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*Review*

# Natural orifice transluminal endoscopic surgery (NOTES) in animals

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## Abstract

Natural orifice transluminal endoscopic surgery (NOTES) is a modern technique of performing surgical procedures developed worldwide. In the last few years, series of NOTES operations were performed in animals and humans. This article describes some surgical procedures performed in animals with use of this new technique.

**Key words:** endoscopy, laparoscopy, dog, pig

## Introduction

Natural orifice transluminal endoscopic surgery (NOTES) is a new technique that does not require an incision of the abdominal cavity wall to create peritoneal access. The technique relies on natural body cavities (mouth, anus, nostrils, vagina and urethra) as gateways to luminal organs whose walls are punctured to access the peritoneal cavity. When instruments are introduced through the oral cavity, the puncture is usually made in the abdominal wall, while the esophageal wall is less often used. When instruments are inserted via the vagina, a puncture is made in the vaginal fornix, and when the surgical site is accessed through the anus, the colonic wall is incised. A puncture is made in the urinary bladder wall to create peritoneal access when the instruments are advanced through the urethra (Box et al. 2008). According to Zorron, the Brazilian NOTES Research Group proposed the NOTES taxonomy in January 2009. In line with the above proposal, NOTES procedures are

divided into four categories: Totally NOTES (T-NOTES), Hybrid NOTES, NOTES-assisted laparoscopy and Natural Orifice Specimen Extraction (NOSE). Totally NOTES, also referred to as Pure NOTES, is a technique that uses transluminal flexible or rigid instruments without any percutaneous assistance or visualization (Zorron 2009). Although Hybrid NOTES relies on various transgastric surgical methods, the key procedures are performed with the use of flexible tools introduced through natural orifices. When natural cavities are used for visualization only, and the remaining procedures are carried out with the involvement of other techniques, the resulting approach is Hybrid NOTES. As described by Palanivelu et al. (2008), Natural Orifice Specimen Extraction (NOSE) refers to a procedure in which an organ or tissue is removed through a natural cavity.

According to Zorron, umbilical surgery relying on various types of single port access (SAS) is a single-trocar laparoscopic procedure rather than natural orifice transumbilical surgery (NOTUS)

because the umbilicus is a natural scar, not a natural orifice. For this reason, Zorron has proposed other terms for the procedure, such as single access surgery (SAS), SPA, transumbilical endoscopic surgery (TUES) or laparoendoscopic single-site surgery (LESS). Zorron (2009) has also proposed a classification of NOTES techniques based on the use of a flexible endoscope and flexible tools. In line with this classification, techniques involving flexible tools are referred to as FLEXNOTES, while procedures performed with the use of rigid instruments are termed RIGNOTES or NOTES using rigid tools only.

### **Potential obstacles to introducing NOTES to clinical practice**

In July 2005, the ASGE/SAGES Working Group on Natural Orifice Transluminal Endoscopic Surgery listed the potential obstacles to introducing NOTES to clinical practice. They are: peritoneal access, closure of peritoneal access site, prevention of infections, development of suturing instruments, development of instruments for anastomosis without sutures, spatial orientation, development of multi-tasking platforms for complex procedures, intraperitoneal hemorrhage control, management of iatrogenic intraperitoneal complications, untoward physiological events and compression syndromes.

### **Potential benefits of NOTES**

NOTES delivers a variety of potential benefits. Since the technique relies on natural orifices, the surgery heals without visible scars and has a very good cosmetic effect. The absence of surgical wounds implies fewer complications, less postoperative pain and faster recovery. NOTES procedures could be performed outside the operating room, thus reducing surgical costs. Selected surgical procedures could be performed under sedation rather than full anesthesia. NOTES offers an alternative to laparoscopic surgery in clinically obese patients. The new technique will minimize the psychological trauma of the patient and his/her family.

### **Comparison of transgastric peritoneal access techniques**

(Delius et al. 2008) compared several techniques for transgastric peritoneal access: a 1.5 to 2 cm longitudinal incision, balloon dilation after needle knife puncture, via a short submucosal tunnel and via an

elongated submucosal tunnel. A needle knife is used to perform a longitudinal incision in the abdominal wall. After making the incision, the needle knife is removed and the endoscope is introduced through the abdominal wall. Balloon dilation after gastroscopic incision supports the performance of a 2 to 3 mm incision in the abdominal wall. The incision is dilated by through-the-scope balloon dilation. The balloon is partially dilated to advance the endoscope through the abdominal wall. (Kalloo et al. 2004) alternately used a pull-type sphincterotome and a dilation balloon inserted over the guidewire to dilate the incision in the abdominal wall. To create transgastric access via a short submucosal tunnel, the submucosa is injected with a saline solution, and a 3 to 4 cm long incision is made in the mucosa using a needle knife. Loose tissue at the submucosal level is bluntly separated, and the mucosa is partially separated from the muscular layer. An endoscope is inserted into the submucosal space using the shaft of the forceps as a guide. With the use of the leading edge of the endoscope, loose tissue is separated to form a tunnel with a length of approximately 4 cm. The serous and muscular layer is incised with a needle knife at the distal end of the tunnel to insert the endoscope into the peritoneal cavity. An elongated submucosal tunnel is formed using the same technique that is applied to shape a short submucosal tunnel, the only difference being that the tunnel is elongated to around 8 cm. According to researchers, the submucosal tunnel procedure is the safest yet the most time-consuming technique of creating peritoneal access.

### **Exploration of the peritoneal cavity**

The first study describing a transgastric approach to the peritoneal cavity was published by (Kalloo et al. 2004). The peritoneal cavity was accessed by needle knife puncture of the ventral abdominal wall, followed by extension of the incision either with a pull-type sphincterotome or by balloon dilation. An endoscope was inserted in the peritoneal cavity through the gastric incision, and it was insufflated with air for examination.

(Fong et al. 2007) performed transcolonic peritoneoscopy in pigs. A double channel endoscope was inserted 15 to 29 cm into the rectum. A puncture was made in the ventral colonic wall using a needle knife and a prototype incision and closure device. Directly after the insertion of the endoscope into the peritoneal cavity, the Veress needle was positioned in the median line. In some animals, it was used for CO<sup>2</sup> insufflation to create pneumoperitoneum, and in others – to control pneumoperitoneum pressure cre-

ated by the air insufflated by the endoscope. During the examination, the animals were placed in different positions to enhance the visibility of organs selected. During transcolonic access, the following organs were easily identified: stomach, liver, gall bladder, spleen, small intestine and colon. The urinary bladder was not fully visible, and the ovaries, fallopian tubes and the uterus were not identified.

(Lima et al. 2006) carried out a peritoneoscopy with access through the urinary bladder. The ventral wall of the urinary bladder was incised with scissors inserted through the ureteroscope's working channel. An open-ended urethral catheter was introduced into the peritoneal cavity through the incision. Guidewire was advanced through the urethral catheter into the peritoneal cavity. The puncture in the urinary bladder wall was then enlarged with a dilator of a ureteroscope sheath enveloped by a flexible over tube. The obtained image of internal organs was quite satisfactory, in particular in the anterior view of the abdominal cavity, including the liver, gall bladder, stomach, spleen and diaphragm.

### **Exploration of the extraperitoneal space**

(Zacharopoulou et al. 2009) carried out a transvaginal exploration of extraperitoneal space in pigs using the NOTES technique. The animals were placed in dorsal recumbency and a double-channel endoscope was inserted through the vagina. An incision with a length of 1 cm was made with a needle knife under endoscopic control, and it was bluntly enlarged with the use of fingers. The incision was made on the left or the right side of the vagina, depending on whether the left or the right side of extraperitoneal space was to be examined. An endoscope was advanced through the incision in the vagina into extraperitoneal space and an extraperitoneal tunnel was created with the use of carbon dioxide and by flexing and straightening the gastroscope. Following passage through the pelvic cavity, the extraperitoneal tunnel was continued in the cephalic direction along the psoas muscle which served as a guide. According to the authors, the following organs were easily identified in the left part of the extraperitoneal space: common iliac vessels, iliac lymph nodes, ureter, ventral aorta with lymph nodes, adrenal gland and pancreas. Epigastric vessels, the posterior jejunal vein with lymph nodes, kidneys and the adrenal gland were observed in the right side of the extraperitoneal space.

### **Nephrectomy**

(Lima et al. 2007) relied on the Totally NOTES technique to carry out nephrectomy in pigs with com-

bined access through the stomach and urinary bladder. A rigid ureteroscope was inserted into the urinary bladder, and the bladder's lumen was enlarged with CO<sub>2</sub>. A small incision was made in the urinary bladder mucosa to perform cystotomy with the use of a catheter. The puncture in the urinary bladder wall was then enlarged with a dilator of a ureteroscope sheath enveloped by a flexible over tube. A ureteroscope was inserted into the peritoneal cavity in an over tube to create pneumoperitoneum and to control its pressure. A double-channel gastroscope was inserted into the stomach through the esophagus, and it was advanced into the peritoneal cavity through a puncture in the ventral abdominal wall made with needle knife cauterization via the gastroscope's working channel. Prior to the insertion of the gastroscope into the peritoneal cavity, the puncture in the urinary bladder wall was enlarged with a papillotomy knife. The animals were placed in lateral recumbency to expose the kidney on the opposing side. The parietal peritoneum was mobilized along the posterior pole of the kidney through cauterization with a needle knife introduced through the gastroscope and with grasping forceps advanced through the ureteroscope's working channel. Following peritoneum removal from the renal hilus and separation of its vessels, the ureteroscope was removed, and it was replaced with a harmonic scalpel that was used to incise the renal artery and vein. The kidney was separated with a needle knife and a harmonic scalpel, and the ureter was incised in mid-length.

(Isyariyawongse et al. 2008) carried out Pure NOTES nephrectomy with the use of laparoscopic tools inserted through the vagina. A gastroscope was first inserted into the stomach using the modified percutaneous endoscopic gastrostomy (PEG) technique. A 3 mm incision was made in the gastric wall by endoscopic electrocautery. The incision was enlarged with the use of an endoscopic balloon to create access to the peritoneal cavity. The gastroscope was advanced into the peritoneal cavity, pneumoperitoneum was created and a single-channel pediatric gastroscope was inserted into the vagina. Using needle knife electrocautery, a longitudinal incision was made in the vaginal fornix, and the endoscope was inserted into the peritoneal cavity. A laparoscopic trocar/endoscopic tube was inserted above the endoscope to create a NOTES port. The endoscope was removed, and a laparoscopic insufflator was connected to the NOTES port. The kidney was separated using laparoscopic sharp dissectors inserted through a modified transvaginal trocar device with the use of endoscopic rat-toothed forceps introduced via the working channel of an endoscope in a transgastric examination. The renal artery, the renal vein and the ureter were incised simultaneously using a laparoscopic stapling

device placed via a vaginal trocar. Following separation from the peritoneum, the kidney was grasped with a laparoscopic retrieval device and removed through the vaginal port.

(Metzelder et al. 2009) carried out a NOTES nephrectomy in pigs using the Brigid hybrid technique. Tools were inserted via two ports, one in the umbilicus and one in the urinary bladder. The parietal peritoneum covering the kidney was suspended with the use of a device inserted through the trocar in the urinary bladder and it was cut with endoscopic scissors placed via a working channel in the umbilical trocar. The anterior and posterior poles were separated by monopolar hook cautery with the use of grasping forceps inserted through the port in the urinary bladder. The renal artery and the renal vein were separated and ligated using several approaches, including endoclips, surgical knots in the abdominal cavity or the endo-ligasure sealing device, after which they were incised. The more distal section of the ureter was cut following the use of endoclips or the endo-ligasure sealing device. The kidney was placed in the endobag, it was morcellated and retrieved through the umbilical trocar.

### Splenectomy

(Kantsevoy et al. 2005) used a flexible endoscope to perform per-oral transgastric splenectomy in pigs. Following the per-oral introduction of a double-channel endoscope into the stomach, the abdominal wall was punctured with a needle knife. The opening was enlarged using a pull-type sphincterotome. An endoscope was advanced into the peritoneal cavity and insufflated with endoscopic air. To access spleen vessels, the network was cauterized and incised with an endoscopic snare. Spleen vessels were ligated using endoscopic loops and clips. When the spleen was mobilized, the incision in the abdominal wall was enlarged with a sphincterotome, and the spleen was retrieved into the stomach.

(Tagaya and Kubota 2009) carried out an endoscope- and laparoscope-controlled splenectomy in pigs and dogs using laparoscopic tools. An endoscope was inserted into the abdominal cavity through the gastric wall, while laparoscopic tools were advanced into the abdominal cavity via three trocars in the abdominal wall. Spleen vessels were ligated with laparoscopic clips and cut with laparoscopic shears, and the spleen was retrieved into the stomach using a polypectomy snare.

### Ligation of Fallopian tubes (oviducts)

(Jagannath et al. 2005) described the procedure of ligating Fallopian tubes in pigs with the use of the

NOTES technique. The Fallopian tube was ligated by per-oral transgastric endoscopy using a double-channel endoscope. The abdominal wall was punctured using a needle knife and a dilation balloon. The endoscope was inserted into the abdominal cavity, and the fallopian tubes were held with grasping forceps placed through an open endoloop. The fallopian tube was pulled through the endoloop, and the endoloop was placed on the uterine tube. The second endoloop was placed on the same Fallopian tube using an identical method. According to the researchers, the procedure involved a ligation of the Fallopian tubes, but the presented figures indicate that uterine horns were ligated.

### Oophorectomy

(Wagh et al. 2006) carried out a transgastric oophorectomy and tubectomy in a pig model. The gastroduodenoscope was inserted transorally into the stomach, and the ventral abdominal wall was punctured with a needle knife. Whenever necessary, the incision was enlarged with a through-the-scope balloon to allow passage of the gastroduodenoscope. An endoloop was placed around the ovary, the ipsilateral tube and mesosalpings. Tubectomy and oophorectomy were performed using snare cautery above the endoloop. The tissue was grasped with a snare and removed by retrieving the endoscope through the stomach and the oral cavity.

(Freeman 2009) performed NOTES oophorectomy in dogs. The endoscope was introduced into the stomach transorally, and the gastrostomy site was selected through transillumination and the application of pressure on the ventral side of the abdomen as close as possible to the greater curvature, similarly to gastrostomy tube placement techniques. A catheter was introduced percutaneously to insert the guidewire into the stomach. It was advanced through the endoscope by a hexagonal snare. The guidewire was used to place the needle knife in the gastrostomy site. The endoscope was advanced into the abdominal cavity, pneumoperitoneum was created and the ovary was lifted with grasping forceps introduced via the working channel. An endoscopic snare inserted via the second channel was placed on the suspensory ligament, the ovarian pedicle and the Fallopian tube. The above structures were cut using a monopolar electrocauter. The ovary was removed from the abdominal cavity using the method described by (Wagh et al. 2006).

### Partial hysterectomy

(Merrifield et al. 2006) carried out partial transgastric hysterectomy in pigs. A gastroduodenoscope was

introduced transorally into the stomach, and the abdominal wall was punctured using the method described by (Kalloo et al. 2004). An endoscope was inserted into the abdominal cavity, and the animal was placed in a head-down position to move the intestine away from the uterus. Grasping forceps were pulled through an open endoloop to grip the uterus, and they were retrieved into the endoloop with the uterus. An endoloop was placed around uterine tissue. Grasping forceps were advanced through an open snare, the uterus was gripped and removed into the snare. The uterine body and the uterine horn were incised above the endoloop with the use of snare cautery. The resected uterus section was grasped with a snare and retrieved from the peritoneal cavity.

### **Partial gastrectomy**

(Nakajima et al. 2008) were the first researchers to perform partial gastrectomy in pigs with the involvement of the NOTES technique. Transvaginal access to the abdominal cavity was created. Prior to endoscope placement in the stomach, three laparoscopic ports were inserted into the abdominal cavity to create pneumoperitoneum, enhance visualization and attach the uterus and its broad ligament to the abdominal wall with the use of sutures and staplers to expose the vaginal wall. The vaginal wall was punctured with a needle knife introduced via one of the two working channels of an endoscope, and an endoscope was inserted into the peritoneal cavity. To enable stomach manipulation, a second endoscope was introduced transorally and it was looped along the greater curvature. Clockwise torque was applied to lift the greater curvature ventrally. The gastrocolic ligament was grasped with endoscopic forceps inserted via the working channel of the first endoscope to facilitate its incision. The gastrocolic ligament was cut using a needle knife or an IT knife with an electrosurgical unit. After full mobilization of the stomach, the first endoscope was removed and it was replaced with a computer-powered linear stapling device with a flexible shaft. The device was used to perform a stapled gastrectomy of the ventral abdominal wall. The resected fragment of the stomach was placed in the endoscopic retrieval net, and it was removed from the abdominal cavity through the vagina.

### **Gastroenterostomy**

(Kantsev et al. 2005) performed transgastric gastrojejunostomy in pigs. The endoscope was introduced transorally into the stomach, and the ventral abdominal wall was punctured with a needle knife and a sphin-

cterotome. The endoscope was inserted into the peritoneal cavity through an incision in the gastric wall. Jejunal loops were grasped with endoscopic forceps, they were pulled into the stomach, fixed with a holding suture and attached to the abdominal wall using a prototype endosuture device (Eagle Claw). A 15 mm incision was made in the antimesentric border of the jejunal loop using a needle knife with combination of pure cautery. A second suture line joining the incised edges was made with the use of the same prototype endosuture device. (Bergström et al. 2006) used thin endoscopic forceps and snares introduced simultaneously via both endoscopic channels. The forceps were inserted through an open snare to grasp the antimesentric border of the small intestine. The intestine was pulled into the stomach and sutured to the stomach using a new technique. An Echotip 19-gauge needle was provided with a metal clip connected to 160 cm 3-0 polypropylene thread. The needle was inserted through the endoscope and passed through the intestinal wall. The clamp with the thread were released by advancing the mandrin, and they were left in the site. This procedure was repeated in the abdominal wall, and thread pairs were tied as described by (Waninger et al. 1996). Six to eight suture pairs were placed to secure the anastomosis.

### **Lymph node biopsy**

(Cahill et al. 2008) performed transgastric biopsy of mesenteric lymph nodes in pigs. A double-channel endoscope was introduced into the stomach, the ventral abdominal wall was punctured with a needle knife and an endoscope was advanced into the peritoneal cavity. The animals were placed in the steep Trendelenburg position to expose the colon. The colon was manipulated with the aid of an externally controlled magnet. Mesenteric lymph nodes were excised with the synchronized use of a blunt tip monopolar electrode and endoscopic graspers introduced via working channels. Lymph nodes were grasped with a snare or standard endoscopic instruments and were retrieved from the abdominal cavity via the stomach and the esophagus.

### **Pancreatectomy**

(Ryou et al. 2007) performed combined transcolonic and transvaginal distal pancreatectomy in pigs. A prototype R-scope was introduced into the colon, the bowel wall was incised using a needle knife, and the R-scope was advanced into the peritoneal cavity. The animals were moved from a horizontal to an inclined position to expose the pancreas. The posterior part of

the pancreas was separated from the extraperitoneal cavity by hook-knife electrocautery, air-dissection with a sclerosing needle and large alligator clamps. The pancreas was lifted on the perpendicular elevators of the R-scope, and the base of the pancreas was incised horizontally. A gastroduodenoscope was inserted into the vagina, colpotomy was performed using a needle knife and the gastroduodenoscope was advanced into the peritoneal cavity. The gastroduodenoscope was removed and replaced with a linear stapler. Stapler jaws were opened and clamped onto the pancreas. Bursting pressure was adjusted and the stapler was fired. The excised section was removed via the colon using a 2.8 cm Roth retrieval net.

### Cholecystectomy

(Park et al. 2005) performed transgastric cholecystectomy in pigs. The gall bladder was removed using two methods. The first method involved two double-channel endoscopes introduced transgastrically, while the second relied on one endoscope advanced through the stomach and a grasping instrument inserted via the abdominal wall.

The gall bladder was localized, and the endoscopes were placed as closely as possible to the organ. The gall bladder was grasped and moved in the direction of the cystic duct. The objective of the above procedure was to place the endoscope in the direct proximity of the gall bladder. It could be performed with the use of two endoscopes, a double-channel endoscope and an endoscope with a pair of forceps introduced via the abdominal wall. The cystic duct was exposed by flexible graspers and gripping the gall bladder alternately. The gall bladder was grasped and separated with a needle knife. Clips were placed on the separated cystic duct and the artery, the gall bladder was lifted and separated from the liver. The separated gall bladder was grasped with a snare, pulled through the puncture in the abdominal wall and retrieved through the esophagus.

The authors tested the usefulness of suture cutting devices and endoscopic scissors in separating the gall bladder, and in their opinion, the applied instruments did not meet cholecystectomy requirements.

(Parreta et al. 2008) used a double-channel video gastroscope to perform transgastric cholecystectomy. The gall bladder was separated from the liver using an endoscopic grasper and a monopolar electrode with a round tip.

(Scott et al. 2007) described transvaginal cholecystectomy. Multiple instruments forming a magnetic anchoring and guidance system (MAGS) were used. Vaginectomy was performed by electrocautery, and an endoscope was introduced. Pneumoperitoneum was cre-

ated, the endoscope was removed and replaced with a rigid port through which pneumoperitoneum was maintained and instruments were inserted. The gall bladder was separated using a cautery and flexible graspers. The cystic duct and the artery were closed with endoclips. The gall bladder was withdrawn from the abdominal cavity using a snare or Roth net.

(Rolanda et al. 2007) performed cholecystectomy with combined access through the stomach and the urinary bladder. An ureteroscopy with a working channel was inserted through the urinary bladder, and a double-channel endoscope was advanced through the stomach. Clamps were passed through the ureteroscopy to grasp the gall bladder and expose the cystic duct. The gall bladder was separated using clamps and a coagulation electrode, inserted through the gastroscope's working channel. The cystic duct and the artery were separated and closed with endoclips. The gall bladder was removed via the stomach with the use of clamps inserted through the gastroscope.

### Summary

In recent years, research was carried out mainly on animals, including porcine and, less frequently, canine models. The NOTES technique has already been used in human surgery, but it has not yet been introduced to general medical practice as most procedures have been performed on individuals or small groups of patients and the risk related to the technique remains insufficiently documented. Few long-term survival studies have been performed on animals, and the method is not yet suited for testing on humans. Despite numerous advantages offered by NOTES, the technique needs to be further investigated before it is introduced to human medicine and veterinary practice.

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