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Transvaginal Laparoscopically-Assisted Endoscopic Appendectomy: A Major Hybrid Natural Orifice Transluminal Endoscopic Surgery Case Series in Asia

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This paper represents an evaluation of a hybrid approach to natural orifice transluminal endoscopic surgery (NOTES) and its performance relative to conventional procedures. Globally, numerous institutions have successfully implemented minimally invasive surgeries by applying NOTES techniques and achieved decreased morbidity while performing incision-less surgery. However, these techniques are still not common in surgical practice in China and Pakistan. Documenting the experiences and challenges encountered in implementing NOTES in such environments can provide guidance for NOTES implementation elsewhere. From May 2010 to April 2012, 16 human transvaginal appendectomies were carried out applying a hybrid NOTES technique using a solo-umbilical trocar, which provided a safe access for laparoscopic assistance during surgical procedure. After removal of the appendix transvaginally, the colpotomy was sutured

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under direct vision with absorbable stitches. The outcomes of cases treated with hybrid NOTES techniques were compared to those of conventional laparoscopic appendectomy. All patients underwent a successful surgical procedure with no intra- or postoperative complications and provided no specific complaints during the 10th day and a monthly follow-up for 2 years. The patients convalesced promptly with healthy and satisfactory cosmetic results. Compared to conventional laparoscopic appendectomy, the hybrid NOTES operation had less postoperative pain, lower cost, and shorter hospitalization. Hybrid NOTES procedures can be performed safely using a solo-umbilical trocar. Our initial experience reveals that this hybrid technique is practically feasible and associated with minimal postoperative pain, reasonable convalescence time, and improved cosmetic outcomes.

Key words: Natural orifice translumenal endoscopic surgery (NOTES) – Appendectomy – Endoscopy – Transvaginal – Laparoscopy

Surgical techniques have seen tremendous progress in recent decades, aimed at applying less aggressive surgical methodology while maintaining full ability to achieve resection or repair. One of the most important developments in this respect is the advent of natural orifice translumenal endoscopic surgery (NOTES). Despite the difficulties in implementing NOTES in new environments, surgical domains steadily embrace this minimally invasive surgical technique. Apart from the obvious avoidance of an abdominal wall incision and the associated complications, the NOTES approach generally minimizes postoperative pain and provides highly satisfying cosmetic results in comparison to conventional laparoscopic procedures. Nonetheless, NOTES still is associated with various technical obstacles, such as achieving safe access to the targeted organ while creating a leakproof suture line, maintaining spatial orientation, and avoiding complications caused by abdominal infections.

Gettman *et al*[1] initially reported the feasibility of NOTES techniques in 2002 by performing transvaginal nephrectomy in an animal model, and Kalloo *et al*[2] performed transgastric liver biopsies in a porcine model in 2000 and reported the results in 2004. Subsequently, additional NOTES procedures using a transgastric route, such as gastrojejunostomy,[3] tubal ligation,[4] cholecystectomy,[5] and pancreatectomy[6] were successfully applied in animal models. In addition, various transluminal accesses such as transcolonic, transurethral, and transvaginal explorations were successfully performed.[7–9] The success in animal models prompted exploration of NOTES techniques in a clinical setting as well.

NOTES was first attempted in humans by Reddy and Rao; however, their work was only incompletely reported in the scientific literature, thus delaying widespread implementation of NOTES. Nevertheless, since 2007, application of transvaginal NOTES procedures in humans for cholecystectomy[10–12] and tubal ligation[13] has been reported. In 2008, Palanivelu *et al*[14] reported their experience with transvaginal endoscopic appendectomy in 6 patients; 1 operation was successfully performed using pure NOTES technique, whereas the rest required conversion to either laparoscopically assisted transvaginal endoscopic appendectomy or conventional laparoscopy. Thus, the literature indicates that NOTES represents an important avenue for the future development of improved surgical procedures.

Implementation of NOTES in novel settings is, however, not straightforward, and this is an area in which we seek to contribute. For more than 2 decades, our research team has been trying to advance the use of minimally invasive surgery at our institution. In 1992, our team performed a laparoscopic cholecystectomy (LC) and laparoscopic exploration of both intra- and extrahepatic bile ducts, acquiring abundant laparoscopic experience in the field of minimally invasive surgery.[15] Since December 2007, we have been vigorously researching the feasibility of minimally invasive procedures in live pig models to ensure operative safety and to identify an optimal method for the clinical application of NOTES techniques. To gain access to the peritoneal cavity, various endoscopic routes were investigated in porcine models, among which the transvaginal channel was considered the best approach for performing cholecystectomy and appendectomy. Hence, we[16] performed the use of a hybrid NOTES technique for transvaginal cholecys-

Table 1 Demographic data for 16 transvaginal appendectomy patients

Age (years)	42.5 ± 8.73
BMI (kg/m^2)	21.25 ± 2.94
ASA physical class 1:2	11:5
Symptomatic appendicitis	9
Appendiceal polyps	7

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

tectomy in 2010 for the first time in China. The relative success of this novel mode of hybrid NOTES compared to conventional approaches remains unexplored.

Since May 2010, we have successfully carried out a series of 16 transvaginal laparoscopically assisted endoscopic appendectomies using hybrid NOTES techniques. Our experience can be useful for practitioners elsewhere who may be contemplating the implementation of NOTES. Furthermore, we feel that determining the relative performance of hybrid NOTES would be useful, as this approach is relatively easy to be introduced in centers with little experience. Thus, here we report our preliminary experience in using the hybrid NOTES techniques for transvaginal appendectomies in China and Pakistan.

Methods

Patient cohort

Our NOTES research team at Qilu Hospital, Shandong University in China and Lady Reading Hospital in Pakistan is a devoted multidisciplinary group including gynecologists, endoscopists, and surgeons. We performed a large number of animal experiments for about 16 months before performing an initial clinical hybrid NOTES operation. Patients (Table 1) with symptomatic appendicitis or enlarged appendiceal polyps and no severe pelvic adhesion due to a previous surgery were given the option of transvaginal endoscopic appendectomy or conventional laparoscopic surgery. The final decision regarding the operative methodology was made by the patient.

In our cohort, randomly 16 out of 52 patients chose the hybrid NOTES procedure, whereas 36 patients underwent conventional laparoscopic appendectomy (CLA) as a consequence of patient objections, which were based on either cultural objections towards the hybrid NOTES approach or on strong conservative opinions with regard to medicine of the patient. Each patient was consulted, and full consent was obtained. A routine blood test, gynecologic examination, computed tomography (CT) scan, and abdominal ultrasonography were performed preoperatively. The patients were kept on nothing per oral overnight, and prophylactic antibiotics were given preoperatively.

Execution of Hybrid NOTES

The patient, placed in a dorsal lithotomy position, was given general anesthesia, and a capnoperitoneum was insufflated via a Veress needle in the umbilical fundus through a 5-mm incision. A 5-mm trocar replaced the Veress needle to introduce a 30° laparoscope for a complete abdominal cavity inspection. An experienced gynecologist then performed a posterior cul-de-sac colpotomy of 1 cm under laparoscopic guidance, while the patient was in a 30° Lloyd–Davies position. Through this incision, a 7-mm soft silicone tube with a 5-mm extra-long grasper (YOUSHI Medical Instruments Co Ltd, Zhejiang, China) was inserted to retract the appendix (Fig. 1A). Along with the soft silicone tube and grasper, we used a standard single-channel flexible gastroscope to enter the peritoneal cavity (Olympus Optical Co Ltd, Tokyo, Japan; Fig. 1B). For further steps, the endoscope alone provided the abdominal view rather than the laparoscope.

The appendix dissecting instruments were introduced through the umbilical trocar. While the patient was still in the Lloyd–Davies position, peritoneoscopy was performed, after which the ileocecal junction was located, resulting in exposure of the appendix. Starting from the base of the appendix, the mesoappendix was prepared using coagulation forceps to begin the initial fenestration. The appendicular artery was clipped with laparoscopic clips (Fig. 1C), the base of the appendix was ligated with an endoloop (Fig. 1D), and laparoscopic scissors were used to dissect appendix through the umbilical trocar. The appendix was mobilized from the ileocecal site with the grasper and an electric hook (Fig. 1E).

After the appendectomy, the laparoscope was again introduced through the umbilical trocar to guide transvaginal retrieval of the specimen (Fig. 1F). Under direct vision, 2/0 absorbable threads were used to seal the posterior cul-de-sac colpotomy with continuous sutures (Fig. 1G). The vagina was packed with sterile gauze, maintaining prevention of bleeding and fistula formation. No drainage was placed. Postoperatively, the patients were routinely given a patient-controlled analgesia (PCA) pump, which

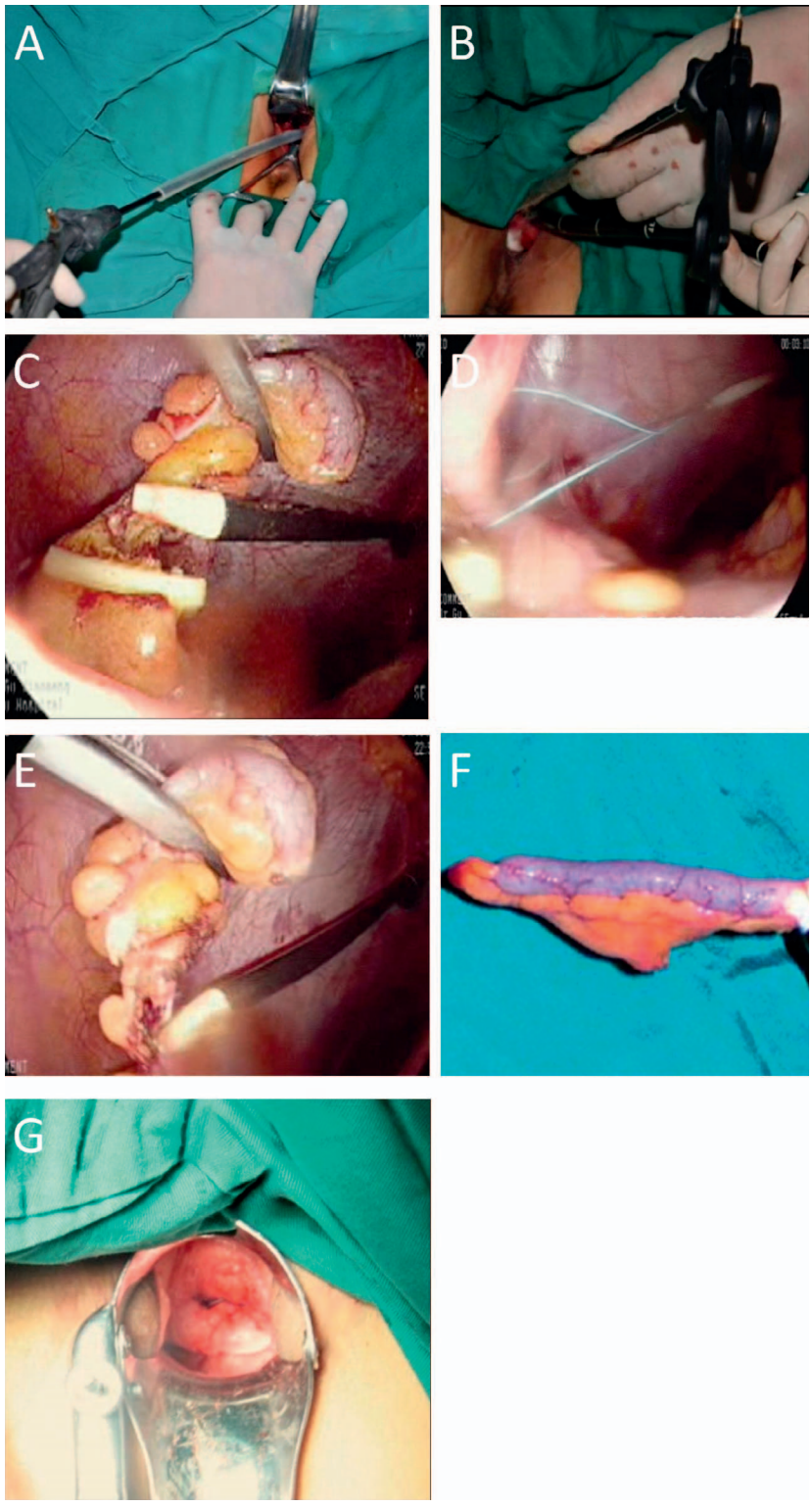

Fig. 1 Illustration of the procedure. (A) Initiation of the procedure with introduction of additional instrumentation. A soft silicone tube facilitates the transvaginal introduction of a 5-mm extra-long grasper. (B) Transvaginal introduction of a single-channel flexible gastroscope to the peritoneal cavity. (C) Clipping of the appendicular artery. (D) Ligation of the base of the appendix by an endoloop through the umbilicus. (E) Mobilization of the appendix from the ileocecal site with an electric hook introduced through the umbilical trocar. (F) Retrieval of the appendix. (G) Uninterrupted suturing to close the vaginal defect under direct visual control.

administered 10 mg tropisetron and 1 mg fentanyl. After 24 hours, the vaginal packing was removed.

Contraindications

Because this was a new technique in our hospital, initially, we selected relatively simple cases for which to perform the hybrid NOTES procedure. The inclusion criteria for hybrid NOTES consisted of patients presenting with mild clinical symptoms. Patients below the age of 20 years or above 65 years with a body mass index (BMI) greater than 30 were excluded. In addition, unmarried women or women with an active reproductive wish and patients with an increased risk of medical comorbidities, bleeding, or clotting disorders were avoided as well. Contraindications also included deep endometriosis, suspected adnexal lesions, previous pelvic surgery, and a history of pelvic inflammatory disease.[17]

After the first 4 successful hybrid NOTES operations were performed with no intra- or postoperative complications, patients with a history of previous pelvic and abdominal surgery or obesity were also considered to meet the candidacy criteria. One patient with a history of hysterectomy, and 4 patients with previous abdominal surgeries such as liver resection and cesarean section were also operated successfully.

Evaluation of hybrid NOTES performance

To evaluate the performance of the hybrid NOTES procedure, the results were compared with those in 36 patients who simultaneously underwent CLA. SAS version 9.1.3 (SAS Institute Inc, Cary, North Carolina) was used to perform statistical analysis of the data. Continuous variables are reported as mean $\pm$ standard deviation values. Student's t test was used to detect and analyze significant differences ($P < 0.05$).

Results

From May 2010 through April 2012, 16 appendectomies were carried out with the hybrid NOTES technique. For all patients, transvaginal laparoscopically-assisted endoscopic appendectomies (TLAEAs) were successfully executed without any intraoperative complications or conversion either to the conventional laparoscopy or open surgery. With retroflection, the endoscopic vision provided a comprehensive orientation within the surgical site. The duration of the surgery was 86.88 $\pm$ 36.62 minutes (range, 40–190 minutes). Notably, the first case had a recorded time of more than 3 hours, whereas that of later consecutive cases was less than 2 hours. Blood loss was statistically approximated at 24.5 mL and thus negligible.

Postoperatively, none of the patients experienced any complications such as leakage, hemorrhage, or problems related to colpotomy and vaginal or abdominal visceral pain. Oral intake was allowed on the same evening postoperatively. In our cohort, 9 patients were discharged on the second postoperative day (POD2), 3 patients on POD3, and 1 patient on POD4. Three elderly patients required hospitalization for a further 5 days. The average hospital stay was 2.9 days. Compared to the conventional laparoscopic operation, the hybrid NOTES approach resulted in a small abdominal incision, mild pain, and less analgesic requirement, and early postoperative ambulation. Patients who underwent hybrid NOTES, displayed rapid recovery, a short average hospitalization, a substantially reduced number of further treatments, and satisfactory cosmetic results regarding the abdominal wall with almost no visible operation-induced scaring (Table 2). The patients completely recovered and resumed daily life activities within 10 days postoperatively. During 2 years of regular monthly check-up and follow-up, no complications were reported, and the patients were found in a healthy condition with no apparent scars. Thus, we concluded that hybrid NOTES has been implemented successfully in our center.

Discussion

Although NOTES is rapidly becoming the operation of choice for a large variety of cases, its implementation in new settings is still not straightforward. To the best of our knowledge, this sequential case series of transvaginal endoscopic appendectomies constitutes the first clinical report of this procedure ever published in China and Pakistan and represents a major clinical hybrid NOTES series in Asia. Our exploratory results certify the feasibility and safe application of the hybrid NOTES approach to transvaginal laparoscopically assisted endoscopic appendectomy in settings comparable to ours.

A main purpose of the NOTES procedure is the possibility to obtain entirely scarless surgical results. Regarding the use of transcolonic or transgastric orifices, they are still considered risky and remain controversial. Moreover, the potential risks of postoperative infection and internal leakage remain significant. Despite the large number of gastrostomy

Table 2 Clinical results comparing NOTES to conventional laparoscopy appendectomy (CLA) in our initial patient cohort

	NOTES (n = 16)	CLA (n = 36)	|t|	*P* value
Pain scores (VAS)	2.06 ± 0.85	4.56 ± 1.38	7.94	<0.0001
Time of PCA pump requests (h)	18.50 ± 3.20	30.78 ± 4.41	9.99	<0.0001
Operation time (min)	86.88 ± 36.62	56.47 ± 8.35	3.28	0.0048
Blood loss (mL)	24.5 ± 2.56	24.25 ± 4.05	0.23	0.8212
Hospitalization (days)	2.88 ± 1.20	5.81 ± 0.98	9.27	<0.0001
Cost of hospitalization (10^4¥)	1.20 ± 0.07	1.48 ± 0.19	7.60	<0.0001

P values calculated using Student's *t* test.

PCA, patient-controlled analgesia; VAS, visual analog scale.

techniques explored through animal experimentation, a safe gastric wall closure remains challenging and the procedures are associated with peritonitis and fistula formation.[18–20]

In contrast, the transvaginal approach is superior to the transgastric approach and has been used by gynecologists, both therapeutically and diagnostically, since the early 1900s. Dmitri von Ott described the first ventroscopy through colpotomy in 1901,[21] and in 1949, gynecologists incidentally performed the first transvaginal appendectomy during vaginal hysterectomy.[22] Importantly, with a slight endoscopic retroflection, the transvaginal approach provides a clear view of the appendix. A major limitation of transvaginal NOTES procedure is that it is only applicable in female patients. In addition, its implementation in a clinical setting requires substantial preparation.

In preparation for pure NOTES transvaginal appendectomies, we repeatedly performed animal experiments. Even though the current endoscopic instrumentation allows almost intuitive feasibility for performing pure NOTES, the inexperienced surgeons still face major unexpected obstacles, making the procedure initially risky and challenging. Transvaginal introduction of the grasper and endoscope has the tendency to cause occult injury to the surrounding internal organs, especially the uterine adnexa and the rectum. Moreover, endoclips are not completely occlusive, causing leakage, especially as they detach relatively easily and are not designed to properly clip the vermiform part of the appendix. In addition, both the endoscope and the operative instruments are positioned in a symmetrical manner, which can cause poor triangulation and hampering manipulation and operational efficacy. Consistent with our experience in this respect, Palanivelu *et al*[14] reported that due to technical problems with pure NOTES, cases were regularly converted to CLA. Bernhardt *et al*,[23] pursued NOTES, but in our study hybrid NOTES appears better suited for recurring subacute appendicitis rather than treatment of acute appendicitis. Thus, a view emerges that although pure NOTES is minimally invasive, it is fraught with technical difficulties that limit its application to highly selected cases of transvaginal appendectomy. Hence, the reports of recently introduced techniques, as we have provided in the present study, are important.

It is expected that NOTES will become safer and generally improved upon with its more widespread application. At present, there are no dedicated pure NOTES devices or platforms available for accomplishing completely scarless surgery, which is a shortcoming. Similar to the approach employed by others,[24,25] we modified the pure NOTES operation to a more hybrid technique involving laparoscopic assistance approaching through a solo-umbilical trocar. The transvaginal insertion and removal of the endoscope and other instruments, the measurement and maintenance of the capnoperitoneum, and the dissection and clipping of the vermiform appendix structure were monitored through a solo-umbilical trocar using conventional laparoscopic instruments.

Despite the occasional presence of moderate pelvic adhesion, laparoscopic guidance provides easy exploration of the pelvis and helps to prevent any injury that might occur in the peritoneal cavity during the surgical procedure due to lack of experience. It is difficult to retrieve the appendix with thin endoscopic graspers, which do not sustain a stable grip. In order to overcome this problem, we introduced a 60-cm-long, specially designed transvaginal grasper, which was placed in a soft silicone tube to prevent any injury due to multiple entries and to provide enough strength for retraction. Similarly, we expect that other centers will find the need to design and apply dedicated novel surgical instruments upon implementing hybrid NOTES, but

obviously further studies are needed to confirm this notion.

With the help of laparoscopic guidance, access through the vagina was rapid and easily obtained in our series of 16 patients. After the hybrid NOTES operation, the umbilical incision was invisible. The patients showed faster recovery with less pain compared to those who underwent CLA, as the vaginal incision is less painful and less exposed to infection in comparison to the abdominal wound. The hybrid NOTES operation was associated with less postoperative pain, a shorter stay and lower cost of hospitalization, and better cosmetic outcomes without any obvious visible scar on the abdominal wall. Usually, the patients were discharged on POD2, and postoperative recovery showed that this technique can be applied clinically without any complication. This excellent initial experience with hybrid NOTES indicates that its introduction in new centers is not necessarily problematic.

Transvaginal hybrid NOTES is still somewhat experimental, and thus, its complete risks remain unclear at present. For example, the possibility of infertility after a transvaginal hybrid NOTES procedure must be considered. Overall, we feel that further development and systematic comparison with conventional laparoscopic surgery remains warranted to ensure the efficacy and safety of NOTES procedures and to reduce risks and complications.

Conclusion

The outcomes in our case series, especially cosmetic and pain-related, were worthy and that specifically designed endoscopic instruments for pure NOTES procedures are not yet available, we believe that the hybrid technique using a solo-umbilical trocar is an excellent clinical approach to perform transvaginal appendectomy. This technique is more feasible and less risky because it provides a safe transvaginal access, bidirectional manipulation in the abdominal cavity, and a transumbilical view when required. Nevertheless, we recognize the need for further technical improvement of NOTES procedures.

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