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MINIREVIEWS

# Gastrointestinal tract access for urological natural orifice transluminal endoscopic surgery

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# Abstract

We conducted a literature review of natural orifice

transluminal endoscopic surgery (NOTES), focusing on urologic procedures with gastrointestinal tract access, to update on the development of this novel surgical approach. As part of the methods, a comprehensive electronic literature search for NOTES was conducted using PubMed and Cochrane Library from March 2002 to February 2016 for papers reporting urologic procedures performed utilizing gastrointestinal tract access. A total of 11 peer-reviewed studies examining utility of gastrointestinal access for NOTES urologic procedures were noted, with the first report in 2007. The procedures reported in the studies were total/radical nephrectomy, partial nephrectomy, adrenalectomy, and prostatectomy. The transgastric approach was identified in five studies examining total/radical nephrectomy (n = 2), partial nephrectomy (n = 1), partial cystectomy (n = 1)= 1), and adrenalectomy (n = 1). Six studies evaluated transrectal approach for NOTES, describing total/radical nephrectomy (n = 3), partial nephrectomy (n = 1), robotic nephrectomy with adrenalectomy (n = 1) and prostatectomy (n = 1). Feasibility was reported in all studies. Most studies were preclinical and acute, and limited by concerns regarding restricted instrumentation and infection risk. We concluded that gastrointestinal access for urologic NOTES demonstrates promise as described by outlined feasibility studies in preclinical models. Nonetheless, clinical application awaits further advancements in surgical technology and concerns regarding infectious potential.

Key words: Gastrointestinal tract; Transrectal; Urology; Natural orifice transluminal endoscopic surgery

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**Core tip:** Gastrointestinal (transgastric and transrectal) access is technically feasible for natural orifice transluminal endoscopic surgery (NOTES) in a number of major urological procedures, and is an attractive alterna-



tive with similar outcomes and distinct advantages compared to transvaginal NOTES. The recent adaptation of robotic technology to transrectal NOTES points the way toward future horizons. Further testing and device development is required prior to clinical application.

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## INTRODUCTION

The introduction of minimally invasive urologic surgery has ushered in a new era of surgical advancements that aim to improve surgical outcomes such as decreasing morbidity, expediting patient recovery, and minimizing scars<sup>[1]</sup>. Procedures which were initially laparoscopic, progressed to single-site and robotically assisted minimally invasive techniques and are now made possible *via* natural orifice transluminal endoscopic surgery (NOTES)<sup>[2,3]</sup>.

Indeed, the promise of NOTES has been the next quantum leap of minimally invasive surgery to further decrease wound morbidity and to further diminish the surgical footprint has outcomes associated with traditional laparoscopic surgery. The past ten plus years have seen a dizzying array of feasibility experiments in general surgical, urological and gynecologic natural orifice procedures, with more limited clinical applications. Nonetheless, NOTES currently remains on the margins of surgical practice, restricted to an "avant-garde" of surgical innovators. In urologic practice, NOTES applications have been mostly transvaginal, though given the substantial male patient population, a need to consider alternative points has been imperative. As such, the gastrointestinal tract may present an alternative with greater applicability to the urologic patient population. We conducted a systematic review of the utilization of gastrointestinal tract access in the performance of urological procedures.

### MATERIALS AND METHODS

A systemic electronic literature search was conducted to identify any publications relating to gastrointestinal tract access for urological NOTES using PubMed (http:// www.pubmed.gov/) and Cochrane Library (http://www. cochranelibrary.com/) from March 2002 to February 2016. Several combinations of the following search terms were used to identify pertinent publications: "Natural Orifice Transluminal Endoscopic Surgery", "transrectal", "trans anal", "transgastric", "gastrointestinal tract access", "urology", "NOTES", "nephrectomy", "cystectomy", "adrenalectomy", and "prostatectomy". Only peer-reviewed published series of urological NOTES procedures were included in the analysis of current state of gastrointestinal tract access urological NOTES. We excluded reviews, editorials, and abstracts.

#### Historical context

The coining of NOTES as the exact term was agreed on by the American Society of Gastrointestinal Endoscopy (ASGE) and the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Working Group in 2005<sup>[1]</sup>. The first pre-clinical example of natural orifice surgery in urology was completed in 2002 by Gettman et al<sup>[4]</sup> when a transvaginal laparoscopic nephrectomy in a porcine model was completed. Since that time, various procedures in urology have been proven possible by NOTES, including partial and radical nephrectomy, cystectomy and prostatectomy<sup>[5]</sup>. Transoral, transgastric, transvaginal, transvesical and transrectal routes have been utilized<sup>[5-7]</sup>. Additionally, NOTES has included various surgical approaches, including laparoscopic and robotic assisted techniques<sup>[5-7]</sup>. Initial barriers to NOTES, outlined by the SAGES/ASGE Working Group<sup>[1]</sup>, included: Access to peritoneal cavity, gastric (intestinal) closure, prevention of infection, development of suturing and anastomotic devices, spatial orientation, development of a multitasking platform to accomplish procedures, management of intraperitoneal complications, physiologic untoward events, compression syndromes, and training. Gastrointestinal tract access NOTES for urologic procedures still remains firmly in pre-clinical research stages; however, there is great potential in extending the availability of NOTES to a greater clinical context. A total of 11 pre-clinical studies utilizing gastrointestinal tract access for NOTES urologic procedures were identified (Tables 1 and 2).

#### TRANSGASTRIC UROLOGICAL NOTES

Five studies were identified that investigated utility of transgastric approach for urologic NOTES. Two studies demonstrated feasibility of total nephrectomy, one for partial nephrectomy, partial cystectomy, and adrenalectomy, respectively (Table 1).

#### Transgastric nephrectomy and partial nephrectomy

In 2007 Lima *et a*<sup>(8)</sup></sup> first demonstrated feasibility of transgastric access in urologic NOTES for total nephrectomy. This porcine acute study utilized a combined transgastric and transvesical approach*via*an ureteroscope and a gastroscope to successfully perform nephrectomy in all planned procedures (<math>n = 6), with median operative time of 120 min. The initial two procedures were notable for mild hemorrhage after renal vessel ligation; however, this was avoided in remaining operations by the application of surgical clips prior to ultrasonic ligation of the vessels. The findings of the study were limited by a lack of closure of gastrostomy due to absence of endoscopic suturing devices and lack of specimen extraction<sup>[8]</sup>.</sup>

Isariyawongse *et al*<sup>(9]</sup> investigated utility of NOTES nephrectomy utilizing a hybrid transgastric and trans-



Table 1	Transgastric gastrointestina	tract access urological natur	al orifice transluminal endoscopic surgery
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Ref.	Access	Procedures	Model	Summary
Lima <i>et al</i> <sup>[8]</sup> , 2007	Transgastric; transvesical	Nephrectomy ( $n = 6$ )	Porcine	Initial mild hemorrhage appropriately corrected in remaining group
Isariyawongse <i>et al</i> <sup>[9]</sup> , 2008	Transgastric; transvaginal	Nephrectomy $(n = 1)$	Porcine	Successful bilateral nephrectomies achieved with both
				transvaginal and transgastric approaches
Sawyer <i>et al</i> <sup>[12]</sup> , 2009	Transgastric; transuretrhal	Partial cystectomy ( $n = 5$ )	Porcine	Successful completion of pure transurethral NOTES
				transure thral $(n = 4)$ and pure transgastric NOTES $(n = 1)$
Boylu <i>et al</i> <sup>[10]</sup> , 2010	Transgastric; hybrid	Partial nephrectomy $(n = 1)$	Porcine	Use of thulium laser in successful partial nephrectomy
Fritscher-Ravens <i>et al</i> <sup>[11]</sup> , 2008	Transgastric	Adrenalectomy ( $n = 10$ )	Porcine	A comparitave study of NOTES alone <i>vs</i> NOTES and endoscopic ultrasound guidance NOTES

NOTES: Natural orifice transluminal endoscopic surgery.

#### Table 2 Transrectal gastrointestinal tract access urological natural orifice transluminal endoscopic surgery

Ref.	Access	Procedures	Model	Summary
Bazzi et al <sup>[13]</sup> , 2011	Transrectal hybrid	Nephrectomy $(n = 3)$	Porcine	First report of transrectal hybridized NOTES
Bazzi et al <sup>[15]</sup> , 2012	Transrectal hybrid	Nephrectomy $(n = 4)$	Cadaver	Successful nephrectomy in a cadaveric model with intact
				specimen extraction
Eyraud <i>et al</i> <sup>[18]</sup> , 2013	Transrectal hybrid	Robot assisted nephrectomy	Cadaver	First investigation of robotic nephrectomy and adrenalectomy.
		and adrenalectomy $(n = 1)$		Successful adaptation of robot to NOTES platform
Bazzi et al <sup>[17]</sup> , 2013	Transrectal hybrid;	Partial nephrectomy ( $n = 10$ )	Porcine	No significant in access or operative times for transrectal or
	Transvaginal hybrid			transvaginal approaches to partial nephrectomy
Park <i>et al</i> <sup>[16]</sup> , 2014	Transvaginal; transrectal;	Nephrectomy $(n = 15)$	Porcine	Survival model; no difference in evidence of infection or injury
	Conventional laparoscopy			at necropsy; no difference in inflammatory markers
Akça <i>et al</i> <sup>[19]</sup> , 2015	Transrectal	Prostatectomy $(n = 1)$	Cadaver	Proof of principle for transrectal approach for NOTES
				prostatectomy

NOTES: Natural orifice transluminal endoscopic surgery.

vaginal approach. Successful bilateral nephrectomy was performed by first visualizing the abdominal cavity *via* a transgastric endoscope and using the transgastric endoscope to establish a transvaginal NOTES port. Total operative time was 40 min for the right nephrectomy and 20 min for the left. The combined transgastrictransvaginal approach allowed for excellent visualization, multitude of readily available instruments to perform basic surgical tasks, and successful specimen extraction through a transvaginal route<sup>[9]</sup>.

Boylu *et al*<sup>[10]</sup> successfully demonstrated the feasibility of transgastric NOTES partial nephrectomy hemostasis in the porcine model. The procedure utilized a therapeutic gastroscope (Olympus GIF-2T160, Melville, NY, United States) combined with a thulium laser (RevoLix; AllMed Systems, Pleasanton, CA, United States) to gain access to the peritoneum, visualize and complete excision the left kidney's upper pole without additional hemostatic measures. The specimen was extracted using an endoscopic wire loop *via* the stomach and the gastrostomy was closed with metal clips. Total operative time was 240 min. Limitations described by the authors included excess smoke produced by the thulium laser as well as lack of appropriate entrapment sacks for safe specimen removal *via* a gastroscope<sup>[10]</sup>.

#### Transgastric adrenalectomy

Fritscher-Ravens *et al*<sup>[11]</sup> demonstrated adrenal gland removal in pigs using NOTES alone or with endoscopic ultrasound guidance (EUS). The study showed that

adrenal gland removal failed in all NOTES-only procedures (n = 4) in which it was attempted while it was successful in six NOTES-EUS (n = 6) cases. The NOTES-only cases of adrenalectomy were halted due to lack of safe access to the organ and bleeding during attempted access. Successful adrenalectomy was achieved in the NOTES-EUS group without complication with a mean duration of 78 min. In addition to successful adrenalectomy in the combined NOTES-EUS approach, the study demonstrated successful closing of the gastrostomy using an endoscopic suturing system<sup>[11]</sup>.

#### Transgastric partial cystectomy

NOTES partial cystectomy in a porcine model was described by Sawyer *et al*<sup>[12]</sup>. The study outlined both two approaches: Transgastric with a urethral assist port and pure transurethral. Both approaches allowed for the completion of successful partial cystectomy with specimen excision and defect reapproximation with endoscopic clips. Transgastric partial cystectomy was performed in one porcine model with an operative time of 93 min. The authors noted that despite being more invasive, the transgastric approach offered better visualization of target anatomy and ability to sample lymph nodes for malignant pathology<sup>[12]</sup>.

# TRANSRECTAL UROLOGIC NOTES

Six studies investigated utility of transrectal NOTES for urologic procedures. Three studies demonstrated



feasibility of total nephrectomy, one for partial nephrectomy, total nephrectomy and adrenalectomy, and prostatectomy, respectively (Table 2).

#### Transrectal NOTES nephrectomy

Bazzi et al<sup>[13]</sup> described the first transrectal NOTES nephrectomy in an acute porcine model utilizing a transrectal access technique described by Ramamoorthy et al<sup>[14]</sup>. This form of access involved creation of a submucosal tunnel in the anus, and dissection along the posterior rectal wall and access into the retroperitoneum, which was monitored by a transumbilical port which was also used for additional retraction, thus fitting into the "hybrid" NOTES model. Three cases of transrectal hybrid NOTES nephrectomy were successfully completed without conversion to conventional laparoscopic or open surgery and without significant intra-abdominal bleeding. Median operative time was 180 min and estimated blood loss was < 50 mL for all cases. The setting of a transrectal access with nephrectomy provided the advantages of a larger access point for instruments and specimen retrieval, easier closure of the access site compared to the transgastric approach, and the ability for application of the approach in both sexes, compared to transvaginal access. The success of this initial report provided proof-of-principle for the transrectal approach as an alternative to the primary transvaginal approach<sup>[13]</sup>.

Bazzi *et al*<sup>[15]</sup> described feasibility of transrectal hybrid NOTES nephrectomy in four human cadavers. Similar to prior work, the hybrid approach utilized a periumbilical transabdominal laparoscopic port. All four cases were performed successfully with a mean operative time of 175 min and no conversions of operative approach. The periumbilical port was utilized for guidance of transrectal access, assistance in renal mobilization, and in deployment of the stapler. However, more than 75% of the procedure was performed *via* instrumentation inserted *via* the transrectal access<sup>[15]</sup>.

Park *et al*<sup>[16]</sup> compared feasibility and safety of transrectal (n = 5), transvaginal (n = 5) and conventional laparoscopic (n = 5) total nephrectomy in a survival porcine model, and examined inflammatory cytokines between the groups. They noted that all procedures were successfully completed without conversion, and while operative time was longer for transrectal and transvaginal approaches (84 min *vs* 61 min *vs* 24 min, respectively, P < 0.001), there were no signs of visceral injury or peritonitis on postmortem examination at the 1 wk mark. Furthermore, none of the laboratory parameters, including white blood cell count, tumor necrosis factor- $\alpha$ , interleukin (IL)-1, and IL-6 differed among the groups during the entire experimental period<sup>[16]</sup>.

### Transrectal NOTES partial nephrectomy

Bazzi *et al*<sup>(17)</sup> compared transrectal (<math>n = 5) and transvaginal (n = 5) approaches for hybrid NOTES partial nephrectomy in an acute porcine model. In this study, 10 porcine models (5 transrectal, 5 transvaginal) un-</sup>

derwent partial nephrectomy. Following transrectal and transvaginal access, the SPIDER (Transenterix, Morrisville, NC, United States) articulating dissecting and suturing platform, was deployed. The procedure was completed successfully in all 10 cases without need for conversion. There were no significant differences when comparing transrectal and transvaginal approaches for access time (29.2 min *vs* 29.6 min, P = 0.944), operative time (196 min *vs* 183 min, P = 0.631) or estimated blood loss (59 mL *vs* 54 mL, P = 0.631)<sup>[17]</sup>.

# Transrectal NOTES robotic nephrectomy and adrenalectomy

Eyraud *et al*<sup>[18]</sup> demonstrated feasibility of robotic (Da Vinci SI, Intuitive Surgical, Sunnyvale, CA, United States) assisted hybrid transrectal NOTES nephrectomy and adrenalectomy in a male cadaver. Transrectal access was achieved by a submucosal tunnel followed by placement of a robotic 8 mm-trocar. This was followed by placement of periumbilical 12 mm and 8 mm robotic ports, and a transrectal 8 mm robotic ports. The procedure was successfully completed with an operative time of 145 min, of which 20 min was for access/robotic docking and 20 min was for rectal closure<sup>[18]</sup>.

#### Transrectal NOTES prostatectomy

Akça *et al*<sup>[19]</sup> described transrectal NOTES prostatectomy in a cadaveric model. The cadaver was placed in an exaggerated lithotomy position, the anterior rectal wall was incised, and a single port device (GelPOINT<sup>®</sup>, Applied Medical, Santa Margarita, CA, United States) was deployed, through which all working and camera ports were inserted through. The authors reported ease of exposure of the posterior surface of the prostate and seminal vesicles with intact specimen extraction, and pointed the way for further testing with respect to feasibility of lymph node dissection using the transrectal route<sup>[19]</sup>.

# **FUTURE DIRECTIONS**

In order for transrectal NOTES to evolve into a clinically viable option, advances in device development and addressing concerns regarding infection risk with outcomes comparable to conventional laparoscopy must be demonstrated<sup>[20]</sup>. Single port surgery can lead to reduced maneuverability and difficult laparoscopic suturing skills, thus further developments will likely incorporate robotic platforms to overcome these limitations<sup>[21]</sup>. Transrectal NOTES has continued to gain influence in the setting of colorectal surgery, and further advancement in urology will require emulation of this field<sup>[22]</sup>. From this foundation of colorectal procedures, urologic applications can continue to advance.

Robotic assistance in NOTES has been suggested as a way to increase surgical feasibility and procedure applicability<sup>[23]</sup>. As the robotic platform continues to expand in its scope of utilization in urologic surgery,

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applications of robotics in NOTES may follow. As robotic technology continues to evolve in the direction of decreased instrument profile and flexible articulation, haptic feedback and improved optics, robotic NOTES may reach that critical tipping point of fusion of technical feasibility, adoption, desirability by patients and ultimately, acceptance by medical and surgical establishments to enter the mainstream of the surgical armamentarium.

Concerns regarding infectious potential of transiting viscera have been a significant hindrance to acceptance and application of NOTES, and this is especially true with the transrectal approach. Given high bacterial prevalence in the gastrointestinal tract, post-operative infections continue to be a major concern regarding transrectal NOTES<sup>[24]</sup>. Device innovation is working to decrease this risk as well. Recently, Senft et al<sup>[25]</sup> demonstrated the efficacy of ColoShield (A.M.I., Feldkirch, Austria), a colon occlusion device, in reducing peritoneal contamination in transrectal NOTES. The occlusion device is inserted 15-20 cm above the anus, inflated to ensure a tight seal with the colonic wall, and maintained in the position through the duration of the surgery. The device acts as a physical impediment in the colon to prevent any unwanted fecal contamination. Device innovations such as this will certainly play a role in the future of transrectal NOTES.

# CONCLUSION

Transvaginal NOTES, although feasible for urologic procedures, has limited applicability to the female population<sup>[26]</sup>. The introduction and exploration of gastrointestinal tract as a urological NOTES entry site opens up the realm of the minimally invasive technique to a much larger population. Urologic transrectal and transgastric NOTES has thus far included nephrectomy, partial nephrectomy, adrenalectomy, and prostatectomy, as well as robotic-assisted techniques. Future pre-clinical survival studies are requisite to determine the potential of urologic transrectal NOTES, with emphasis on improved instrumentation, robotic assistance, and avoidance of infection.

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