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Current Status of Natural Orifice Trans-endoscopic Surgery (NOTES) and Laparoendoscopic Single Site Surgery (LESS) in Urologic Surgery

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ABSTRACT

Laparoendoscopic single site surgery (LESS) and natural orifice transluminal endoscopic surgery (NOTES) represent novel approaches in urological surgery. To perform a review of the literature in order describe the current status of LESS and NOTES in Urology. References for this manuscript were obtained by performing a review of the available literature in PubMed from 01-01-02 to 15-05-09. Search terms included single port, single site, NOTES, LESS and single incision. A total of 412 manuscripts were initially identified. Out of these, 64 manuscripts were selected based in their urological content.
The manuscript features subheadings for experimental and clinical studies, as NOTES-LESS is a new surgical technique and its future evolution will probably rely in initial verified feasibility. A subheading for reviews presents information regarding common language and consensus for the techniques. The issue of complications published in clinical series and the future needs of NOTES-LESS, are also presented.

Key words: *laparoscopy; urology; robotic surgery; minimally invasive procedures; NOTES; LESS*
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INTRODUCTION

Natural orifice transluminal endoscopic surgery (NOTES) involves the intentional penetration of hollow viscera with an endoscope in order to access the abdominal cavity and perform an intraabdominal operation (1). In 2002, Gettman et al. reported the first experience with NOTES, performing transvaginal nephrectomies in pigs (2). The initial clinical experience in NOTES was performed by Antony Kalloo in transgastric surgery in 2004 (3).

Closely related to NOTES, laparo-endoscopic single-site surgery (LESS) describes minimally access surgical procedures that are performed through a single incision/location (4). Rane et al. published the first true LESS experience in abstract form in 2007, performing a transumbilical laparoscopic nephrectomy (5).

Currently, the application of NOTES-LESS has been expanding in the clinical setting and several experiences have been reported. The preliminary experience with NOTES has confronted several ques-

tions, such as the safety entrance into a healthy hollow organ lumen and adequate closure methods (6). Single site surgery has likewise faced questions regarding the added difficulty from lack of triangulation of instruments. Nonetheless, Urology has significantly participated in the development of minimal access surgical techniques, and NOTES-LESS is steadily gaining momentum in our field.

RATIONALE FOR NOTES AND LESS

NOTES-LESS are attractive surgical approaches due to several potential benefits and advantages. With NOTES there are no abdominal incisions and, therefore, abdominal wound infections and incisional hernias could be potentially avoided. This could also translate into less pain and improved cosmesis. In NOTES, the translumenal access to the peritoneal cavity may have definite advantages in situations whereby the transcutaneous path into the peritoneal cavity is not optimal, as in obese patients (7). Of further interest, consistently reduced levels of TNF-alpha have been observed in experimental experiences with NOTES in animal models in the late postoperative period. This suggests an immunomodulatory effect of the NOTES not present in laparoscopy or laparotomy (8).

LESS likewise offers the potential advantages of a more rapid recovery, fewer adhesions, fewer opportunities for hernias, and less postoperative ileum. Esthetically, use of a single incision minimizes the visible evidence of surgical intervention. This is most notable when the natural scar of the umbilicus is used for the port site. Furthermore, the risk related to the use of ports has been reported in 0.003-0.3% for both vascular and visceral injuries (9).

THE CHALLENGE OF NOTES AND LESS

Both NOTES-LESS drastically limit the surgeon's ability to choose the site of entry for operative instruments. Therefore, the advantages NOTES-LESS are gained with the caveat of difficult surgical performance due to the lack of space.

NOTES present the additional challenges of access to the peritoneal cavity through a hollow viscus. The safety of this strategy is of utmost importance, and studies are needed to evaluate the long-term consequences of the breach of a hollow viscus of the gastrointestinal or urinary tract. Flexible or small-bore instruments are required to utilize natural orifices, and this can present a challenge in maintaining orientation within the surgical space. Adequate transmission of force through flexible instruments for dissection and retraction may also present added complexity. Overcoming these limitations in NOTES and LESS require a great deal of laparoscopic experience and skill, and the application of novel instruments and techniques.

THE STEPWISE PROGRESS OF MINIMAL ACCESS SURGERY

The purpose of the laparoscopic approach has been clear: to provide improved tolerability and decreased morbidity while delivering the same or better clinical outcomes as open surgery (10). Laparoscopic surgery was not generated de novo; rather, it was developed by applying the techniques and standards developed in open surgery to the laparoscopic environment.

A similar evolutionary process has contributed to the progress of NOTES-LESS. Early laboratory research has been focused on feasibility. Animal and cadaveric models have been used to demonstrate the possible applications of NOTES and LESS, including transgastric peritoneoscopy, tubal ligation, gastrojejunostomy, partial hysterectomy, oophorectomy, and transcolonic exploration, liver biopsy and cholecystectomy (11). Investigation has also been brought to the operative suite - ablative and reconstructive procedures using NOTES-LESS have been reported by many surgical teams, utilizing a variety of techniques, devices and approaches.

NOTES-LESS IN UROLOGY

Laboratory (Table-1)

The initial experience in urologic minimal access surgery came in 2002, when Gettman et al.

performed transvaginal laparoscopic dissection and nephrectomy in 6 porcine models (2). They acknowledged the limitations imposed by both the porcine anatomy and available laparoscopic instruments at the time.

Lima et al. have presented several experiences in pig models were they have described transvesical access (12), and transvesical transdiaphragmatic endoscopic thoracoscopy (13). Lima et al. have also presented a combined approach in the experimental setting, in which they installed a transvesical tube into the peritoneal cavity under cystoscopic guidance; and a flexible gastroscope was passed orally, then into the peritoneal cavity via a gastrotomy. They performed 6 nephrectomies with instruments introduced by both approaches (14). Crouzet et al. described transgastric and transvaginal renal cryoablations in a porcine model, accomplished without complications (15). Several approaches have been described for NOTES-LESS nephrectomy, including transvaginal hybrid NOTES nephrectomy in a porcine model (16,17), pure NOTES transvaginal technique (18) and NOTES nephrectomy using magnetic anchoring and guidance system instrumentation (19).

Robotic assistance has been introduced to facilitate NOTES procedures using the da Vinci robotic interface. Box et al. performed robotic-assisted hybrid NOTES renal surgery, completing a right nephrectomy. They utilized transvaginal and transcolonic ports for the robotic arms, and a transumbilical port for the camera. While this approach avoided camera/instrument conflict, the authors noted significant instrument/instrument conflict due to inability to separate the ports by greater than 7.5 cm (20). Haber et al. reported on their experience with robot-assisted transvaginal hybrid NOTES, which enabled them to completed pyeloplasties, nephrectomies and partial nephrectomies in porcine models. They acknowledged success with both ablative and reconstructive procedures, noting that the wristed robotic instruments and 3D vision made intracorporeal suturing possible, and that the robotic platform allowed the surgeon to operate through ports that are too widely separated to allow a single surgeon to manipulate them simultaneously (21).

While the majority of laboratory research in NOTES-LESS has focused on NOTES applications, significant experimental experience has also been gained in LESS. A research group was formed to build a prototype system of magnetically anchored instruments for trocar-free laparoscopy. The system was then evaluated in vivo in a porcine laparoscopic nephrectomy model with promising results (22). A novel approach to the robot-assisted LESS radical prostatectomy was completed by Desai et al. in 2 human cadavers, utilizing a transvesical approach. Again, articulated robotic instruments facilitated the complex motions need for vesico-urethral anastomosis and bladder closure (23). An interesting work of radical prostatectomy performed transvesically has been presented in a cadaver model. The entire resection was performed with the laser and a rigid offset 27F nephroscope was used to perform the vesicourethral anastomosis using a laparoscopic suture device and knot pusher in an interrupted fashion (24).

Bridging Studies

Surgeons have taken their experimentally gained experience in LESS, and then applied it clinically, reporting both experiences simultaneously. Raman and colleagues presented single keyhole nephrectomy in a porcine model, followed by the same procedure in three human patients (25). Barret et al. described a robot-assisted LESS radical prostatectomy completed in a cadaveric model, and the technique was then transitioned to a human patient. The team used standard laparoscopic ports gathered at a single umbilical incision. Despite some instrument clashing that made exchanging robotic instruments difficult, they reported good results with an operative time of 150 minutes (26).

Clinical (Table-2)

Clinically, NOTES experience has been much more limited than LESS. Gettman et al. performed transvesical peritoneoscopy using a flexible ureteroscope in a patient who subsequently underwent standard robotic-assisted laparoscopic prostatectomy. The cystotomy was performed via a cystoscope, but with guidance from the previously

Table 1 *– Experimental data.*

Authors	Number/ procedures	Approach	Comments
Gettman et al. (2002) 2	6 Nephrectomies.	1 pure transvaginal and 5 combined transvaginal and transabdominal approaches.	First publication on NOTES and first pure transvaginal nephrectomy in porcine model.
Lima et al. (2006) 12	8 Transvesical peritoneoscopies.	Transvesical placement of peritoneal Endo-Eye™, and ureteroscope.	Porcine model, performed liver biopsy and falciform liver section.
Lima et al. (2007) 13	6 Transvesical thorascopies.	Transvesical entry of peritoneum, then into plural cavity with an ureteroscope.	Porcine model, lung biopsies performed without complications.
Lima et al. (2007) 14	6 Nephrectomies	Combined transvesical and transvaginal approach.	Porcine model, completed without complications.
Zeltser et al. (2007) 22	2 Nephrectomies.	15 mm Transumbilical trocar.	Prototype magnetic anchoring and guidance system camera in porcine model.
Clayman et al. (2007) 16	1 Nephrectomy.	Transvaginal single port NOTES nephrectomy.	Use of the multiport TransPort platform in porcine model.
Raman et al. (2007) 25	8 Nephrectomies.	Transumbilical 25mm single-port in 3 cases and 10mm + 2 5mm ports in 5 cases.	Experience from porcine models was used in human nephrectomies (see Clinical Data).
Box et al. (2008) 20	1 Nephrectomy.	Combined transvaginal and transcolonic, single port, robot-assisted nephrectomy.	First robotic NOTES experience in porcine model.
Haber et al. (2008) 21	10 Pyeloplasties; 10 Partial nephrectomies; 10 Nephrectomies.	R-NOTES combined transumbilical and transvaginal.	Robot allows suturing using both umbilical and vaginal access simultaneously in porcine model.
Isariyawongse et al. (2008) 17	1 Bilateral nephrectomy.	NOTES access, transgastric and transvaginal.	To prove the technical feasibility of NOTES nephrectomy with standard laparoscopic and endoscopic instruments in porcine model.

Table 1 *– continued.*

Crouzet et al. (2008)15	4 Renal cryoablations.	Transvaginal and transgastric approach.	Porcine model, no complications.
Desai et al. (2008)23	2 Radical prostatectomies.	Robotic transvesical approach.	Clashing da Vinci arms is worse with single-port than in a multi-port cadaveric procedure, but closure easier.
Barret et al. (2009) 26	1 Radical prostatectomy.	Robotic transumbilical extraperitoneal approach.	LESS radical prostatectomy experience in cadaver was transitioned in human radical prostatectomy procedure (see Clinical Data).
Haber et al. (2009) 18	5 Total nephrectomies.	Transvaginal approach with single and dual channel gastroscope.	Pure NOTES transvaginal nephrectomy was verified as feasible in the porcine model. Authors state the need for further development of instrumentation.
Humphreys et al. (2009) 24	4 NOTES radical prostatectomies.	Transvesical approach.	The entire resection was performed with the laser in a cadaver model. A rigid offset 27F nephroscope was used to perform the vesicourethral anastomosis using a laparoscopic suture device and knot pusher in an interrupted fashion.
Raman et al. (2009) 19	2 Nephrectomies.	Magnetic anchoring and guidance system (MAGS). 40-cm dual-lumen rigid access port inserted into the peritoneal cavity. A MAGS camera and cauterizer were deployed through the port and manipulated across the peritoneal surface by way of magnetic coupling via an external magnet. A prototype 70-cm articulating laparoscopic grasper introduced through the vaginal access port facilitated dissection after deployment of the MAGS instruments.	NOTES nephrectomy using MAGS instrumentation was verified feasible in the porcine model. Authors stated that the approach might improve shortcomings of previously reported NOTES nephrectomies regarding triangulation.

Table 2 – Clinical data.

Authors	Number/procedures	Approach	Comments
Milliken et al. (2006) 30	22 Insertions of peritoneal dialysis catheters.	Supraumbilical port.	Partial omentectomy and the catheter placement in the pelvis under vision.
Gettman et al. (2007) 27	1 Transvesical peritoneoscopy.	Endoscopic transurethro-transvesical.	First publication on the feasibility of transvesical peritoneoscopy.
Desai et al. (2008) 39	1 Nephrectomy; 1 Pyeloplasty.	Transumbilical single port.	The procedures were performed with the help of R-Port and curved at the shaft instruments.
Kaouk et al. (2008) 33	4 Renal cryotherapy procedures; 1 Kidney biopsy; 1 Radical nephrectomy; 4 Abdominal sacrocolpopexies.	Transumbilical or retroperitoneal.	Using the Uni-X Single Port Access Laparoscopic System, a single port, multichannel cannula with specially designed curved laparoscopic instrumentation.
Raman et al. (2007) 25	3 Radical nephrectomies.	Transumbilical.	The experimental experience on porcine models was transited into human procedures.
Kaouk et al. (2007) 34	3 Varicocelectomies.	Transumbilical.	First report on use of multicannula single laparoscopic port in children.
Kaouk et al. (2008) 52	4 Radical prostatectomies.	Transumbilical.	Use of multichannel port, urethrovesical anastomosis with a free-hand interrupted suturing and extracorporeal knot tying.
Ponsky et al. (2008) 35	1 Nephrectomy.	SAS transperitonealy.	Use of GelPort requires 7cm incision.
Desai et al. (2009) 41	4 Pyeloplasties; 1 Ileal ureter; 1 Ureteroneocystostomy.	Transumbilical.	The use of R-port allows to exteriorize the bowel for isolating the ileum segment and restoring the continuity.
Desai et al. (2008) 43	3 Simple prostatectomies.	Transvesical.	Report on initial experience with single port transvesical enucleation of the prostate.
Kaouk et al. (2008) 53	1 Radical prostatectomy; 1 Pyeloplasty; 1 Radical nephrectomy.	Transumbilical.	Robotic single port surgeries via multichannel port.
Branco et al. (2008) 29	1 Nephrectomy.	Transvaginal Hybrid NOTES.	Transumbilical camera, transvaginal instruments, with an additional subxyphoid trocar for a right nephrectomy.
Goel et al. (2008) 32	6 Renal cryoablations.	Single port access.	4 retroperitoneal through lumbar incision, 2 transperitoneal through umbilical site.

Table 2 – continued.

Rane et al. (2008) 31	2 Simple nephrectomies; 1 Orchiopexy; 1 Orchiectomy; 1 Ureterolithotomy.	Single port access.	Nephrectomies performed through port at mid-axillary line, other procedures through umbilicus. Use of R-Port described.
Castellucci et al. (2008) 37	1 Adrenalectomy.	Transperitoneal supraumbilical.	Single port adrenalectomy via triangular port arrangement.
Kaouk et al. (2008) 46	7 Partial nephrectomies.	Transumbilical.	5 cases of single-port laparoscopic and 2 cases of single-port robotic partial nephrectomies. Single port laparoscopic and single port robotic partial nephrectomy is feasible for select exophytic tumors. Robotics may improve surgical capabilities during single-port surgery.
Gill et al. (2008) 38	4 Live donor nephrectomy.	Transumbilical.	Initial experience with E-NOTES donor nephrectomy.
Aron et al. (2008) 39	5 Partial nephrectomies.	Single transumbilical port.	4 completed U-LESS; 1 required an additional port.
Barret et al. (2009) 26	1 Radical prostatectomy	Transumbilical extraperitoneal.	The experimental experience on cadaver model was transited robotic radical prostatectomy into human patient.
White et al. (2009) 36	5 Cryotherapy; 1 partial nephrectomy; 1 metastectomy; 1 renal cyst decortications.	Retroperitoneal single port.	Single port retroperitoneal surgery is feasible and offers comparable surgical outcomes and superior cosmesis and pain control compared with traditional retroperitoneoscopy.
Sotelo et al. (2009) 29	4 Transvaginal nephrectomies. 1 totally accomplished with the technique.	Multichannel access port in both the vagina and the umbilicus.	Transvaginal nephrectomy is feasible in the highly selected patient with favorable intraoperative circumstances, considerable refinements in technique and technology are necessary.
Sotelo et al. (2009) 42	1 Transumbilical simple prostatectomy; 20 Transvesical simple prostatectomies; 1 Simple nephrectomy (NS); 1 Enterocystoplasty augmentation; 5 Simple hysterectomies.	Multi-channel access.	LESS is a feasible and reproducible surgical option in urogynecologic surgical treatment.

established laparoscopic instruments. This experience represents the first published clinical experience in urologic NOTES (27).

Branco et al. published a report of a hybrid NOTES simple nephrectomy, in which an endoscope was placed through the posterior vaginal cul-de-sac, along with 5 mm ports at the umbilicus and below the xiphod. The specimen was extracted through the vaginal incision. The authors noted difficulty grasping intra-abdominal organs with endoscopic instruments; as well as problems with lateral viewing using the endoscope, necessitating the use of a 5 mm 30^{o} scope during portions of the case (28). Recently, transvaginal nephrectomy was reassessed by Sotelo et al. with a hybrid approach (29).

In contrast to NOTES, clinical experience with LESS is more extensively published. There are reports on peritoneal dialysis catheter placement using a single umbilical port in pediatric patients (30), simple nephrectomy, orchiopexy, orchiectomy and ureterolithotomy (31). The Cleveland Clinic (formally known as the Cleveland Clinic Foundation) has extensively presented their experience with LESS-NOTES. Kaouk et al. presented a clinical series of ten patients operated by single-port technique for different urological procedures (32). Their early results show feasibility along with good outcomes. This institution has also reported on LESS renal cryotherapies (33), and varicocelectomy (34).

The radical nephrectomy technique with single port surgery has also been assessed by Ponsky and coworkers (35). This experience was undertaken in a patient with an enhancing renal tumor. The technique featured three trocars through a GelPort device and the use of only standard laparoscopic instruments. Renal surgery for different procedures has also been evaluated in retroperitoneal single port access (36).

Additional extirpative surgeries have been accomplished using LESS. Castellucci et al. have reported details of a LESS adrenalectomy (37). Gill et al. performed LESS left donor nephrectomies (38).

Reconstructive procedures add new dimensions of complexity to LESS procedures. Aron et al. reported five single-port partial nephrectomies; of which only one required an additional 5 mm port (39). Desai et al. presented transumbilical nephrectomy and pyeloplasty using the R-Port; 2 mm needle-ports were used in these cases as well. Procedures were successfully accomplished with no extra-umbilical skin incisions and adequate results (40). Desai et al. used LESS to complete bilateral pyeloplasties, ileal ureteral interposition, and psoas hitch ureteroneocystostomy (41). Sotelo et al. have presented a series of NOTES-LESS procedures including enterocystoplasty augmentation (42).

Pelvic surgery involving reconstruction has also been accomplished. Desai et al. completed transvesical LESS simple prostatectomies utilizing an R-port placed through the bladder dome (43). Kaouk et al. completed LESS radical prostatectomies using a Uni-X port at the umbilicus, and flexible shaft laparoscopic instruments. After dividing the bladder neck, the surgical team found it difficult to maintain adequate traction to dissect the seminal vesicles; therefore they proceeded to the apical dissection and completed the surgery in a retrograde manner. Anastomotic sutures were tied extracorporeally. There were no intra operative complications; however, one patient developed a recto-urethral fistula 2 months postoperatively (44).

Similar to the experimental experience, robotic technology has been used to augment clinical LESS procedures. Kaouk et al. completed a radical prostatectomy, a dismembered pyeloplasty, and a radical nephrectomy via LESS placement of da Vinci robotic instruments (45). The procedures were completed without additional ports or instruments, and no complications were reported. There is also a report of a series of robotic LESS partial nephrectomies (46).

Comparative Studies

Raman et al. performed a retrospective case-controlled study comparing the outcomes of 11 LESS nephrectomies to 22 matched, conventional laparoscopic nephrectomies. LESS nephrectomies were shown to be feasible, with comparable interoperative times, blood loss and complication rates; the study failed to demonstrate any significant improvement in analgesic use or convalescence (47). While this study is retrospective, it represents an important step in validating LESS procedures in comparison to standard approaches.

NOTES-LESS Reviews, Nomenclature, Consensus Papers (Table-3)

Outside of the realm of original research, the increasing enthusiasm for NOTES-LESS has been reflected in a growing body of articles, which summarize and review the details of this topic. This has included a number of review articles, often written by individuals actively participating in NOTES-LESS research. Our search revealed 20 review articles addressing current status and future development of NOTES-LESS techniques (48-65). Additionally, a Urology Working Group on NOTES was formed in November 2007, and subsequently generated a consensus statement on NOTES-LESS. In this statement, they expressed enthusiasm for the future of NOTES and LESS, but recognized that NOTES remains a research topic in need of further development before widespread clinical application (66). The Urologic Working Group on NOTES also observed the plethora of names and acronyms relating to NOTES-LESS; in order to clarify and standardize the language describing these techniques, they published and article defining NOTES-LESS, and provided a framework for standard language to describe these procedures (67).

FUTURE ENDEAVORS

When Gettman et al. performed the first NOTES procedure, he noted the difficulty of the procedure given the limits of the available instruments (2). This has been a recurring theme in the NOTES-LESS literature that has followed: lack of mobility demands highly developed laparoscopic skills to overcome. In order to broadly apply these techniques, new instruments specially suited to these procedures will likely need to be developed. Curved or articulating instruments, streamlined or flexible optics, and robotic assistance have all been applied toward this end. On the horizon, novel devices such as flexible robotics may bring us closer to the wide application of NOTES-LESS.

Creating these new devices, and the new approaches to utilize them, will require open, inquisitive minds to constantly rethink the problems and imagine solutions. Urologists are uniquely suited to this task. Urologists are already well versed in laparoscopic, endoscopic and radiologic modalities that will likely be needed to perform minimal access procedures. The specialty also has a "pioneering spirit" that readily embraces new and innovative techniques (66). Along with open minds, there is also the need for healthy scientific skepticism. NOTES- LESS cannot be embraced simply because they are new. They must be carefully validated, both experimentally and clinically, focusing on patient safety and an evidence-based assessment of the benefits of these approaches. The future needs of NOTES-LESS are specific studies to evaluate the technique. At this point, we probably do not need more feasibility studies and the work should be focused primarily in improving and refining techniques, in order to proceed with comparison. The prospect of a randomized prospective study seems far away, but the idea should be kept in mind, even if it seems unlikely to ever happened, as we all have seen in the fields of laparoscopic adrenalectomy and laparoscopic radical prostatectomy. Meantime, solid reports of complications should be incorporated in the clinical work as limited information is available at this point (Table-4); in order to clearly define limitations and potential improvement of outcomes and also very important to consider the need for surgical certification to perform this approaches.

CONCLUSIONS

NOTES-LESS are novel techniques that hold tremendous promise for delivering safe, effective treatment of urologic disease but they also pose great obstacles. Investigators have applied a great deal of innovation and skill to begin to overcome these challenges. The big part of the NOTES-LESS experience has been performed in renal surgery and this field is probably the most fitted for future development. Further progress will likely rely on novel technologies, as well as innovative minds to imagine and apply them. Finally, NOTES-LESS will need careful validation in comparison to the current standard of care to ensure that they deliver the improved outcomes of which they seem capable.

Table 3 – Reviews/Related Publications.

Authors	Reviewed Period	Number of Publications Reviewed or Searching Strategy	Comments
Raman et al. (2007)	2002-2007	23	Mini review on the status of SILS (single incision laparoscopic surgery) and NOTES, describing future directions and concluding on the future exploration of the technique.
Gettman et al. (2008)	2002-2008	32	A review on current NOTES technique status since first publication on transvaginal nephrectomy by the authors in 2002, concluding the need of new technologies to appear to make NOTES the next clinical frontier.
Canes et al. (2008)	1969-2008	31	A review on history of E-NOTES across surgical disciplines for the past 40 years. The review covers questions of nomenclature, surgical technique, instrumentation and perioperative outcomes.
Tracy et al. (2008)	1960-2008	39	A review on LESS, covering instrumentation descriptions, surgical techniques, analysis of the comparative studies on benefits of LESS, concluding on the need of the future research to unveil the benefits over standard laparoscopy.
Swain (2008)	1993 - 2008	39	Review of current status of NOTES nephrectomy, with review of history of NOTES surgery and current experimental approaches.
Lima et al. (2008)	2002-2008	33	Review on NOTES history, development, applications, experimental and human studies, current limitations and urological role in the technique, that states the urologists are welcomed to contribute into the development of the novel approach.
Cindolo et al. (2008)	2002-2008	16	Short review on NOTES in urology, covering history, current status, techniques, future potentials, concluding that NOTES are still at the development phase.
Gettman et al. (2008)	----------	----------	Consensus statement concerning NOTES and LESS, and detailing the formation of the Urology Working Group on NOTES. Highlights the potential of NOTES and LESS, as well as the challenges and need for scientific confirmation of benefits.
Box et al. (2008)	----------	----------	Nomenclature of NOTES and LESS surgical procedure; defining terms to describe procedures in order to provide standardized terminology for NOTES and LESS operations.
Lima et al. (2009)	2002-2008	Manuscripts and abstracts of annual meetings of the American Urological Association, the European Association of Urology, and the World Congress of Endourology from 2007.	NOTES procedures remain highly complex operations in the urology. In an attempt to overcome these limitations, the hybrid approach (adding a single abdominal port access) or the pure NOTES combined approach (joining multiple natural orifice ports) as proposed in the literature.

Table 3 – continued.

Kommu et al. (2009)	1965-2008	Reports in major urological meeting abstracts, Embase and Medline.	Advances in instrumentation have been essential to achieve adequate results in LESS-NOTES urological surgery. Testing survival in animals is also necessary to further expand these techniques. Improved instrumentation and technology together with increasing experience in LESS-NOTES approaches have prompted the transition from porcine models to human patients.
Irwin et al. (2009)	---------- ------	Comprehensive review on LESS.	Success of LESS surgery is associated with familiarity of current practitioners with advanced laparoscopic techniques and technology. Advancements in instrumentation and future robotics platforms will expand the technique. Prospective studies comparing safety and effectiveness of NOTES-LESS with the laparoscopic and robotic approaches will objectively determine its role in surgical practice.
Box et al. (2009)	----------	Transvaginal access.	Transvaginal approach may be the best suited NOTES portal in selected patients.
Xavier et al. (2009)	----------	Transgastric access.	Application of transgastric NOTES in urology has been limited to case reports in the porcine model, and no urologic procedure has been performed solely via a transgastric route.
Ponsky et al. (2009)	----------	Feasibility and future of NOTES in Urology.	Experimental experience has showed the feasibility of NOTES and provided insight into the technical innovations necessary to improve the technique. NOTES is starting to be deployed in clinical experiences in both hybrid laparoscopic-endoscopic cases and pure procedures. Critical evaluation of outcomes is mandatory.
Canes et al. (2009)	----------	Deployment of flexible robotics and in vivo mini-robots for NOTES.	NOTES present specific instrumentation challenges (lack of stable platforms, loss of spatial orientation, and limited instrument tip maneuverability) that might be overcome with incorporation of robotic technology. Development of such technology is a challenge that has already been approached in Urology.
Granberg et al. (2009)	----------	Transvesical NOTES in Urology.	Initial studies have demonstrated the feasibility of transvesical NOTES. This technique has the potential to develop into a viable technology in the clinical setting, but it remains in phase of development.
Shin & Kalloo (2009)	----------	Transcolonic NOTES in Urology.	NOTES represent the symbiosis of the concepts of both minimally invasive surgery and interventional endoscopy. The transcolonic approach to the peritoneal cavity is presented.
Gamboa et al. (2009)	----------	Education and training for NOTES.	Development of guidelines for training will be necessary for the safe adoption of NOTES. Educational experience coined in laparoscopy (animal and cadaveric laboratories) will have an impact in the development of knowledge and surgical skills for NOTES.
Rasswei-ler et al. (2009)	----------	Imaging and navigation for NOTES.	Image-guided soft-tissue navigation represents a logic option to diminish the hazards of the technically challenging procedures of NOTES in Urology.

Table 4 *– Report on complications in NOTES-LESS clinical series.*

Authors	Number/procedures	Approach	Complications reported
Garg et al. (2005)	26 Nephrectomies	Extraperitoneal single port	1 Pleura perforation – managed intraoperatively 1 Vena cava hemorrhage – managed intraoperatively
Kiyokowa et al. (2006)	21 Prostatectomies	Retropubic extraperitoneal	No complications reported
Milliken et al. (2006)	22 Insertion of peritoneal dialysis catheters	Supraumbilical port	1 rectal injury
Gettman et al. (2007)	1 Transvesical peritoneoscopy	Endoscopic transurethro-transvesical	1 leak – resolved within 24 hours 1 exit-site infection – resolved via oral flucloxacillin 1 blockage due to fibrin clot – resolved with urokinase 1 blockage 2 weeks later - reoperation
Desai et al. (2007)	1 Nephrectomy; 1 Pyeloplasty	Transumbilical single port	No complications reported
Kaouk et al. (2007)	4 Renal cryotherapy procedures; 1 Kidney biopsy; 1 Radical nephrectomy; 4 Abdominal sacrocolpopexies.	Transumbilical or retroperitoneal	1 Postop complication in cryo procedure resolved via ventilation mask and blood transfusions (CT scan revealed small perinephric hematoma).
Raman et al. (2007)	3 Radical nephrectomies	Transumbilical	No complications reported

Table 4– continued.

Kaouk et al. (2007)	3 Varicocelectomies	Transumbilical	No complications reported
Kaouk et al. (2008)	4 Radical prostatectomies	Transumbilical	No intraoperative or postoperative complication 1 delayed complication – rectourethral fistula managed with mucosal advancement flap.
Ponsky et al. (2008)	1 Nephrectomy	SAS Transperitonealy	No complications reported
Desai et al. (2008)	4 Pyeloplasties 1 Ileal ureter 1 Ureteroneocystostomy	Transumbilical	No complications reported
Desai et al. (2008)	3 Simple prostatectomies	Transvesical	1 inadvertent enterotomy – fixed intraoperatively.
Kaouk et al. (2008)	1 Radical prostatectomy 1 Pyeloplasty 1 Radical nephrectomy	Transumbilical	No complications reported.
Castellucci et al. (2008)	1 Adrenalectomy	Transperitoneal supraumbilical	No complications reported
Kauok et al. (2008)	7 Partial nephrectomies	Transumbilical	1 intraoperative bleeding from tumor bed – managed intraoperatively with conversion to standard laparoscopy and blood transfusions.
Gill et al. (2008)	4 Live donor nephrectomy	Transumbilical	No complications reported
Barret et al. (2009)	1 Radical nephrectomy	Transumbilical extraperitoneal.	No complications reported

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CONFLICT OF INTEREST

None declared.

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