



Asian Focus

Natural orifice transluminal endoscopic surgery in urology: The Chinese experience



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Urology;
Chinese experience

Abstract *Objective:* To describe the Chinese experience of natural orifice transluminal endoscopic surgery (NOTES) in urology.

Methods: From December 2008 to May 2017, 35 animal experiments and 305 clinical surgeries of NOTES or natural orifices specimen extractions (NOSE) were performed in China. The animal experiments included five kidney biopsies, 24 nephrectomies and six partial nephrectomies. The clinical surgeries included 12 transvaginal NOSE (TV-NOSE), 266 hybrid transvaginal NOTES (TV-NOTES) and 27 pure TV-NOTES. The TV-NOSE procedure was performed in five transumbilical laparoendoscopic single-site (U-LESS) nephrectomies, four suprapubic-assisted laparoendoscopic single-site surgery (SA-LESS) nephroureterectomies, and three laparoscopic radical cystectomies. The hybrid TV-NOTES procedure included 210 nephrectomies, 31 adrenalectomies, eight nephroureterectomies, 13 partial nephrectomies, and four heminephrectomies. The pure TV-NOTES procedure included five renal cyst decortications and 22 nephrectomies. *Results:* A total of 29 animal experiments were successfully performed. One partial nephrectomy was converted to standard laparoscopic surgery. Two kidney biopsies and two nephrectomies were unsuccessful. A total of 297 clinical surgeries were successfully performed. Six patients who underwent hybrid TV-NOTES were converted to open surgery. Two patients who underwent pure TV-NOTES were converted to SA-LESS. There were 22 major complications, 16 occurred intraoperatively and six postoperatively. The mean visual analog score

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(VAS) of 48 h after the operation was 2.5 points in TV-NOSE, 2.3 points in hybrid TV-NOTES and 1.7 points in pure TV-NOTES. The mean follow-up of 50.6 (3.0–87.0) months showed that all patients were in good condition. The umbilicus scars were nearly invisible in TV-NOSE and hybrid TV-NOTES. The vaginal incision healed well.

Conclusions: TV-NOSE and TV-NOTES are feasible, safe, and effective with little injury, low pain, fast recovery, and good cosmetic outcomes in properly selected patients. They are worth consideration for urological clinical practice.

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1. Introduction

Natural orifice transluminal endoscopic surgery (NOTES) is an innovational surgical procedure that uses hollow organs (e.g., vagina, bladder, gastrointestinal tract) to access the peritoneal or thoracic cavity for disease diagnosis and treatment [1]. It is regarded as the third generation surgery following open surgery and laparoscopic surgery and its advantages include little injury, low pain, fast recovery and good cosmetic results [2].

The first report of a NOTES procedure dated from gynecologic surgery during the 1970s, when culdoscopic sterilizations were first published [3]. In urology, the concept of NOTES was initiated with natural orifices specimen extraction (NOSE). In 1993, Breda et al. [4] first reported vaginal extraction of an intact kidney following a laparoscopic nephrectomy. Then a larger series was reported by Gill et al. [5] in 2002. In 2004, Kalloo et al. [6] first presented the concept of NOTES with successfully performing liver biopsy in a porcine model by transgastric approach. Then in 2007, Lima et al. [7] performed the first NOTES nephrectomy by combined transgastric and transvesical approaches in a porcine model. Human NOTES was first performed for appendectomy via transgastric approach by Rao et al. [8] in 2007, and the first hybrid transvaginal NOTES (TV-NOTES) nephrectomy in a human body was reported by Branco et al. [9] in 2008. Later, hybrid TV-NOTES simple, radical, living donor nephrectomy and heminephrectomy were successively reported [10–13]. In 2010, Kaouk et al. [14] reported the first pure TV-NOTES nephrectomy in clinical practice. However, due to the limitations of operative instruments and high technical difficulties, NOTES was still precluded from widespread adoption. Although NOTES has been successfully completed experimentally by transgastric, transrectal, transvaginal, and transvesical approaches [15–18], transvaginal access is an ideal approach and the most commonly used in NOTES in urology now.

In China, NOTES in urology initially trailed several years behind other countries; however once started, it developed fast and a Chinese system of urological NOTES was then gradually established. Herein, we detailed the Chinese experience of NOTES in urology from animal experiment to clinical practice, and from hybrid to pure NOTES.

2. Materials and methods

From December 2008 to May 2017, 35 animal experiments and 305 clinical surgeries of NOTES or NOSE were performed in China. The experimental data and clinical data were retrospectively analyzed. The animal experiments included five kidney biopsies, six nephrectomies and six partial nephrectomies by combined transvesical and transgastric approach, six nephrectomies by combined transvesical and transvaginal approach, six hybrid transvaginal nephrectomies and six hybrid transrectal nephrectomies. There were 305 patients subjected to clinical surgeries, including 12 transvaginal NOSE (TV-NOSE), 266 hybrid TV-NOTES and 27 pure TV-NOTES (Table 1). TV-NOSE consisted in the performance of a laparoscopic procedure with the extraction of the specimen through the vagina. It was performed in five transumbilical laparoendoscopic single-site nephrectomies (U-LESS-N), four suprapubic-assisted laparoendoscopic single-site surgery nephroureterectomies (SA-LESS-NU), and three laparoscopic radical cystectomies (LRC). The hybrid TV-NOTES procedure was performed in 210 nephrectomies, 31 adrenalectomies, eight nephroureterectomies, 13 partial nephrectomies and four heminephrectomies. The pure TV-NOTES procedure was performed in five renal cyst decortications and 22 nephrectomies.

The study was approved by the ethics committee of Gannan Medical University (2010118). All patients were adequately informed of the possible risks and benefits of this new approach and signed a written consent agreeing to undergo the described procedure.

2.1. Operative technique

2.1.1. Animal experiment of NOTES in urology

Under general anesthesia, pigs underwent pure NOTES by combined transvesical and transgastric approach, hybrid NOTES by combined transvesical and transvaginal approach, or hybrid NOTES by transvaginal or transrectal approach. During the pure NOTES by combined transvesical and transgastric approach, no abdominal trocar was placed. The transvesical access was established by incising the top wall of the bladder with a needle knife with cautery through a ureteroscope. The transgastric access was established by incising the wall of the

stomach using the same method and then a gastroscope was inserted. Dissection was performed through the vesical trocar under the vision from the gastroscope. The kidney biopsy, nephrectomy, or partial nephrectomy was performed and the specimen was extracted through the bladder in the partial nephrectomy procedure, but not taken out in the nephrectomy procedure. The vesical and gastric wounds were not closed and the pigs were sacrificed at the end of the procedure. During the hybrid NOTES by combined transvesical and transvaginal approach, one trocar was placed at the umbilicus and a conventional 30° laparoscope was inserted. The transvesical access was established in the same way. The transvaginal access was established by incising the posterior vaginal fornix using the same method. Dissection was performed through the vesical and vaginal trocars. The nephrectomy was performed and the specimen was extracted through the vagina. The vesical and vaginal wounds were not closed and the pigs were sacrificed at the end of the procedure. During the hybrid NOTES by transvaginal or transrectal approach, two trocars were placed at the margin of the umbilicus and one trocar was placed either through the vagina (TV-NOTES) by incising the posterior vaginal fornix or rectum (transrectal NOTES) by incising the anterior wall of rectum 2 cm above the dentate line. The transrectal or transvaginal trocar into the abdominal cavity was visualized using a flexible-tip 5.4 mm 0° laparoscope (Olympus Optical, Tokyo, Japan) through the umbilical trocar. The laparoscope was then placed through the vaginal or rectal trocar. Dissection was performed through the umbilical trocars and visualized by the vaginal or rectal laparoscope. The nephrectomy was performed and the specimen was extracted through the vagina or rectum. The vaginal or rectum wound was closed transvaginally or transrectally with a 2/0 absorbable suture.

Table 1 Baseline characteristics of all 305 patients.

Characteristics	Value
Age, mean, range, year	39.5 (23–76)
BMI, mean, range, kg/m ²	21.5 (15.4–29.6)
Classification of diseases, <i>n</i>	
Adrenal tumors	31
Renal tumors	49
Non-functional kidneys	194
Renal tuberculosis	7
Renal cysts	5
Duplex kidneys	4
Renal pelvis and ureteral tumors	12
Bladder tumors	3
Tumor size, mean, range, cm	5.0 (3.2–6.8)
Previous operation history, <i>n</i>	
Pelvic operation	22
Abdominal operation	12
ASA score, mean, range	2 (1–3)

ASA, American Society of Anesthesiologists; BMI, body mass index.

2.2. Clinical application of NOTES in urology

2.2.1. Patients selection

The indications for TV-NOSE and TV-NOTES were women with previous vaginal delivery. The exclusion criteria were as follows: Body mass index (>30 kg/m²), unmarried status, preparation for pregnancy, pelvic inflammatory disease, vaginal narrowing, and severe cervical erosion (evaluated by a gynecologist). All patients were informed of the possible risks and signed a written consent agreeing to undergo the described procedure. The baseline characteristics of all the selected patients are shown in [Table 1](#).

2.2.2. Preoperative preparation

Vaginal irrigation was performed with iodophors and oral antibiotics including norfloxacin and metronidazole were given for 3 days before the operation. All patients had a clear liquid diet 1 day preoperatively and underwent a mechanical bowel preparation with the enema in the morning of surgery.

2.2.3. Surgical procedure

Under general anesthesia, a nasogastric tube and a transurethral catheter were placed to decompress the stomach and bladder. Patients were subjected to TV-NOSE, hybrid TV-NOTES, or pure TV-NOTES procedures.

In TV-NOSE procedures, the patients were placed in the lithotomy position, with the affected side elevated at 60° for U-LESS-N and SA-LESS-NU, or with Trendelenburg position by 25° for LRC. During U-LESS-N procedures, three trocars were placed through a 3 cm arciform periumbilical incision. During SA-LESS-NU procedures, two trocars were placed at the medial margin of the umbilicus and another trocar was placed below the pubic hairline. During LRC procedures, five trocars were inserted through the abdominal wall as the method of standard laparoscopic radical cystectomy [19]. A standard 30° laparoscope or a flexible-tip 5.4 mm 0° laparoscope and conventional laparoscopic instruments were used for dissections according to the method of standard laparoscopic nephrectomy (simple and radical) [20], nephroureterectomy [21], and radical cystectomy, respectively. The specimen was placed inside a homemade bag and removed through vagina by a 3–4 cm incision at the posterior vaginal fornix. Cutaneous ureterostomy was performed at the end of LRC.

In hybrid TV-NOTES procedures, the patients were placed in the lithotomy position with the affected side elevated at 60°. A 5 mm trocar and a 10 mm trocar were placed at the medial margins of the umbilicus. A 10 mm trocar or a lengthened 5 mm trocar was placed through the posterior vaginal fornix into the pelvic cavity under direct vision using a conventional 30° laparoscope or a flexible-tip 5.4 mm 0° laparoscope from the umbilical trocar. After confirming that no pelvic organs were injured, the laparoscope was placed through the vaginal trocar. Dissections were performed through the umbilical trocars using conventional laparoscopic instruments according to the method of standard laparoscopic nephrectomy (simple and radical), adrenalectomy [22], nephroureterectomy, partial

nephrectomy [23], and heminephrectomy [24], respectively. During simple nephrectomy procedures, the perirenal extra-fascial nephrectomy was performed for infective non-functioning kidney with perinephric adhesion. The renal artery was doubly clipped with its surrounding fibrous tissues, and the kidney was mobilized outside Gerota's fascia. During nephroureterectomy procedures, a resectoscope was inserted into the bladder after the distal ureter was dissected and blocked under laparoscopy, and pneumovesicium method was applied with carbon dioxide insufflation [25]. The distal ureter was disconnected from the bladder wall by dissecting circumferentially through the entire detrusor muscle. Then the ureter was isolated completely and a radical nephrectomy was laparoscopically performed. The specimen was placed inside a homemade bag and extracted by extending the vaginal incision.

In pure TV-NOTES procedures, the patients were placed in the lithotomy position with affected side elevated at 30° and with Trendelenburg position by 25° to minimize the intestinal canal within the pelvic cavity as much as possible. A 3 mm incision was made at the posterior vaginal fornix, and a 5 mm trocar was introduced into the pelvic cavity guided by a 5 mm blunt forceps. A flexible-tip 5.4 mm 0° laparoscope was inserted into the pelvic cavity confirming no organs were injured. Then, the posterior vaginal fornix incision was enlarged to about 3 cm length with sponge forceps, and a self-developed three-channel ZOU-port (Zhouji Medical Instruments Co Ltd, Zhejiang, China) was deployed across the vaginal incision, through which the laparoscope and all laparoscopic instruments were introduced into the abdominal cavity. Then the patient was placed in a dorsally elevated position by 25° with the affected side elevated at 60°. Dissection was entirely performed through the transvaginal ZOU-port. Various self-developed, extra-long and flexible-tip forceps, aspirators and Hem-o-lok applier (Zhouji Medical Instruments Co Ltd), and extra-long 5-mm harmonic scalpel (Ethicon Endosurgery, Cincinnati, OH, USA) were used for dissections according to the method of standard laparoscopic renal cyst decortication [26] and nephrectomy (simple and radical), respectively. The specimen was placed inside a homemade bag (made with a sterile protective plastic bag) and extracted through the vaginal incision.

At the end of the procedure, one or no drainage tube was placed in the operative region through an abdominal trocar, and one drainage tube was placed in the pelvic cavity via the vaginal incision in each patient. The vaginal wound was closed transvaginally with a 2/0 absorbable suture. A vaginal tamponade for 24 h after surgery using a sterile vaginal pack dressing was applied in all patients.

2.2.4. Evaluation of surgical outcome

The operative time, estimated blood loss, intraoperative and postoperative complications, and postoperative hospital stay were used to evaluate the safety, feasibility, and efficacy of the operation. The visual analog score (VAS) [27] of 48 h after the operation was used for evaluation of postoperative pain. The cosmetic result was evaluated according to the Patient Scar Assessment Questionnaire and Scoring System (PSAQ) [28] 3 months after surgery. A complete sexual abstinence lasting 3 months was advised

for all cases. Sexual function was investigated by administering the Female Sexual Function Index (FSFI) [29] 1 week before and 3 months after the operation, and the total score was compared. The quality of life was assessed by Short Form 36 Health Survey Questionnaires (SF-36) [30] 1 week before and 3 months after surgery, and the total score was compared.

2.3. Statistical analysis

Statistical analysis was performed using SPSS 14.0 (IBM Corp, Armonk, NY, USA). The paired *t*-test was used to compare differences between preoperative and postoperative FSFI and SF-36 total scores, respectively, with $p < 0.05$ considered as indicating statistical significance.

3. Results

A total of 29 animal experiments were successfully performed. One partial nephrectomy was converted to laparoscopic surgery. Two kidney biopsies and two nephrectomies by combined transvesical and transvaginal approach failed to be completed.

A total of 297 clinical surgeries including 12 TV-NOSE, 260 hybrid TV-NOTES and 25 pure TV-NOTES were successfully performed. Six patients who underwent hybrid TV-NOTES were converted to open surgery, including one adrenalectomy due to spleen injury and five nephrectomies due to inferior vena cava injury ($n=2$), colon injury ($n=2$), and renal vascular injury ($n=1$). Two patients that underwent pure TV-NOTES nephrectomy were converted to SA-LESS nephrectomy, one for rectum injury and one for failure in progression of the procedure. The mean operative time, mean estimated blood loss, cases of transfusion and major complications, and postoperative hospital stay are listed in Table 2. Ten patients in all received a transfusion. The mean ischemia time was 20 min for partial nephrectomy. A total of 22 major complications occurred, including 16 major intraoperative complications and six major postoperative complications. The intraoperative major complications included pleural injury, spleen injury, colon injury, rectal injury, bladder rupture, inferior vena cava injury, renal vascular injury, and iliac vein injury. The postoperative major complications included secondary hemorrhage and iliac artery thrombosis.

The mean VAS of 48 h after the operation was 2.5 points in TV-NOSE, 2.3 points in hybrid TV-NOTES and 1.7 points in pure TV-NOTES. At a mean follow-up of 50.6 (3–87) months, all patients were in good condition. The umbilical scars were nearly invisible in TV-NOSE and hybrid TV-NOTES. The vaginal incisions healed well and there was no evidence of infection of the pelvic or abdominal cavities, umbilical hernias, or uterine prolapse. Three months after surgery, the PSAQ score was 38.1 (31–58). There was no change in the FSFI score (28.5 preoperatively, 28.2 postoperatively, $p > 0.05$) and the SF-36 score showed a significant improvement (Table 3). After the operation, four patients were impregnated naturally without any hormone assistance or assisted reproductive technology and underwent successful deliveries. Three of them gave

Table 2 Perioperative data for the 305 patients.

Surgical procedures	Cases, <i>n</i>	Successful cases, <i>n</i>	Mean operative time (range), min	Mean estimated blood loss (range), mL	Patients receiving transfusion, <i>n</i> (%)	Intraoperative major complications, <i>n</i> (%)	Postoperative major complications, <i>n</i> (%)	Postoperative hospital stay, mean (range), day
TV-NOSE	12	12						
Nephrectomy	5	5	136 (110–160)	66 (40–100)	0	0	0	4.8 (4–6)
Nephroureterectomy	4	4	150 (120–210)	180 (80–350)	0	0	0	8.2 (7–9)
Radical cystectomy	3	3	232 (210–255)	383 (300–500)	0	0	0	9.3 (7–12)
Hybrid TV-NOTES	266	260						
Adrenalectomy	31	30	65 (45–310)	110 (20–800)	1 (3.2%)	1 (3.2%)	0	6.5 (4–13)
Nephrectomy	210	205	96 (70–280)	72 (30–800)	6 (2.9%)	12 (5.7%)	3 (1.4%)	7.0 (4–10)
Partial nephrectomy	13	13	115 (110–190)	130 (50–450)	1 (7.7%)	1 (7.7%)	1 (7.7%)	7.4 (4–10)
Heminephroureterectomy	4	4	98 (87–110)	225 (160–300)	0	0	0	7.0 (6–8)
Nephroureterectomy	8	8	180 (160–245)	183 (100–500)	1 (12.5%)	1 (12.5%)	0	8.3 (7–9)
Pure TV-NOTES	27	25						
Nephrectomy	22	20	190 (160–320)	170 (100–500)	1 (4.5%)	1 (4.5%)	2 (9.1%)	5.8 (4–10)
Renal cyst excision	5	5	80 (60–90)	25 (20–50)	0	0	0	3.8 (3–4)

TV-NOSE, transvaginal natural orifice specimen extraction; TV-NOTES, transvaginal natural orifice transluminal endoscopic surgery.

Table 3 The score of VAS, PSAQ, FSFI and SF-36.

Surgical procedures	Cases, <i>n</i>	Postoperative 48 h VAS, mean (range)	PSAQ score, mean (range)	FSFI score, mean (range)		SF-36 score, mean (range)		<i>p</i> -Value	
				1 week preoperatively	3 months postoperatively	1 week preoperatively	3 months postoperatively	FSFI	SF-36
TV-NOSE	12	2.5 (2–4)	37.3 (32–48)	26.2 (25.3–29.5)	25.6 (25.1–28.7)	39.8 (33.1–44.9)	50.2 (43.7–62.6)	0.502	0.041
Hybrid TV-NOTES	266	2.3 (1–4)	38.2 (31–58)	27.2 (22.7–30.8)	26.2 (22.5–30.6)	39.2 (32.2–45.8)	53.2 (41.6–65.8)	0.430	0.037
Pure TV-NOTES	27	1.7 (1–3)	None	31.2 (26.5–32.6)	30.7 (26.5–32.2)	38.3 (32.7–44.6)	52.9 (42.8–66.3)	0.388	0.033
Total	305	2.2 (1–4)	38.1 (31–58)	28.5 (22.7–32.6)	28.2 (22.5–32.2)	38.6 (32.2–45.8)	53.1 (41.6–66.3)	0.403	0.036

FSFI, female sexual function index; PSAQ, patient scar assessment questionnaire and scoring system; SF-36, short form 36 health survey questionnaires; TV-NOSE, transvaginal natural orifice specimen extraction; TV-NOTES, transvaginal natural orifice transluminal endoscopic surgery; VAS, visual analog score.

birth through vaginal delivery and one by caesarean because of nuchal cord entanglement. Mothers and children are all in good condition to date.

4. Discussion

NOTES is a significant innovation in surgical fields and is regarded as the third generation surgery following open surgery and laparoscopic surgery. The most obvious advantage of NOTES is excellent cosmetic results with no scar or invisible scar on the body's surface, especially for large specimen extraction. Currently, due to the limitations of operative instruments and techniques, NOTES in urology in humans has only been successfully accomplished in several hospitals all over the world. Whatever, NOTES has become a new direction in modern minimally invasive surgery and increasingly used in the surgical treatment of women with urinary diseases.

The animal experiment of NOTES in urology in China was first performed in Changhai Hospital, Shanghai in December 2008 by combined transgastric and transvesical approach for kidney biopsy in a porcine model. The urologists at Changhai Hospital then successively performed NOTES nephrectomy in porcine models by combined transvesical and transvaginal approach and by combined transvesical and transgastric approach, and partial nephrectomy by combined transvesical and transgastric approach. In 2012, the urologists at our First Affiliated Hospital of Gannan Medical University successively performed hybrid transvaginal and hybrid transrectal NOTES nephrectomy in porcine models. The animal experiments were necessary and useful for surgeons to adapt to the different vision and surgical approach of NOTES before transition to clinical practice.

Although NOTES has been successfully completed in animal experiments by transgastric, transrectal, transvaginal, and transvesical approach, the majority of NOTES in urology in humans were performed by transvaginal approach. Most NOTES procedures applied a hybrid approach in which at least one umbilical laparoscopic port was used for visualization [31]. Compared to other approaches, transvaginal approach has the following advantages [32]: (1) There is a low risk of postoperative incision infection and leakage because of less pathogenic bacteria and rich blood supply in vagina; (2) the vagina is a quick and convenient access into abdominal cavity for the thin tissue at the posterior vaginal fornix which is close to the rectum womb pit; (3) the postoperative pain is minor because the vaginal fornix mucosa does not have somatic nerve sensation and was unphased to cutting; (4) the vagina has good extensibility and elasticity that is suitable for the use of rigid instruments and extraction of specimens; (5) the vaginal incision can be safely established and closed under direct vision. Collectively, patients experience psychological and cosmetic benefits, leading to faster recoveries.

In China to date, TV-NOTES in urology in humans has only been performed at our First Affiliated Hospital of Gannan Medical University. The TV-NOTES nephrectomy schedule evolved in a stepwise process. It started with five cases of U-LESS nephrectomy with TV-NOSE. Although NOSE was not considered NOTES by some scholars [33,34], NOSE was an

effective technique by itself and an ideal stepping stone to NOTES. In May 2010, we successfully performed the first hybrid TV-NOTES simple nephrectomy for a non-functioning kidney. Then we successively performed hybrid TV-NOTES adrenalectomy, radical nephrectomy, partial nephrectomy, heminephrectomy, and nephroureterectomy. In these procedures, vaginal access was used to insert a laparoscope and two umbilical trocars were used as main working ports. For the transition to pure TV-NOTES, we performed 25 more challenging cases of hybrid TV-NOTES nephrectomy, with a single umbilical trocar used to provide visualization and a multi-instrument access port deployed across the vaginal incision. With the introduction of extra-long bent instruments and self-developed three-channel ZOU-port, we began to perform pure TV-NOTES starting with five cases of renal cyst decortication. Then in January 2011, we successfully performed the first pure TV-NOTES simple nephrectomy for a non-functioning kidney.

In TV-NOTES, there was no operative triangulation for facilitated dissection along normal anatomic planes as in standard laparoscopic surgery, which resulted in clashing, suboptimal exposure, and imprecise tissue dissociation and hemostasis. The flexible-tip laparoscope with a streamlined profile and the light cable placed 90° to the lens, provided good visualization and reduced conflict with other instruments. If the liver or spleen was found to interfere with the operation, it was better to expose the surgical field by suspending the liver and spleen with a suture on the abdominal wall. When removing a large specimen, it was best to keep in line with the longitudinal axis of the vagina, avoiding rough pulling and preventing tears of the vagina.

In pure TV-NOTES procedures, the placement of transvaginal port was a very crucial step. Placement was blind without the umbilical port and the detection of laparoscope monitoring, which increased the risk of organ injury such as the rectum. One patient suffered rectal injury when placing the vaginal port early in surgery. To prevent future complications, patients could be placed in the Trendelenburg position to avoid the bowel loops stacking in the pelvic cavity. Moreover, the preoperative bowel preparation should be performed beforehand to allow any injured bowel to be sutured immediately and avoid secondary operations. The dissection of the cephalad aspect of the renal hilum and the upper pole of the kidney was challenging, because of the considerable distance and difficulty to obtain the correct working angle. We used self-developed extra-long prebent or flexible instruments which could minimize instrument clashing and help provide intracorporeal instrument triangulation, proper tissue retraction and better force distribution for dissection. The ZOU-port we used was long enough to bypass the pelvic organs which minimized pelvic organ injury during the operation. Furthermore, the original length of the port was 25 cm and the port material was plastic elastomeric, which could be cut at will with a knife to adapt the issue of individual anatomic differences. Modifying the port was helpful and allowed the instruments to better transverse the abdominal cavity. Although these improved instruments facilitated the surgical procedure, they were still relatively laborious. The development of purpose-specific robotic platforms may overcome the current limitations of NOTES [35].

The postoperative pain, cosmetic result, and quality of life were important concerns of patients. Compared with other minimally-invasive surgery, the TV-NOTES procedure provided decreased postoperative pain, improved cosmetic result, and earlier recovery [36,37]. The low VAS and no narcotic pain medications used showed that TV-NOTES procedure was associated with less pain because the vaginal incision was less sensitive than abdominal wound. The umbilicus scars were nearly invisible and the vaginal incision healed well. There was no umbilical hernia or uterine prolapse. The patients were satisfied with the good cosmesis by a low PSAQ score. And the quality of life evaluated using SF-36 was significantly higher 3 months after surgery than before surgery.

The safety and complications of TV-NOTES were concerned by both surgeons and patients. The major complications included pleural injury, spleen injury, colon injury, rectal injury, bladder rupture, inferior vena cava injury, renal vascular injury, iliac vein injury, secondary hemorrhage, and thrombosis. One patient underwent emergency thrombectomy for right iliac artery thrombosis after the operation. The incidence of major complications in our study was about 7.2% (22/305). There was no significant difference in the incidence of complications compared with standard laparoscopic surgery [38]. These major complications were mainly owed to shortcomings of technical experience with the transvaginal access in the early period and dense adhesion with adjacent organs. Fortunately, all complications were well disposed and there was no intra-operative or postoperative death case. Proper case selection and comprehensive assessment before surgery are important for determining the suitability of TV-NOTES. Patients who are obese (BMI >30 kg/m²) or too tall are not fit for NOTES. In addition, patients with a large specimen or specimens (the transverse diameter >7 cm) are not suitable. Meanwhile, whenever there is a risk of injuring the patient, it is necessary to converse to standard laparoscopy or open surgery.

The effects of TV-NOTES on postoperative sexual function, pregnancy, and fertility function were another major concern of both surgeons and patients. In this study, FSFI score 3 months after surgery was not significantly different from before surgery in sexually active women. Previous studies in vaginal surgery in gynecology suggested that there was no significant effect on sexual function or fertility function [39]. No significant differences were found for postoperative sexual function, changes in menorrhagia, or vaginal discharge reported by Bulian et al. [40]. A part of patients felt sexual life significantly improved and painful sexual intercourse decreased after surgery. A prospective cohort study of 106 cases of sexually active women patients after TV-NOTES reported by Linke et al. [41] showed that five patients conceived naturally within 1 year after surgery and three of them gave birth through vaginal delivery, one of them gave birth by caesarean and the other patient underwent spontaneous abortion resulted from non-surgical related bacterial infection. During the post-operative follow-up in our center, four patients were impregnated naturally without accepting any drugs or assisted reproductive technology and underwent delivery after surgery. Three of them gave birth to babies vaginally and one by caesarean due to umbilical cord entangled

neck. One patient conceived twice naturally after surgery and successively gave birth to two boys through vaginal delivery. Mothers and children are all in good condition to date.

In our opinion, with animal experiments and clinical experiences, TV-NOSE and TV-NOTES are feasible, safe and effective in appropriate patients, with advantages of little injury, low pain, fast recovery, and good cosmetic results. There is no significant effect on sexual function, pregnancy and fertility function after surgery, but significant improvement is still needed for TV-NOTES, including improvement of operative skills and instruments, especially the further improvement of instruments. The operative skills and instruments were developed slowly in recent years and most NOTES were performed with the assistance of a laparoscope. Combined approaches may promote the NOTES procedure. We believe that with the further improvement of instruments and the operative skills, NOTES will be pushed to the next level, and it will play a greater role in the treatment of urological diseases.

In this study, we mainly describe the experience of NOTES in urology. A controlled study compared with other minimally invasive approaches is needed to further describe the advantages of NOTES. In additional, randomized multi-center and long-term follow-up studies are needed to better evaluate the outcomes of NOTES.

5. Conclusion

TV-NOSE and TV-NOTES are feasible, safe and effective with little injury, low pain, fast recovery and good cosmetic outcomes in properly selected patients. They are worth applying in urological clinical practice.

Author contributions

Study concept and design: Xiaofeng Zou, Guoxi Zhang, Tianpeng Xie.

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Conflicts of interest

The authors declare no conflict of interest.

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