



# Adrenal natural orifice transluminal endoscopic surgery (NOTES): a step too far?

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**Abstract:** Surgical approach to adrenal gland has evolved from open to minimally invasive surgery. With the advent of technology, multiple techniques and approaches are available in a surgeon's armamentarium today to deal with adrenal nodules that require surgical intervention. Each approach has its own advantages and disadvantages. The era of minimal invasive surgery has fuelled our quest for better cosmesis, faster recovery, early return to work and reduced hospital stay. While minimal invasive method is the preferred approach for most benign adrenal masses less than 6 cm, its application for large adrenal lesions as well as adrenocortical carcinoma is still debatable. Single incision minimal invasive procedures further try to reduce the incisions and wound morbidity. With the aim to completely remove visible scars and possibly reduced morbidity, the concept of natural orifice transluminal endoscopic surgery (NOTES) has been proposed by some surgeons as well as interventional gastroenterologist. In NOTES, the peritoneal cavity is accessed through a hollow viscus to perform therapeutic as well as diagnostic procedures. While the theoretical advantages of scar less surgery and its advantages sound encouraging, the precise indications and its potential advantages for adrenal pathologies is yet to be defined. It should in no way, compromise our goal of safe patient surgery and outcomes.

**Keywords:** Natural orifice surgery; natural orifice transluminal endoscopic surgery (NOTES); transvaginal surgery; endoluminal surgery; adrenalectomy

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## Introduction

Surgery on adrenal gland is challenging, irrespective of the pathology. In addition to the surgical proximity to vital organs and major vessels, the physiological interaction of the adrenal hormones is also at play. Both in hormonally active glands as well as in insufficiency, perioperative optimisation and post-operative support is paramount. Adrenal gland surgery is done for a wide variety of reasons, from adrenal tumours to functional adenomas, lesions with suspicion of cortical carcinomas to metastatic deposits. Based upon pathology and laterality the surgery can range from total to partial adrenalectomy.

Ever since Gagner performed the first laparoscopic adrenalectomy in 1991 (1) laparoscopic adrenalectomy is considered gold standard for small and medium sized benign adrenal tumours (1,2). Though we find isolated cases describing resections of large adrenal mass, ranging up to 15 cm (1,3), application of laparoscopic adrenalectomy for lesion >6 cm is still debatable and lacks consensus (4-7). Today, more surgeons prefer to use the retroperitoneal approach for adrenal lesions, as it offers all the benefits of minimal invasive surgery, with the added advantage of avoiding violation of peritoneum (8-10). The benefits of laparoscopic surgery are many: safe, feasible, better

cosmesis, reduced pain, shorter hospital stay, early recovery after surgery and reduced wound morbidity, particularly in obese (7,10).

Over the years, surgeons and researchers quest for even smaller incisions has led to the advent of novel techniques like laparo-endoscopic single site surgery (LESS) (11) and natural orifice transluminal endoscopic surgery (NOTES) (12). While the principle of access to abdomen in LESS remains the same as for any laparoscopy, NOTES is an emerging technique wherein the peritoneal cavity is accessed through a hollow viscus or natural orifice, e.g., vaginal vault, stomach, etc., to perform a variety of diagnostic and interventional procedures, allowing a totally scarless surgery. NOTES offer us new possibilities and challenges in term of the technique, endoscopic expertise and scope for technological innovation. But for any new technique to be successful, the fundamental principles of patient safety and post-operative outcomes cannot be comprised. The cost benefit analysis also needs to be weighed, as compared to conventional minimal invasive techniques.

### Evolution of NOTES

The goal of any minimally invasive procedure is to minimising access related trauma by reducing the size and number of abdominal incisions (13,14). NOTES as a concept was put forward in 1990's by a team of researchers who called it "flexible transluminal endoscopy" (15). The term NOTES was coined in year 2005 by the American Society of Gastrointestinal Endoscopy and the Society of American Gastrointestinal and Endoscopic Surgeons working group (16). The idea of elimination of any visible surgical scar seemed so promising that more and more researchers started experimenting with this concept, both in animal studies as well as isolated cases in humans. Natural orifices like vagina, anus, mouth and urethra were utilised to gain access (17).

In animal models a variety of surgical procedures were performed, including transgastric adrenalectomy (18). The potential benefits suggested when compared to convention open and minimal invasive procedures were reduced pain, wound related complications, port site hernia, reduced hospital stay, improved cosmesis and patient satisfaction (19). The greatest advantage suggested for NOTES was retrieval of the specimen, avoiding the need for large incisions.

Kaloo *et al.* in 2003, utilised NOTES to perform liver biopsies (20). Marescaux *et al.* in 2007 reported the first transvaginal cholecystectomy (21). Ever since, the

acceptability of NOTES has spread, with more surgeons translating it into clinical practice. In the following years, the spread of NOTES was limited due to limitations of technology, inappropriate instrumentation and standardization of techniques. However, for the few years multiple abdominal and retroperitoneal surgeries have been performed using NOTES, and these include cholecystectomy, appendicectomy, adnexal and tubal surgery, hernia repair, splenectomy and nephrectomy (16).

### NOTES for adrenalectomy

In 2002, Gettman *et al.* completed and reported in animal model the use of NOTES for nephrectomy using transvaginal access (22). Following this, multiple researchers have demonstrated the application of NOTES in surgeries in the retroperitoneum, namely total and partial nephrectomy, cystectomies and prostatectomies, utilising transgastric, transrectal, transvesical and transvaginal access (23-25). Endoscopic instruments, combined with laparoscopic assistance and robotic assisted surgery were used in these studies involving animals or cadavers (23,26,27).

Fritscher-Ravens *et al.* in their studies on porcine model reported transgastric adrenalectomy using pure NOTES and NOTES in combination with endoscopic ultrasound (EUS) (28). They performed pure NOTES in four pigs and combined NOTES with EUS in six pigs. They failed to safely perform and complete adrenalectomy in the NOTES only group, due to excessive bleeding during access and lack of safety. But in the remaining cases under EUS guidance adrenalectomy was performed safely, with a mean operative time of 78 min.

Similarly, Perretta *et al.* in 2009, performed retroperitoneal right and left adrenalectomy in female pigs through the transvaginal access with a mean operative time of 70 minutes (29). No intra-operative complications were reported. They also reproduced the transvaginal access in cadaver model and demonstrated proper identification of all the retroperitoneal anatomy and landmarks. They suggested that this technique may benefit particularly in obese patients and patients with multiple abdominal surgeries. They also suggested that by avoiding the peritoneal breach, the cardio-pulmonary complications associated with carbo-peritoneum could be avoided. The same team further reported their experience with animal and cadaveric experiments on retroperitoneal surgeries using pure NOTES in 2009 (30).

In 2013, Eyraud *et al.* demonstrated feasibility of robotic assisted transrectal hybrid NOTES nephrectomy and

adrenalectomy in a male cadaver (31). They placed an 8-mm transrectal robotic trocar, followed by periumbilical trocars. They were able to successfully complete the procedure in 145 min, including the rectal closure. Based on the available evidence it is too early to reach a conclusion regarding wider application and acceptability of NOTES in adrenal surgery outside the purview of research and experimental studies.

One of the first clinical experience in transvaginal NOTES assisted adrenalectomy was reported by Zou *et al.* on 11 patients (32). They used conventional laparoscopic instruments through umbilical access and a 30-degree laparoscope through posterior vaginal fornix. The same posterior vaginal fornix incision was used to extract the resected specimen. They reported splenic injury in one patient with Cushing disease for whom they needed to perform splenectomy and hence conversion to open. The median operative time was 102 min (80–310 min) with a median estimated blood loss of 80 mL. The median size of adrenal mass was 4.7 cm (2.2 to 6.6 cm). As all patient were females, they performed Female Sexual Function Index, pre- and postoperatively and found no difference in the median scores. Except the patient who needed conversion to open, all the other patients were satisfied with the cosmetic outcome. They concluded that transvaginal NOTES assisted laparoscopic adrenalectomy is safe and feasible for adrenal tumours in female patients.

In the absence of large series, comparative studies, standardization of techniques and instrumentation, it is advisable to tread with caution when offering patients NOTES adrenalectomy. However, theoretically there are potential benefits of reduced post-operative pain, wound related complications mainly surgical site infections and port site hernias. The immunomodulatory effects of NOTES by a reduction in TNF-alpha levels in the postoperative period in NOTES subgroup as compared to laparoscopy and laparotomy groups were demonstrated in a swine model by McGee *et al.* (33). Similarly, benefits in obese patients have been shown for transvaginal cholecystectomy (34).

### Pitfalls in NOTES adrenalectomy

There is a lot to be learned about NOTES, a novel operative technique for abdominal surgery. Most of the published literature about application of NOTES for adrenal as well as other retroperitoneal pathologies is based on animal studies and isolated case reports. It remains to be seen whether the animal models can be successfully

replicated in larger human studies. Hence, it is difficult to prove the benefits of NOTES when compared to conventional laparoscopic surgery (35).

Standardization of the procedure is still awaited, ideal access route yet to be defined. Most of the published animal, cadaveric and isolated case reports published have utilised transvaginal access, which is considered the safest access route. But this approach cannot be used in males, who will invariably account for half of the cases. Most animal studies which show the intra-peritoneal access techniques in NOTES to be safe, were conducted in virgin abdomens (20,36). This technique may be difficult in patients with previous surgeries.

In 2006, the Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) published a white paper advised a zero tolerance for NOTES associated complications (37). A difficult problem is the safe closure of the luminal access site and NOSCAR considers this to be the main obstacle. They have pitched for achieving 100% success in closure of luminal access, for which researchers must develop better anastomotic or suturing devices. Palanivelu *et al.* reported a complication rate of 16% in their series of NOTES transvaginal cholecystectomy (38).

Access related surgical site infections, inadvertent injuries, bleeding, post-operative leaks have been reported, and we are yet to address these issues conclusively. Instrument sterilisation is not clearly defined. Learning curve with regards to achieving expertise in endoscopy, orientation with flexible scope in a retroflexed view leading to an off-axis movement of instruments are potential issues (39). Other issues particularly in transgastric or trans-rectal access techniques is inadvertent bowel distention caused due to air leaking into the bowel (39).

The steep learning curve in NOTES and difficulties in its incorporation into surgical residency programs is another issue raised (40,41). Current residency programs are already falling short to incorporate a variety of open, conventional laparoscopy, LESS procedures, robotic surgery and this may be burdened with addition of another technique. Once NOTES reach the stage of human trials, maintaining a balance between quality of care, patient safety during service delivery and residency training issues need to be considered.

To conclude, over the last decade NOTES is gaining popularity, especially the concept of scarless abdomen seems promising to most surgeons. Whilst its use has increased over the years, mainly in animal studies and small sample human studies, the technique is not without its problems.

Some of the unaddressed issues include academic protocols, medico-legal issues, patient safety and bureaucratic and administrative challenges. Experimental studies have been conducted in NOTES adrenalectomy but require larger studies, with focus on clinical outcomes, cost effectiveness and benefits. At this point in time; adrenal NOTES is probably a step too far.

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## Footnote

*Conflicts of Interest:* The authors have no conflicts of interest to declare.

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