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NOTES Hybrid Transvaginal Radical Nephrectomy for Tumor: Stepwise Progression Toward a First Successful Clinical Case

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Abstract

Background: Natural orifice transluminal endoscopic surgery (NOTES) has been used to perform nephrectomy in the laboratory; however, clinical reports to date have used multiple abdominal trocars to assist the transvaginal procedure.

Objective: To present our stepwise technique development and the first successful clinical case of NOTES transvaginal radical nephrectomy for tumor with umbilical assistance without extraumbilical skin incisions.

Design, setting, and participants: The four transvaginal NOTES procedures were performed at two institutions after obtaining institutional review board approval. Various operative steps were developed experimentally in three clinical cases, and on March 7, 2009, we performed the first successful case of NOTES hybrid transvaginal radical nephrectomy without any extraumbilical skin incisions. Using one multichannel access port in the vagina and one in the umbilicus, laparoscopic visualization, intraoperative tissue dissection, and hilar control were performed transvaginally and transumbilically. The intact specimen was extracted transvaginally.

Measurements: All perioperative data were accrued prospectively. A stepwise progression to the successful completion of the fourth case is systematically presented.

Results and limitations: Intraoperatively, at incrementally more advanced stages of the procedure, the first three NOTES clinical cases were electively converted to standard laparoscopy because of rectal injury during vaginal entry, of failure to progress, and of gradual bleeding during upper-pole dissection after transvaginal hilar control, respectively. The fourth case was successfully completed via transvaginal and umbilical access without conversion to standard laparoscopy. Operative time was 3.7 h, estimated blood loss was 150 cm³, and hospital stay was 1 d. Final pathology confirmed a 220-g, pT1b, 7-cm, grade 2, clear-cell renal cell carcinoma with negative margins. The patient was readmitted for an intraabdominal collection that responded to drainage and antibiotics.

Conclusions: We report our stepwise progression and the initial successful clinical case of NOTES hybrid transvaginal radical nephrectomy for tumor, assisted with only one umbilical trocar. Although transvaginal nephrectomy is feasible in the highly selected patient with favorable intraoperative circumstances, considerable refinements in technique and technology are necessary if this approach is to advance beyond mere anecdote.

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1. Introduction

Natural orifice transluminal endoscopic surgery (NOTES) represents a developmental field in which natural orifices are employed to gain access for performing surgery inside the body. First described in 2003, NOTES was explored initially in the field of general and gastrointestinal surgery [1]. Although a few patients have undergone pure NOTES appendectomy, most NOTES procedures have been *hybrid*, using transabdominal assistance with one or more standard laparoscopic ports.

The application of NOTES in urology is an even more recent phenomenon. From a historical perspective, in 1993, Breda et al described the first case of laparoscopic nephrectomy with vaginal extraction of the specimen [2]. In 2002, Gill et al reported the technical details and outcomes of laparoscopic nephrectomy with vaginal extraction in a series of 10 cases [3]. In both of these reports, the vagina was used only for specimen extraction. In the laboratory, in 2004, Gettman et al initially reported transvaginal nephrectomy with transabdominal assistance in six farm pigs, with the entire procedure being completed exclusively transvaginally in one animal [4]. In 2007, Lima et al performed combined NOTES transvesical and transgastric nephrectomy [5], and Clayman et al reported hybrid transvaginal porcine nephrectomy [6]. In 2008, Isariyawongse et al [7] and Matthes et al [8] performed transvaginal and transgastric nephrectomy, and Box et al reported hybrid robotic transvaginal NOTES nephrectomy [9], all in the porcine model. Recently, Haber et al reported pure transvaginal NOTES nephrectomy in five pigs [10], and Aron et al reported pure transvaginal NOTES nephrectomy in human cadavers [11].

In the clinical setting, two pioneering reports of hybrid NOTES nephrectomy are available. Branco et al reported the first hybrid NOTES nephrectomy for a nonfunctioning kidney using two transabdominal trocars, one umbilical and one extraumbilical [12]. Alcaraz et al reported hybrid transvaginal NOTES nephrectomy in which the transvaginal route was used only for placement of the laparoscope and ultimate specimen extraction; all intraoperative technical steps of the procedure were performed transabdominally via two extraumbilical laparoscopic trocars [13]. Thus, in both of these reports, extraumbilical trocar was employed.

We report our stepwise technique development and, to our knowledge, the first successful clinical case of NOTES hybrid transvaginal radical nephrectomy without any extraumbilical trocars.

2. Materials and methods

After performing experimental porcine and human cadaver work and obtaining institutional review board (IRB) approval, we attempted NOTES hybrid transvaginal nephrectomy in four patients (three in Cleveland, OH, USA; one in Caracas, Venezuela) between August 2008 and March 7, 2009. During informed consent, patients were informed about risks, benefits, alternatives, and personnel and the novelty of NOTES hybrid nephrectomy. They were informed that transabdominal access via the umbilicus would be secured as a matter of routine in each case and that, at the surgeon's discretion, the procedure would be converted to standard laparoscopic surgery on failure to progress.

Each patient was informed that such elective conversion to standard laparoscopy was not a complication but rather surgical prudence because of the novelty of this procedure.

For the first three cases, only relevant aspects of the surgical technique are described briefly; the surgical technique in the fourth case is described in detail. In the first case, right radical nephrectomy was indicated for a 6-cm renal mass. During transvaginal open posterior colpotomy and insertion of the R-port with its introducer by the gynecologic surgeon, rectal entry occurred. The introducer of the R-port is straight, rigid, and pointed; it is likely that the introducer was inserted at a posteriorly inclined angle, leading to a 2-cm sharp rectal entry. Additionally, the vaginal port was inserted without transabdominal laparoscopic monitoring. After conversion to standard laparoscopic surgery, the 2-cm injury in the sigmoid colon was suture repaired, the right radical nephrectomy was completed in routine manner, and the intact specimen was extracted transvaginally without any post-operative sequelae. In the second case, right radical nephrectomy was indicated for an 8-cm upper-pole mass. Transvaginally, we were able to identify, transect, and laterally retract the ureter; to dissect the lower renal pole; and to control the renal artery with an ENDO GIA stapler. Our inability to adequately and consistently medially retract the duodenum and the overlapping liver, combined with the high location of the large tumor, precluded safe dissection of the renal vein and the suprarenal region. After converting to standard laparoscopy, the radical nephrectomy was completed, and the specimen was entrapped and extracted transvaginally. In the third patient, during left simple nephrectomy for poorly functioning hydronephrotic kidney, individual control of the left renal artery and vein was achieved transvaginally with the ENDO GIA stapler; transumbilical assistance was limited to medial retraction of the colon and placement of Hem-o-lock clips, as necessary. During suprarenal mobilization, gradual bleeding was encountered. On conversion to standard laparoscopy, an unexpected upper-pole vessel was identified and secured, and left nephrectomy was completed.

2.1. Case report

A 65-yr-old female patient was referred with the diagnosis of an incidental left renal mass. Computed axial tomography revealed an organ-confined, 6 × 6-cm, enhancing, central, infiltrating, irregularly shaped mass in the lower pole of the left kidney with evidence of neovascularity, along with a normal opposite kidney (Fig. 1). The patient's serum creatinine was 1.1 mg/dl. She was 1.5 m tall, weighed



Fig. 1 – Computed tomography scan image showing the 7-cm left lower-pole renal mass.

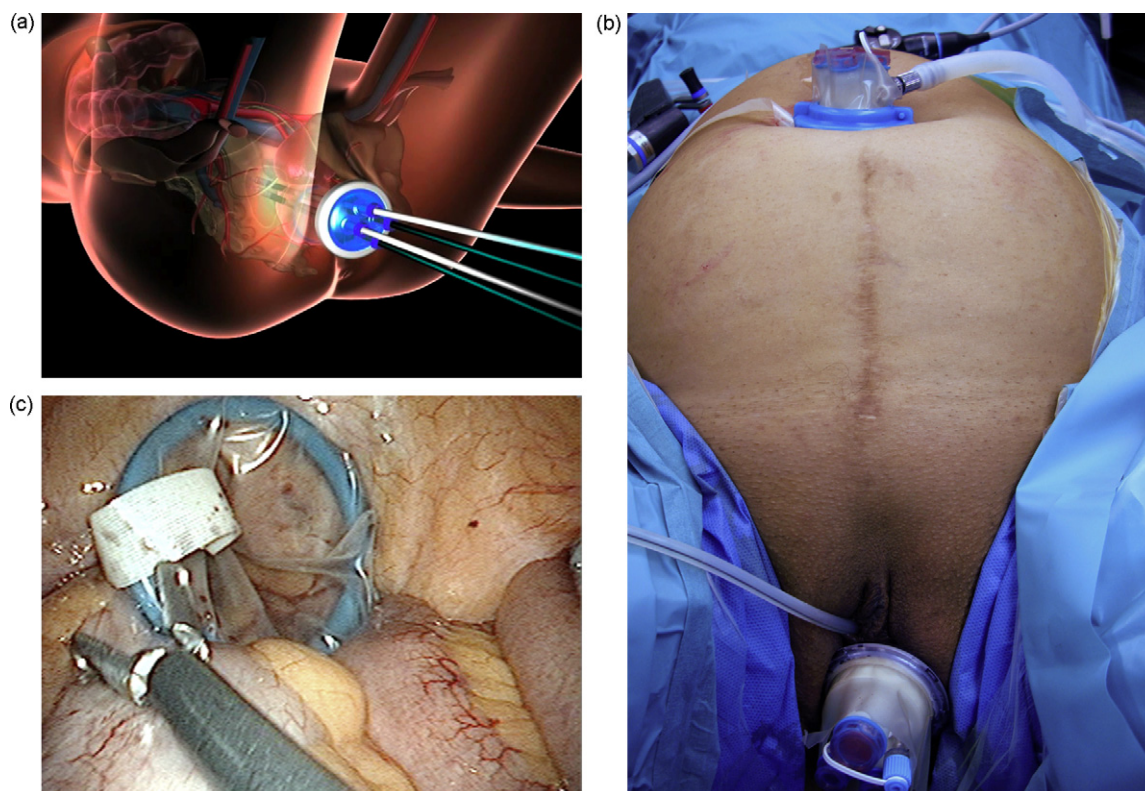


Fig. 2 – (a) Diagrammatic representation of the multichannel transvaginal port. (b) External picture of the patient with the multiaccess three-channel R-Port in position transvaginally and transumbilically. The ports are inserted with the patient supine with lithotomy and Trendelenberg tilt. Once the positions are placed, the table is rotated to the 45° position, maintaining the lithotomy and Trendelenberg positions. (c) Internal picture showing the inner ring of the transvaginal port in position in the cul de sac. It must be noted that absence of the uterus helps in providing adequate space and orientation for internal ring deployment. It also helps in unrestricted entry of instruments from the transvaginal access.

65 kg, and had a body mass index of 29.7. Past surgical history included open surgical hysterectomy for benign disease via a midline infra-umbilical incision. The patient was informed about her various surgical options. She opted for NOTES hybrid transvaginal radical nephrectomy. After IRB approval, informed written consent was obtained from the patient. Surgery was performed on March 7, 2009 (RS).

2.2. Surgical technique

After general anesthesia, the patient was positioned in the 45° right lateral decubitus position, with legs in moderate lithotomy position to allow vaginal access. All bony prominences were meticulously padded, and extremities were maintained in neutral position. A 2.5-cm Z-plasty incision was made within the umbilicus, and a three-channel R-Port (Triport; Advanced Surgical Concepts, Dublin, Ireland) was inserted into the peritoneal cavity and secured. Using a 5-mm, zero-degree laparoscope with a flexible tip (EndoEYE; Olympus Medical, Tokyo, Japan), the abdomen and pelvis were inspected for surgical adhesions, which were lysed under direct vision. Using a finger inserted per vagina, the posterior vaginal fornix was tented upward into clear laparoscopic view. Umbilically inserted ultrasonic shears (SonoSurg; Olympus Surgical, Tokyo, Japan) were used to create a 2–3-cm wide, full-thickness incision in the vaginal vault, through which a transvaginal 3-lumen R-Port was inserted into the pelvis and secured (Fig. 2a–c). Visualization for the procedure was provided by the transvaginal 5-mm, 30° EndoEYE laparoscope. The essential technical aspects of laparoscopic nephrectomy were duplicated. Using a transvaginal suction cannula for retraction and a J-hook, the line of Toldt was incised and the left colon was mobilized medially to identify the psoas muscle. Continued medial traction on the

colon was maintained by a grasper inserted umbilically. Transvaginally, the left ureter was identified, dissected, and sectioned with scissors.

The renal hilum was identified, and the colon was mobilized with retraction by a bariatric aspiration cannula inserted transvaginally. The EndoEYE was now inserted transumbilically, and the renal artery was dissected individually by a combination of transvaginal and umbilical manipulations. The renal artery was clipped with Hem-o-lock clips (Weck Closure Systems, Research Triangle Park, NC, USA) introduced umbilically. Using a combination of transvaginal and umbilical dissection and retraction, three separate renal veins were identified and dissected. These veins were transected with an ENDO GIA stapler inserted umbilically (Fig. 3a and b). The remainder of the kidney was then mobilized circumferentially, taking care to appropriately retract and protect the spleen and the pancreas. An ENDO CATCH II bag was inserted transvaginally under laparoscopic vision from the umbilicus. The specimen was extracted intact through the vagina. The colpotomy incision was suture repaired laparoscopically through the umbilical R-Port using 2-0 vicryl sutures (Fig. 4).

3. Results

Total operative time was 3.7 h, including achieving vaginal access. Estimated blood loss was 150 ml. There were no intraoperative complications. Hospital stay was 1 d. Post-operatively, the patient took only one tablet of non-narcotic analgesic medication for left thigh pain, ostensibly due to intraoperative positioning. She resumed normal activities within the home in 3 d. On day 7, her visual analog scale (VAS)

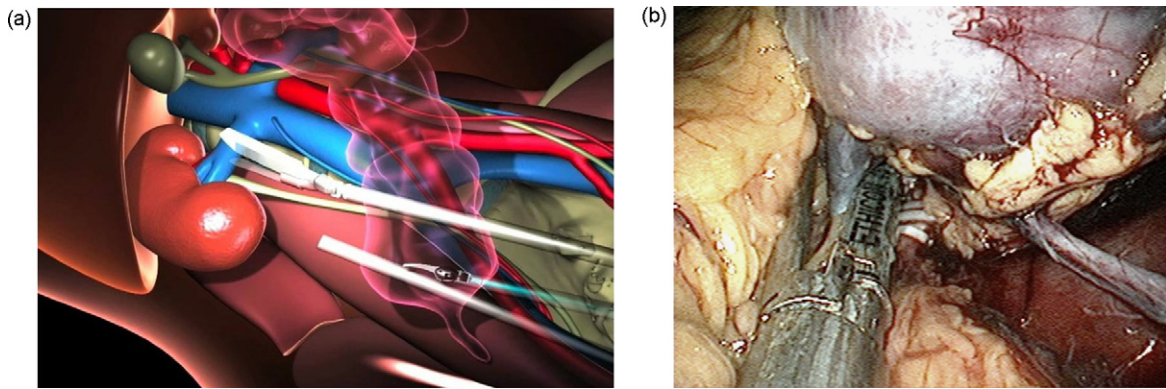


Fig. 3 – (a) Diagrammatic representation of the use of rigid and articulating instruments during our cadaveric NOTES experience. (b) Internal view of hilar control. The renal artery has already been clipped and the renal vein is being controlled with an ENDO GIA stapler. Using the transumbilical access enables precise individual dissection and control of the renal pedicle.

score was 3. Intact specimen weight was 220 g, and final pathology confirmed a pT1b 7 × 6.5 × 6-cm grade 2 clear-cell renal cell carcinoma with negative surgical margins (Fig. 5). The patient was readmitted postoperatively for fever. The CT scan showed a collection in the renal fossa that was drained percutaneously without sequelae.

4. Discussion

Recent advances in laparoscopic surgery have focused on further reducing procedural morbidity and moving toward a *scarless* outcome. NOTES and laparoendoscopic single-site surgery (LESS) are two such approaches that share this common philosophical premise. Over the past few years, significant research efforts have gone into developing NOTES for various surgical applications. While progress

in the laboratory has been considerable, the clinical application of NOTES has understandably lagged.

Our transvaginal NOTES nephrectomy program has evolved as a stepwise progression leading to the clinical success reported in this paper. In 2002, we reported the initial series employing a natural orifice (vagina) for intact specimen extraction after standard four-port laparoscopic radical nephrectomy [3]. Working toward a scar-free approach, more recently we performed single-port transumbilical LESS radical nephrectomy exclusively through the umbilicus in two patients; the intact entrapped specimen was extracted transvaginally, leaving no visible abdominal surgical scar whatsoever (unpublished data). With regard to pure transvaginal NOTES nephrectomy without any transabdominal

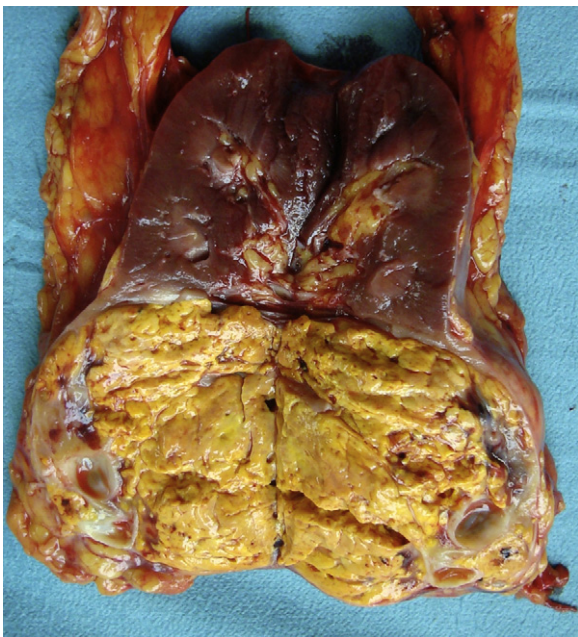


Fig. 4 – Intact excised specimen shows the lower-pole tumor. Note the intact perinephric fat around the specimen that finally revealed a grade 2 clear-cell renal cell carcinoma with negative surgical margins.



Fig. 5 – External image showing the abdomen postoperatively without any visible scar from the procedure. The midline scar of the prior hysterectomy is seen.

assistance, we next investigated the acute porcine model using the flexible gastroscope platform [10]. A flexible dissecting forceps was passed through its working channel, and a rigid retracting instrument or stapler was inserted alongside the gastroscope. Although successful in the porcine model, we believe this flexible platform lacks the tensile strength, versatility, and robustness required for a complex clinical procedure such as human nephrectomy.

As the next step in developing pure NOTES nephrectomy for ultimate clinical application, we investigated the human cadaver model using a rigid transvaginal platform [11]. This procedure utilized a multichannel R-Port, straight and articulating laparoscopic instruments, and a rigid 10-mm, 30° laparoscope (EndoEYE, Olympus Medical, Japan). Because the human cadaver better approximates the anatomy of a live human radical nephrectomy than does, say, the porcine model, it afforded us a more clinically realistic appreciation of potential anatomical and technical problems. Another purpose of the cadaveric experiment was to determine whether a wide-caliber multichannel vaginal port and robust rigid laparoscopic instruments can facilitate clinical nephrectomy.

With the female cadaver secured in steep Trendelenburg lithotomy position and target side rotated up 30–45°, a three-channel R-Port was placed in the umbilicus to monitor the transvaginal procedure. A four-channel Quad-Port was placed through the posterior vaginal fornix into the pelvic cavity. All of the following operative steps were achieved transvaginally using straight/articulating laparoscopic instruments: (1) mobilize/dissect colon and ureter; (2) individually dissect/control renal artery and vein with clips and ENDO GIA stapler, respectively; (3) mobilize kidney completely; (4) entrap intact specimen in ENDO CATCH bag; and (5) extract specimen transvaginally.

Three nephrectomies (two right, one left) were successfully performed; one left-sided procedure was aborted due to adhesions from prior pelvic surgery. In the first two cadavers, transient umbilical assistance was necessary toward the end of the procedure to release postero-superior attachments between the upper-pole kidney and the diaphragm. In the

final case, we were able to perform even this dissection with a transvaginal flexible gastroscope. Thus, in the final cadaver, we were able to confirm the technique of pure transvaginal NOTES nephrectomy, without any transabdominal assistance whatsoever. This cadaveric study provided several learning points: (1) extralong (bariatric) laparoscopic instruments possess the requisite tensile strength and reach to enable clinical transvaginal nephrectomy, (2) the cephalad aspect of the hilum and the upper-pole attachments are problem areas for transvaginal dissection, and (3) flexible instruments can be used adjunctively if occasional operative angles are suboptimal with rigid instruments [11].

In our initial three clinical cases, the procedure could not be completed transvaginally but important milestones were reached. First, the technique of transvaginal deployment of the R-Port was refined. Second, the suitability of a rigid platform, including optics and instruments, for transvaginal NOTES surgery was confirmed clinically. Third, incrementally increasing portions of the actual intraoperative steps, including individual dissection and control of the renal artery and/or vein transvaginally in cases 2 and 3 were realized. Fourth, timely conversion to standard laparoscopy facilitated completion of the procedure, including rectal repair in case 1, without post-operative sequelae. Finally, and most important, we gained increasing confidence with regard to intraoperative visual orientation and laparoscopic dissection from the transvaginal route. Learning points from the clinical cases are summarized in Table 1: (1) until vaginal access techniques are standardized, transabdominal visual guidance during vaginal port placement is advisable; (2) larger kidney specimens, especially upper-pole tumors, are unsuitable for the transvaginal approach at this time; and (3) transvaginal mobilization of the upper-pole kidney requires use of extralong articulating, or flexible instruments. In these three cases, all specimens were extracted transvaginally; no procedure was converted to open surgery.

Based on the above experimental and clinical work performed in Cleveland, the successful NOTES case was performed in Venezuela (RS). An R-Port was secured in the

Table 1 – Lessons learned from our initial three cases of attempted natural orifice transluminal endoscopic surgery (NOTES) hybrid transvaginal nephrectomy

	Case 1	Case 2	Case 3
Operative procedure	Right radical nephrectomy	Right radical nephrectomy	Left simple nephrectomy
Steps accomplished transvaginally	None	<ul style="list-style-type: none"> • Transvaginal access • Colon mobilization • Ureteral division • Arterial mobilization and clipping 	<ul style="list-style-type: none"> • Transvaginal access • Colon mobilization • Ureteral division • One artery clipping • Vein stapling
Problem encountered	Rectal injury during transvaginal access	Failure to progress because of large (8 cm) upper-pole mass	Bleeding and slow progress during upper-pole mobilization
Final disposition	<ul style="list-style-type: none"> • Conversion to standard laparoscopy • Rectal injury repaired laparoscopically and radical nephrectomy completed without sequelae 	Conversion to standard laparoscopy	Conversion to standard laparoscopy
Lessons learned	<ul style="list-style-type: none"> • Vaginal access should occur under abdominal visualization • Do not use R-port introducer blindly 	<ul style="list-style-type: none"> • Proper case selection is critical • Large specimens are unsuitable for NOTES 	<ul style="list-style-type: none"> • Extralong articulating instruments are needed for upper-pole mobilization

umbilicus, and another one was secured in the vagina. Because our patient required a radical nephrectomy for tumor with wide excision for negative margins, we elected to place a multichannel port in the umbilicus (instead of a standard laparoscopic port). The greater versatility of this port enabled precise and individual control of the renal artery and vein at some distance from the specimen, in proximity to the vena cava. We believe individual control of the renal artery and renal vein, rather than en bloc hilar stapling, is preferable, whenever feasible. The 5-mm, zero-degree, flexible-tip digital laparoscope provided excellent visualization and minimized clashing with the retracting and dissecting instruments inserted transvaginally.

Our hybrid NOTES nephrectomy reported in this paper differs from the Branco et al [12] and Alcaraz et al [13] case reports in two important respects: (1) the transvaginal approach was used to perform a majority of our intraoperative dissection, and (2) our patient had no extraumbilical skin incisions whatsoever.

Although consensus is lacking with regard to which steps must be performed transvaginally during a hybrid procedure for it to qualify as NOTES, we feel that, at a minimum, the laparoscopic visualization plus actual intraoperative dissection must be performed transvaginally to differentiate transvaginal hybrid NOTES from transabdominal laparoscopy and vaginal extraction. *Complete or pure* NOTES should involve no transabdominal port placement at all. Any use of a ≥ 5 -mm laparoscopic port inserted through an abdominal skin incision (as opposed to a 2-mm port inserted via only a skin puncture) should be designated as hybrid NOTES. Clearly, if a transabdominal port is inserted intraoperatively at all for whatever reason, it behooves the surgeon to utilize this port optimally to enhance procedural efficacy and patient safety. Akin to a standard laparoscopic port, umbilical placement of the R-Port results in a nonvisible hidden scar, yet provides significantly greater versatility.

Several aspects of instrumentation and patient selection deserve mention. Instruments (Appendix A) that facilitate the procedure include the deflectable-tip digital endoscope, which can provide a perpendicular view to the kidney and hilar structures, even from the transvaginal vantage point. Extralong NOTES-specific articulating instruments are currently under development and may prove invaluable for enabling transvaginal surgery. Transvaginal entry and access to the upper retroperitoneum are facilitated significantly if the patient has had prior hysterectomy. The intact uterus compromises secure deployment of the internal retention ring of the R-Port or Gelpport and can also hinder instrument exchanges intraoperatively. The transvaginal approach is more difficult for obese patients and for larger specimens.

As a parallel development, in recent years, single-port surgery or LESS surgery [14] has evolved rapidly to the point of being used for multiple urologic applications. LESS surgery comprises techniques that employ a single skin incision for performing laparoscopic surgery. Various centers have already reported their experience with a range of ablative and reconstructive LESS urologic procedures, with encouraging early results [15–19]. Thus, within a short time span,

LESS has substantially overtaken NOTES with regard to actual clinical application in urology.

Going forward, we anticipate that, in the optimal patient with suitable body habitus, a purely transvaginal NOTES nephrectomy will become reality. To move from the anecdotal to the routine, advances in technology, including newer robotic systems, will be necessary. At this writing, transvaginal NOTES nephrectomy may be better suited for patients with a benign indication, in whom one can control the renal vessels close to the kidney with judicious en bloc fires of the ENDO GIA stapler. Alternatively, such benign kidneys can be more efficaciously excised by LESS surgery via a single hidden intraumbilical incision and removed by morcellation, thus rendering the vaginal incision redundant. Given the above points, we believe that for the immediate future, transvaginal NOTES nephrectomy will remain an investigational procedure with limited indications in highly selected patients.

5. Conclusions

We report the initial case of NOTES hybrid transvaginal radical nephrectomy for tumor with umbilical assistance, without any extraumbilical skin incisions. Further technical and technological innovation is necessary to elevate this approach beyond mere anecdote.

Author contributions: Rene Sotelo had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Desai, Gill, Sotelo, Aron.

Acquisition of data: de Andrade, Fernández, Ramirez, Moreira, Berger.

Analysis and interpretation of data: Di Grazia, Carmona.

Drafting of the manuscript: Sotelo.

Critical revision of the manuscript for important intellectual content: Desai, Gill, Aron, Carmona.

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Supervision: Gill, Desai, Aron, Sotelo.

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Appendix A

Instruments used:

1. R-Port (Advanced Surgical Concepts, Dublin, Ireland)
2. Laparoscope, 5-mm, zero-degree, flexible tip (EndoEYE, Olympus Medical, Tokyo, Japan)

3. Flexible articulated 5-mm scissors, needle holder (Cambridge Endo)
4. Clamp grip, disposable, 5 mm (folded manually)
5. Laparoscopic needle holder, 5 mm, straight (Olympus Medical, Tokyo, Japan)
6. Suction Cannula, 5 mm irrigation (one manually bent; one 50-cm long)
7. Monopolar 5-mm J-hook electrode (hook)
8. Ultrasonic scissors, 5 mm (SonoSurg, Olympus Medical, Tokyo, Japan)
9. Hem-o-lock clips polymatrix, 5 and 10 mm (Hem-O-Lock, Weck Closure Systems, North Carolina, USA)
10. Linear automatic suture device, 12 mm (ENDO GIA Universal stapler)
11. Loading ENDO GIA universal 45-3,5 mm
12. ENDO CATCH II bag (Covidien, Norfolk, CT, USA)

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