2005;62:293-296.

Hu B, Kalloo AN, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Isakovich NV, Nakajima Y, Kawashima K, Kantsevoy SV. Peroral transgastric endoscopic primary repair of a ventral hernia in a porcine model. Endoscopy 2007;39:390-393.

Ikeda K, Fritscher-Ravens A, Mosse CA, Mills T, Tajiri H, Swain CP. Endoscopic full-thickness resection with sutured closure in a porcine model. Gastrointest Endosc 2005;62:122-129.

Ikeda K, Mosse CA, Park PO, Fritscher-Ravens A, Bergström M, Mills T, Tajiri H, Swain CP. Endoscopic full-thickness resection: circumferential cutting method. Gastrointest Endosc 2006;64:82-89.

Isariyawongse JP, McGee MF, Rosen MJ, Cherullo EE, Ponsky LE. Pure Natural Orifice Transluminal Endoscopic Surgery (NOTES) Nephrectomy using Standard Laparoscopic Instruments in the Porcine Model. J Endourol. 2008;17:[Epub ahead of print]

Jacobeus HC. Uber Die Moglichkeit die Zystoskopie bei Untersuchung seroser Hohlunger anzuwerder. Munch Med Wochenschr 1911;57:2090–2092.

Jagannath SB, Kantsevoy SV, Vaughn CA, Chung SSC, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Scorpio DG, Magee CA, Pipitone LJ, Kalloo AN. Per-oral transgastric ligation of fallopian tubes with long-term survival in a porcine model. Gastrointest Endosc 2005;61:449–453.

Kalk H. Erfahrungen mit der lapprskopie (Zugleich mit Beschreibung Eines Nuen Instrumentes). Z Klin Med 1929;111:303–348.

Kalloo AN, Singh VK, Jagannath SB, Niiyama H, Hill SL, Vaughn CA, Magee CA, Kantsevoy SV. Flexible transgastric peritoneoscopy: a novel approach to diagnostic and therapeutic interventions in the peritoneal cavity. Gastrointest Endosc 2004;60:114–117.

Kantsevoy SV, Hu B, Jagannath SB, Vaughn CA, Beitler DM, Chung SSC, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Pipitone LL, Talamini MA, Kalloo AN. Transgastric endoscopic splenectomy. Is it possible? Surg Endosc 2006; 20:522–525.

Kantsevoy SV, Jagannath SB, Niiyama H, Chung SS, Cotton PB, Gostout CJ, Hawes RH, Pasricha PJ, Magee CA, Vaughn CA, Barlow D, Shimonaka H, Kalloo AN. Endoscopic gastrojejunostomy with survival in a porcine model. Gastrointest Endosc

2005;62:287-292.

Kaouk JH, Haber GP, Goel RK, Desai MM, Aron M, Rackley RR, Moore C, Gill IS. Single-port laparoscopic surgery in urology: initial experience. Urology 2008;71:3-6.

Kelling G. Die Tamponade der Speiseroehre und des magensmit beigsamen instrumenten. Verdhandlungen der Gesellschaft Deutscher Naturtorscher und Aerzte. Vogel verlag, Leipzig 1901;73:117–119.

Lima E, Henriques-Coelho T, Rolanda C, Pego JM, Silva D, Carvalho JL, Correia-Pinto J. Transvesical thoracoscopy: a natural orifice transluminal endoscopic approach for thoracic surgery. Surg Endosc 2007;21:854-854.

Lima E, Rolanda C, Correia-Pinto J. NOTES performed using multiple ports of entry: current experience and potential implications for urologic applications. J Endourol 2008; (in press)

Lima E, Rolanda C, Correia-Pinto J. Transvesical endoscopic peritoneoscopy: intra-abdominal scarless surgery for urologic applications. Curr Urol Rep. 2008;9:50-54.

Lima E, Rolanda C, Osório L, Pego J, Silva D, Henriques-Coelho T, Carvalho J, Bergström M, Park PO, Mosse C, Swain P, Correia-Pinto C. Endoscopic closure of transmural bladder wall perforations. Eur Urol 2008; Jun 13. [Epub ahead of print]

Lima E, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL, Correia-Pinto J. Transvesical endoscopic peritoneoscopy: A novel 5 mm-port for intra-abdominal scarless surgery. J Urol 2006;176:802–805.

Lima E, Rolanda C, Pêgo JM, Henriques-Coelho T, Silva D, Osório L, Moreira I, Carvalho JL, Correia-Pinto J. Third-generation nephrectomy by natural orifice transluminal endoscopic surgery. J Urol 2007;178:2648-2654.

Litynski GS, Mouret P, Dubois F, Perissat J. The laparoscopic breakthrough in Europe. J Soc Laparosc Surg 1999;3:163–167.

Litynski GS. Erich Muhe and the rejection of laparoscopic cholecystectomy: a surgeon ahead of his time. J Soc Laparosc Surg 1998;2:341–346.

Liu R, Chand B, Ponsky J. The future of surgical endoscopy. Endoscopy 2005, 37:38-41.

Lynch TH, Martínez-Piñeiro L, Plas E, Serafetinides E, Türkeri L, Santucci RA, Hohenfellner M; European Association of Urology. European Association of Urology. EAU guidelines on urological trauma. Eur Urol 2005;47:1-15.

Malik A, Mellinger JD, Hazey JW, Dunkin BJ, MacFadyen BV Jr. Endoluminal and transluminal surgery: current status and future possibilities. Surg Endosc 2006;20:1179-1192.

Marescaux J, Dallemagne B, Perretta S, Wattiez A, Mutter D, Coumaros D. Surgery without scars. Report of transluminal cholecystectomy in a human being. Arch Surg 2007;142:823-826.

Marescaux J. Operation Anubis: A new step in NOTES history! Available at http://www.websurg.com/notes/.

McKernan JB. Origin of laparoscopic cholecystectomy in the USA: personal experience. World J Surg 1990; 231:332–333.

Meining A, Wilhelm D, Burian M, Dundoulakis M, Schneider A, von Delius S, Feussner H. Development, standardization, and evaluation of NOTES cholecystectomy using a transsigmoid approach in the porcine model: an acute feasibility study. Endoscopy 2007;39:860-864.

Merrifield BF, Wagh MS, Thompson CC. Peroral transgastric organ resection in the abdomen: feasibility study in pigs. Gastrointest Endosc 2006;63:693–697.

Mintz Y, Horgan S, Cullen J, Ramamoorthy S, Chock A, Savu MK, Easter DW, Talamini MA. NOTES: the hybrid technique. J Laparoendosc Adv Surg Tech A 2007;17:402-406.

Moll F, Rathert P. The surgeon and his intention: Gustav Simon (1824–1876), his first planned nephrectomy and further contributions to urology. World J Urol 1999;17:162-167.

Mouret P. How I developed laparoscopic cholecystectomy. Ann Acad Med Singapore 1996;25:744–747.

Neudecker J, Sauerland S, Neugebauer E, Bergamaschi R, Bonjer HJ, Cuschieri A, Fuchs KH, Jacobi Ch, Jansen FW, Koivusalo AM, Lacy A, McMahon MJ, Millat B, Schwenk W. The European Association for Endoscopic Surgery clinical practice guideline on the pneumoperitoneum for laparoscopic surgery. Surg Endosc. 2002;16:1121-1143.

Newman D. lectures on surgical diseases of kidney. London, 1888.

NIH Consensus Conference. Gallstones and laparoscopic cholecystectomy. JAMA 1993;269:185-188.

Onders R, McGee MF, Marks J, Chak A, Schilz R, Rosen MJ, Ignagni A, Faulx A, Elmo MJ, Schomisch S, Ponsky J. Diaphragm pacing with natural orifice transluminal endoscopic surgery: potential for difficult-to-wean intensive care unit patients. Surg Endosc 2006;21:475–479.

Organ CH. Historical contributions to gasless laparoscopy. In smith RS and Organ CH, eds, Gasless laparoscopy with conventional instruments: the next phase in minimally invasive surgery. San francisco: Norman Pub.,1933;1-10.

Orndoff RH. The peritonesocope in diagnosisof diseases of the abdomen. J Radiol 1920;1:307.

Ott DO. Ventroscopic illumination of the abdominal cavity in pregnancy. Z Akush Zhenskikl Boleznei1901;15:7–8.

Pai RD, Fong DG, Bundga ME, Odze RD, Rattner DW, Thompson CC. Transcolonic endoscopic cholecystectomy: a NOTES survival study in a porcine model (with video). Gastrointest Endosc 2006;64:428–434.

Palmer R. Technique et instrumentation de la coelioscopie gynecologique. Gynecol Obstet (Paris) 1947;46: 420.

Pansadoro A, Franco B, Laurenti C, Pansadoro V. Conservative treatment of intraperitoneal bladder perforation during transurethral resection of bladder tumor. Urology 2002;60:682-684.

Park PO, Bergström M, Ikeda K, Fritscher-Ravens A, Mosse S, Kochman M, Swain P. Endoscopic pyloroplasty with full-thickness transgastric and transduodenal myotomy with sutured closure. Gastrointest Endosc 2007;66:116-120.

Park PO, Bergstrom M, Ikeda K, Fritscher-Ravens A, Swain P. Experimental studies of transgastric gallbladder surgery: cholecystectomy and cholecystogastric anastomosis (videos). Gastrointest Endosc 2005;61:601–606.

Park S, Bergs RA, Eberhart R, Baker L, Fernandez R, Cadeddu JA. Trocar-less instrumentation for laparoscopy: magnetic positioning of intra-abdominal camera and retractor. Ann Surg 2007;245:379-384.

Perretta S, Dallemagne B, Coumaros D, Marescaux J. Natural Orifice Transluminal Endoscopic Surgery. Transgastric Cholecystectomy in a survival porcine model. Surg Endosc 2008;22:1126-1130.

Pham BV, Raju GS, Ahmed I, Brining D, Chung S, Cotton P, Gostout CJ, Hawes RH, Kalloo AN, Kantsevoy SV, Pasricha PJ. Immediate endoscopic closure of colon perforation by using a prototype endoscopic suturing device: feasibility and outcome in a porcine model (with video). Gastrointest Endosc 2006;64:113-119.

Philipi CJ, Fitzgibbons RJ, Salerno GM. Historial review: Diagnostic laparoscopy to laparoscopic cholecystectomy and beyond. In: Zucker KA, ed. Surgical laparoscopy. St lous, MO: Quality Medical Publishing, Inc., 1991;3-21.

Phillips J, Keith D, Keith L. Gynecologic laparoscopy. J Reprod Med 1974;12:215–217.

Picatoste Y, Patino J, Martin GB, Hernandez RR. Cystoscopy (1879–1979): centennial of a transcendental invention. Arch Esp Urol 1980;33:1–18.

Ponsky JL. Gastroenterologists as surgeons: what they need to know. Gastrointest Endosc 2005;61:449-453.

Ponsky LE, Cherullo EE, Sawyer M, Hartke D. Single access site laparoscopic radical nephrectomy: initial clinical experience. J Endourol 2008;22:663-666.

Raju GS, Shibukawa G, Ahmed I, Brining D, Poussard A, Xiao SY, Coe J, Cropper M, Martin D, Hull J. Endoluminal suturing may overcome the limitations of clip closure of a gaping wide colon perforation (with videos). Gastrointest Endosc 2007;65:906-911.

Raman JD, Bensalah K, Bagrodia A, Stern JM, Cadeddu JA. Laboratory and clinical development of single keyhole umbilical nephrectomy. Urology 2007;70:1039-1042.

Rassweiler J, Sentker L, Seemann O, Hatzinger M, Stock C, Frede T. Heilbronn laparoscopic radical prostatectomy. Technique and results after 100 cases. Eur Urol 2001; 40:54-64.

Rathert P. Max Nitze (1848–1906). Invest Urol 1967;5:327-530.

Rattner D, Kalloo A. ASGE/SAGES Working Group on natural orifice transluminal endoscopic surgery. SAGES/ ASGE Working Group on NOTES. Surg Endosc 2006;20:329-333.

Reich H. New techniques in advanced laparoscopic surgery. Clin Obstet Gynecol 1989;3:655–681.

Reynolds W. Jr. The first laparoscopic cholecystectomy. J Soc Laparoendosc Surg 2001;5:89-94.

Richards WO, Rattner DW. Endoluminal and transluminal surgery: no longer if, but when. Surg Endosc 2005,19:461-463.

Rodriguez MI, Ash K, Foley RW, Liston W. Pericardio peritoneal window: a laparoscopic approach. Surg Endosc 1999;13:409–411.

Rolanda C, Lima E, Correia-Pinto J. Searching the best approach for third-generation cholecystectomy. Gastrointest Endosc 2007;65:354.

Rolanda C, Lima E, Pêgo JM, Henriques-Coelho T, Silva D, Carvalho JL, Correia-Pinto J. Third Generation Cholecystectomy by Natural Orifices: Transgastric and Transvesical Combined Approach. Gastrointest Endosc 2007;65:111–117.

Rosin D. History. In Rosin D ed. Minimal Access Medicine and Surgery. Oxford: Radcliffe Medical Press,1993:1–9.

Roviaro GE, Varoli F, Vergani C, Maciocco M. State of the art in thoracoscopic surgery. A personal experience of 2000 videothoracoscopic procedures and an overview of the literature. Surg Endosc 2002;16:881–892.

Ruddick JC. Peritoneoscopy. Surg Gynecol Obstet 1937;65:523–539.

Ruddick JC. Peritoneoscopy. West J Surg 1934;42:392–405.

Ryou M, Fong DG, Pai RD, Tavakkolizadeh A, Rattner DW, Thompson CC. Dual-port distal pancreatectomy using a prototype endoscope and endoscopic stapler: a natural orifice transluminal endoscopic surgery (NOTES) survival study in a porcine model. Endoscopy 2007;39:881-887.

Ryou M, Pai RD, Sauer JS, Rattner DW, Thompson CC. Evaluating an optimal gastric closure method for transgastric surgery. Surg Endosc 2007;21:677-680.

Saleh JW. Laparoscopy. Philadelphia: WB Saunders Co., 1988;vii-viii.

Santambrogio L, Nosotti M, Bellavit N, Mezzetti M. Videothoracoscopy versus thoracotomy for diagnosis of the indeterminate solitary pulmonary nodule. Ann Thorac Surg 1995;59:868–870.

Schuessler WW, Schulam PG, Clayman RV, Kavoussi LR. Laparoscopic radical prostatectomy: initial short-term experience. Urology 1997;50:854-857.

Schuessler WW, Vancaillie TG, Reich H, Griffith DP. Transperitoneal endosurgical lymphadenectomy in patients with localized prostate cancer. J Urol 1991;145:988-991.

Sclabas GM, Swain P, Swanstrom LL. Endoluminal methods for gastrotomy closure in natural orifice transenteric surgery (NOTES). Surg Innov 2006;13:23-30.

Scott DJ, Tang SJ, Fernandez R, Bergs R, Goova MT, Zeltser I, Kehdy FJ, Cadeddu JA. Completely transvaginal NOTES cholecystectomy using magnetically anchored instruments. Surg Endosc 2007;21:2308-2316.

Semm K. Endoscopic appendicectomy. Endoscopy 1983;15:59–64.

Shih SP, Kantsevoy SV, Kalloo AN, Magno P, Giday SA, Ko CW, Isakovich NV, Meireles O, Hanly EJ, Marohn MR. Hybrid minimally invasive surgery-a bridge between laparoscopic and translumenal surgery. Surg Endosc 2007; 21:1450-1453.

Silber SJ, Cohen R. Laparoscopy for cryptorchidism. J Urol 1980;124:928-929.

Sumiyama K, Gostout CJ, Rajan E, Bakken TA, Deters JL, Knipschield MA, Hawes RH, Kalloo AN, Pasricha PJ, Chung S, Kantsevoy SV, Cotton PB. Pilot study of the porcine uterine horn as an in vivo appendicitis model for development of endoscopic transgastric appendectomy. Gastrointest Endosc 2006;64:808-812.

Sumiyama K, Gostout CJ, Rajan E, Bakken TA, Knipschield MA, Chung S, Cotton PB, Hawes RH, Kalloo AN, Kantsevoy SV, Pasricha PJ. Transgastric cholecystectomy: Transgastric accessibility to the gallbladder improved with the SEMF method and a novel multibending therapeutic endoscope. Gastrointes Endosc 2007,65:1028-1034.

Swain P, Park PO. Endoscopic suturing. Best Pract Res Clin Gastroenterol 2004;18:37-47.

Swain P. Endoscopic suturing: now and incoming. Gastrointest Endosc Clin N Am 2007;17:505-520.

Swanstrom LL, Kozarek R, Pasricha PJ, Gross S, Birkett D, Park PO, Saadat V, Ewers

R, Swain P. Development of a new access device for transgastric surgery. J Gastrointest Surg 2005;9:1129-1137.

Türk I, Deger S, Winkelmann B, Schönberger B, Loening SA. Laparoscopic radical cystectomy with continent urinary diversion (rectal sigmoid pouch) performed completely intracorporeally: the initial 5 cases. J Urol 2001;165:1863-1866.

Veress J. Neues Instrument Zur Ausfuhrung von brustoder Bachpunktionen und Pneumothoraybehundlung. Deutsch Med Wochenschr 1938;64:1480–1481.

Vitale GC, Davis BR, Tan T C. The advancing art and science of endoscopy. Am J Surg 2005;190:228-233.

Vitale GC, Lawhon JC, Larson GM, Harrell DJ, Reed DN Jr, MacLeod S. Endoscopic drainage of the pancreatic pseudocyst. Surgery 1999,26:616-623.

Wagh MS, Merrifield BF, Thompson CC. Endoscopic Transgastric Abdominal Exploration and Organ Resection: Initial Experience in a Porcine Model. Clin Gastroenterol and Hepatol 2005;3:892–896.

Wagh MS, Merrifield BF, Thompson CC. Survival studies after endoscopic transgastric oophorectomy and tubectomy in a porcine model. Gastrointest Endosc 2006;63:473-478.

Waller DA, Forty J, Morritt GN. Video-assisted thoracoscopic surgery versus thoracotomy for spontaneous pneumothorax. Ann Thorac Surg 1994;58:372–476.

Weickert U, Jakobs R, Riemann JF. Diagnostic laparoscopy. Endoscopy 2005;37:33-37.

Yee DS, Kalisvaart JF, Borin JF. Preoperative cystoscopy is beneficial in selection of patients for laparoscopic repair of intraperitoneal bladder rupture. J Endourol 2007;21:1145-1148.

Zeltser IS, Bergs R, Fernandez R, Baker L, Eberhart R, Cadeddu JA. Single trocar laparoscopic nephrectomy using magnetic anchoring and guidance system in the porcine model. J Urol 2007;178:288-291.

Zornig C, Emmermann A, von Waldenfels HA, Mofid H. Laparoscopic cholecystectomy without visible scar: combined transvaginal and transumbilical approach. Endoscopy 2007;39:913-915.

Zorron R, Maggioni LC, Pombo L, Oliveira AL, Carvalho GL, Filgueiras M. NOTES transvaginal cholecystectomy: preliminary clinical application. Surg Endosc 2008; 22:542-547.