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ORIGINAL ARTICLE

Ovarian cystectomy by transvaginal natural orifice transluminal endoscopic surgery versus laparoscopy: a randomized controlled trial

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Summary

Purpose: *To compare the effect of transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) and traditional porous laparoscopic surgery on ovarian function after the treatment of benign ovarian tumors.*

Methods: *The women subjected to ovarian cystectomy by V-NOTES /laparoscopy at a tertiary hospital between January 2017 and October 2021 were retrospectively analyzed.*

Results: *There were 80 women assigned randomly into the laparoscopy group (n=40) or V-NOTES (n=40) group. V-NOTES had better control over blood loss (BL) (p=0.015), operation time (OT) (p=0.001) and postoperative time of first ambulation (p=0.000) compared with laparoscopic surgery. Patients in V-NOTES group did not need analgesics after surgery (p=0.012). The levels of Hb (p=0.000), E2 (p=0.016), AFC (p=0.000), PSV (p=0.022), RI (p=0.000) and PI (p>0.05) decreased in the laparoscopy group postoperatively and the decrease was remarkable except for PI. The levels of LH (p=0.030) and FSH (p>0.05) were elevated after laparoscopic surgery. The levels of Hb (p=0.000), FSH (p=0.006), LH (p>0.05), E2 (p>0.05), PSV (p=0.032) and PI (p>0.05) decreased after V-NOTES treatment and the decrease was notable except for LH, E2 and PI. Mean AFC remained unchanged (p>0.05) and RI increased (p>0.05) after V-NOTES. Patients undergoing V-NOTES had a longer postoperative hospital stay than those undergoing laparoscopic surgery (p=0.000).*

Conclusions: *V-NOTES approach brought about much better intraoperative and postoperative outcomes, and a smaller effect on ovarian reserve compared to laparoscopic surgery.*

Key words: *laparoscopy, natural orifice transluminal endoscopic surgery, ovarian cystectomy, benign ovarian tumor*

Introduction

Benign ovarian tumor is one of the tumors with a high incidence in women of childbearing age, accounting for 1/4 to 1/3 of the female benign tumors. The typical main clinical symptoms are compression symptoms, lower abdominal pain and abdominal mass [1]. According to epidemiological investigations, in recent years, with the continuous change of people's lifestyle and environment, the incidence of benign ovarian tumors has shown an increasing trend and has caused serious impact on women's health and quality of life [2,3]. The pathogenesis of ovarian benign tumor is closely related to genetic and environmental factors. Its histological types are complex and prone to malignant transformation, so once diagnosed, active clinical intervention is required [4,5]. Surgical elimination is the primary principle in the treatment of benign ovarian tumors. Women of reproductive age usually have higher requirements for the preservation of ovarian structure and function and the cosmetic effect of the wound, so the selection of surgical methods for this disease is of great importance [6,7].

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As a traditional treatment for benign ovarian tumors, open surgery has a wide surgical field and can effectively remove tumors. However, it often causes greater trauma to patients, resulting in large intraoperative blood loss, slow postoperative recovery and postoperative complications such as urinary retention and incision fat liquefication [8]. Clinical studies have confirmed that surgery is easy to cause traumatic stress on the patient's body, which damages the immune function of patients and is not conducive to postoperative recovery. At the same time, normal ovarian tissue is not difficult to be destroyed during surgery, which affects the ovarian function of patients [6]. Patients may have abnormal endocrine function, reduced number of follicles and decreased quality of oocytes after surgery, leading to decreased fertility of women of reproductive age [9,10]. The large scar usually has serious impact on the appearance. Therefore, the selection of appropriate surgical treatment is of major importance. To reduce the tissue stimulation and injury caused by surgery in patients with benign ovarian tumor, and to ensure the normal ovarian structure and function as far as possible in women of reproductive age is a medical problem that urgently needs to be solved. Laparoscopic surgery is an alternative to traditional open surgery with the advantages of a smaller incision, less postoperative complications, shorter treatment cycle and faster recovery. It has been extensively used in the diagnosis and treatment of obstetrics and gynecology diseases, especially in the treatment of benign ovarian tumors [11]. Although laparoscopic minimally invasive surgery has many advantages, it also has disadvantages, such as impaired immune function of patients [12]. With the continuous application of laparoscopic surgery in benign ovarian tumors, normal ovarian tissues can be protected to a certain extent to minimize damage, but there are still some adverse effects. How to maximize the protection of normal ovarian tissues from damage is still worthy of further study. Natural orifice transluminal endoscopic surgery (NOTES) is a minimally invasive surgery for diagnosis and treatment through the esophagus, stomach, colorectum, bladder, vagina and other natural cavities. It is referred to as the third generation of surgical method after open surgery and laparoscopic surgery [13]. Its features contain small trauma area, no postoperative scar on the abdominal wall, light pain, rapid recovery and good cosmetic effect on the basis of ensuring curative effect [14]. In recent years, NOTES has been widely utilized as a new surgical procedure with the progress of minimally invasive technology and medical science and technology. Among them, an advanced operation through vaginal natural cavity- transvaginal natural orifice transluminal endoscopic surgery (V-NOTES) is developed in recent years [15,16]. The V-NOTES single-port platform was placed through the vagina, and the endoscope and laparoscopic instruments were delivered through the vagina to the abdominal cavity for surgery. As a new minimally invasive treatment method, V- NOTES not only has the advantages similar to traditional vaginal surgery, but also effectively overcomes the disadvantages of vaginal surgery exposure and difficult operation, and has also the advantages of clear surgical field and convenient operation [17]. With the improvement of equipment and technology, the clinical application of V-NOTES in female patients has been reported in recent years, which has confirmed its feasibility, safety and reproducibility, and also indicated that V-NOTES has a good application prospect [18].

As a safe, convenient and effective surgical method, although some achievements have been made in the field of gynecologic diseases, the application of V-NOTES in ovarian benign tumors is still in the exploratory stage. There are few studies on V- NOTES ovarian cyst removal reported in domestic and foreign literature. The effect of this procedure on ovarian function in women of reproductive age is not yet clear. There is no evidence to clarify the extent of patient benefit. In this study, the traditional porous laparoscopic surgery was used as a control to observe the effects of V-NOTES ovarian cyst removal on clinical indicators, aesthetic satisfaction, ovarian function and cellular immunity, and to evaluate the safety and feasibility of this procedure for the removal of benign ovarian tumors. It was to provide a reference for the selection of surgical procedures for benign ovarian tumors. Therefore, it has important clinical application value and social benefits.

Methods

This research was carried out in accordance with the Helsinki Declaration (The World Medical Association Declaration of Helsinki. Recommendations guide physicians in biomedical research involving human subjects. JAMA 1997; 277: 925-6). This study was discussed and approved by the Human Investigation Review Board of Meizhou People's Hospital. All patients signed the informed consent form before surgery and all operations were performed by experienced gynaecologists.

Patients

Patients with surgical indications who came to Meizhou People's Hospital for treatment of benign ovarian tumor from January 2017 and October 2021 were collected as the research subjects. According to the number of the outpatient department, they were randomly divided into the following two groups by random number

method, with 40 patients in each group: 1) Transvaginal single-port laparoscopic surgery group (V-Notes group); 2) Porous laparoscopic surgery group.

The inclusion criteria were: 1) Patients aged from 18 to 55 years; 2) The benign ovarian tumor diagnosed by CT or MRI; 3) Indications of surgical treatment; 4) The activity of uterus and accessory was goodshowed by physical examination; 5) The patients and their families voluntarily signed the informed consent form; (2) Exclusion criteria were: 1) Malignant lesions were found during operation (ice cutting) and post-operation (paraffin); 2) The operation was changed to open abdomen and hole adding; 3) Severe pelvic adhesions caused by multiple operations; 4) Hypoovarianism; 5) Pregnancy or lactation; 6) Narrow or malformed reproductive tract; 7) Suspected ovarian malignancy; 8) Asexual life; 9) Patients who have taken drugs that affect ovarian function.

Surgical techniques

V-NOTES surgery group

In the observation group, transvaginal single site laparoscopy treatment was performed to remove an ovarian cyst. Routine intestinal cleaning preparation and vaginal flushing were performed before operation, and antibiotics were used prophylactically. The patient was placed in the bladder lithotomy position and general anesthesia was administered. Then the labia minora on both sides was fixed to expose the vagina fully. After disinfection of the vulva, vagina and cervix, a 2 cm arc incision was made at the posterior fornix of the vagina into the abdominal cavity. The port was placed into the abdominal cavity, and the ventilation abdominal tube was connected to establish pneumoperitoneum. The video laparoscopy instrument was placed. The camera was inserted through the 10 mm channel, and the separation forceps were inserted through the two 5 mm channels. The capsule was circumferentially cut in the normal tissue of the ovarian hilum. The cyst was separated by blunt dissection and completely removed with the help of curved forceps. The remaining ovarian tissue was sutured with No. 4 absorbable threads. If the cyst was large, part of the cyst fluid could be sucked out first, the wall of the cyst could be pulled outward, and cystectomy was implemented under direct vision. The wound surface was rinsed with normal saline. Absorbable suture

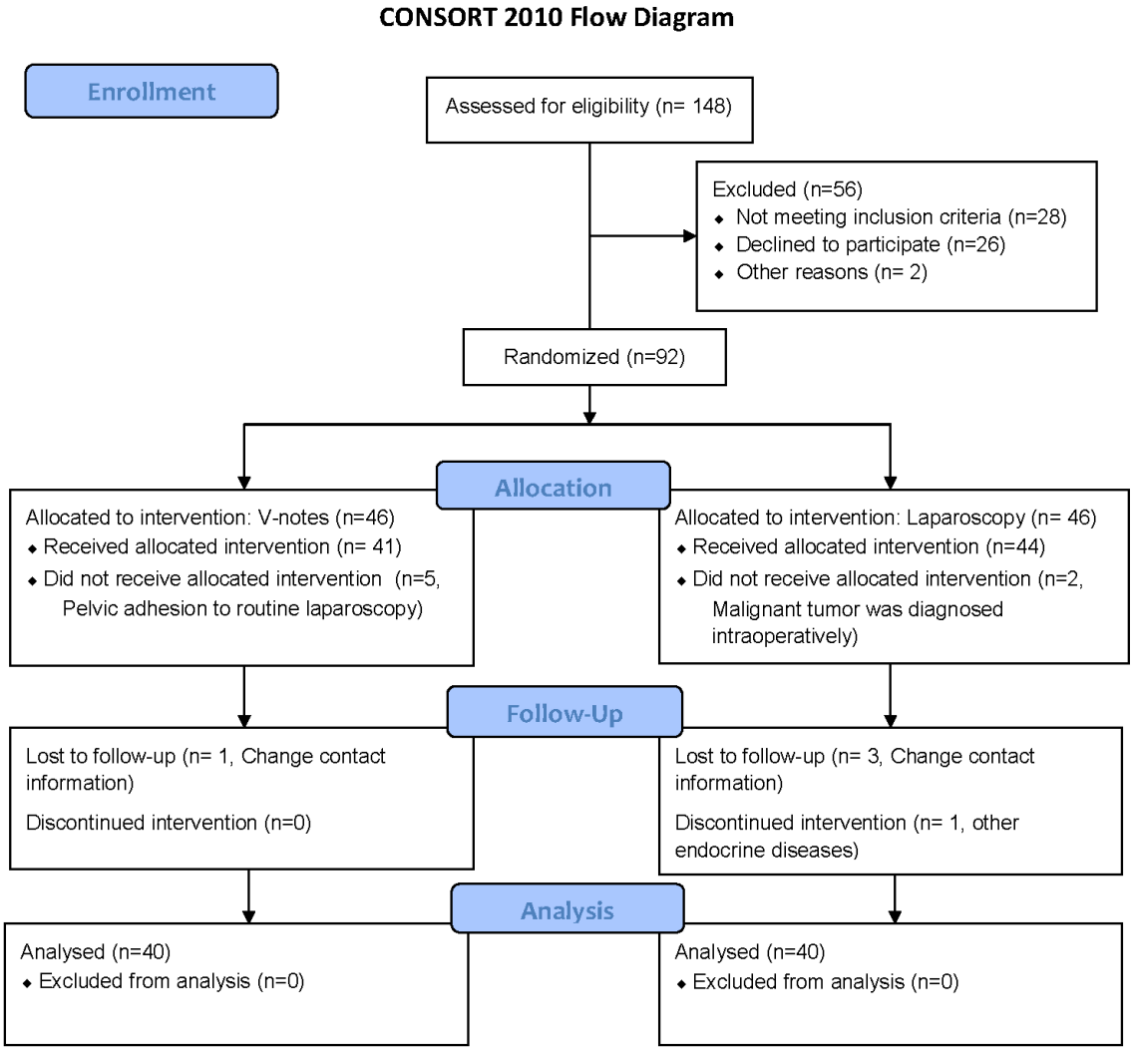

Figure 1. The CONSORT flow chart of the test.

was used to stop bleeding, and electrocoagulation could be used if necessary. The pelvic floor peritoneum and posterior vaginal fornix incision were sutured layer by layer to complete the operation. The catheter and vaginal gauze were retained 2 h after operation, and antibiotics were used to prevent infection within 48 h.

Laparoscopy surgery group

In the control group, porous laparoscopic surgery was performed. The patients were placed in supine position. After successful general anesthesia, a longitudinal skin incision (1 cm in length) was made in the umbilicus and the laparoscope was placed into. Two puncture holes were established in the lower abdomen and the surgical instruments were placed. Then, the ventilation abdominal tube was connected to establish pneumoperitoneum. The subsequent operation steps were the same as those in the observation group. The incision in the abdominal wall was sutured after operation.

Statistics

SPSS17.0 software was used to analyze the statistical data. The measurement data were expressed as mean±standard deviation. Categorical variables were expressed in frequency (percentage). We used the One-Sample Kolmogorov-Smirnov test to confirm the normal distribution of continuous variables. The independent sample t-test was used for the comparison of clinical indicators and laboratory examination indicators between groups, and the paired sample t-test was used for the comparison of indicators related to ovarian function within groups. Data with a normal distribution but uneven variance were compared with the t-test. Non-normal variables were compared using Mann-Whitney

Table 1. Characteristics of women in the V-NOTES group and laparoscopy group

Characteristics	*L (n=40)*	*V-NOTES (n=40)*	*p value*
Age (years)	30.75±10.36 (18-55)	32.75±6.15 (21-45)	0.298[a]
Body mass index (kg/m^2)	22.05±2.82 (17.3-26.4)	23.18±2.93 (18.8-27.4)	0.084[a]
Mass diameter (cm)	7.25±3.04 (2-15)	5.93±2.52 (1.5-13)	0.038[a]
Nulliparae, n (%)	15 (37.5)	5 (12.5)	0.010[b]
Previous abdominal surgery, n (%)	6 (15)	17 (42.5)	0.007[b]

Values are mean ± SD (range) or n (%); [a]t-test; [b]x^2 test.

Table 2. Pathologic diagnoses in the laparoscopy group and V-NOTES group

Characteristics	*L (n=40)* *n (%)*	*V-NOTES (n=40)* *n (%)*	*p value*[a]
Teratoma	15 (37.5)	29 (72.5)	0.000
Cystadenoma	6 (15.0)	9 (22.5)	
Simple cyst	13 (32.5)	0	
Follicular cyst	0	1 (2.5)	
Endometriosis cyst	6 (15.0)	0	
Corpora luteal break and hemorrhage	0	1 (2.5)	

[a]Fisher-exact test

Table 3. Clinical and efficiency outcomes in the laparoscopy group and V-NOTES group

	L (n=40)	*V-NOTES (n=40)*	*p value*
Clinical outcomes			
Blood loss (mL)	26.63±20.30 (5-100)	18.13±6.57 (5-30)	0.015[a]
Anal exhaust (hours)	12.1±4.92 (5-28)	13.2±7.85 (3-46)	0.455[a]
Efficiency outcomes			
Operating time (min)	71.25±32.04 (25-160)	50.88±18.67 (25-95)	0.001[a]
Time of first ambulation after operation (h)	18.03±7.46 (6-36)	5.25±2.10 (2-11)	0.000[a]
Postoperative hospital stay (days)	0.65±0.95 (0-4)	3.80±1.09 (2-6)	0.000[b]
Postoperative analgesics, n (%)	7 (17.5)	0 (0)	0.012[c]

Values are mean ± SD (range) or n (%); [a]t'-test; [b]t-test; [c]Fisher-exact test.

U test. The differences between rates were tested by x^2 or Fisher-exact test, if appropriate. P<0.05 was considered statistically significant.

Results

The CONSORT flow chart of the test is shown in Figure 1. Between January 2017 and October 2021, 148 patients were screened for eligibility, 56 were excluded and 92 patients were randomly assigned to either V-NOTES group or the laparoscopy group. Seven patients underwent other types of surgery due to special conditions, 4 patients were lost to follow-up and 1 person discontinued intervention due to endocrine disease.

A total of 80 patients were enrolled in this study. The baseline characteristics are presented in Table 1. The age of the study population was

Table 4. Changes in ovarian function in the V-NOTES group and laparoscopy group

Variable	*L (n=40)*	*V-NOTES (n=40)*	*p value*[a]
Hb (g/L)			
preoperation	123.50±17.34 (70.00-150.00)	125.05±13.24 (83.00-145.00)	0.654
postoperation	108.88±15.54 (68.00-142.00)	110.50±10.78 (78.00-129.00)	0.588
p value	0.000	0.000	
difference	-14.63±7.86 (-33 - -1)	-14.55±8.24 (-31.00-7.00)	0.967
E2 (pmol/L)			
preoperation	96.90 (<10.00-120.10)	101.46±8.85 (72.61-114.90)	0.118[c]
postoperation	90.20 (10.00-106.00)	97.97±6.97 (75.83-107.50)	0.001[c]
p value	0.016[c]	0.053	
difference	-5.96±10.59 (-31.90-12.29)	-3.49±9.47 (-22.10-13.20)	0.275
FSH (mIU/mL)			
preoperation	5.78±1.34 (2.99-8.45)	7.37±1.83 (4.23-12.73)	0.000
postoperation	6.28±1.61 (2.87-8.58)	6.23±1.72 (2.34-9.34)	0.905
p value	0.139	0.006	
difference	0.49±1.68 (-2.27 - 4.59)	-1.13±2.40 (-9.31 - 3.17)	0.001
LH (mIU/mL)			
preoperation	7.49±1.88 (2.33-12.67)	6.94±2.89 (3.14-16.10)	0.322
postoperation	8.52±2.27 (3.26-11.73)	6.48±2.16 (3.17-12.45)	0.000
p value	0.030	0.418	
difference	1.03±1.85 (-1.50 - 4.74)	-0.46±2.29 (-10.35 - 4.94)	0.002
AFC			
preoperation	8.00 (2.00-10.00)	7.00 (1.00-18.00)	0.648[c]
postoperation	5.00 (1.00-8.00)	7.00 (2.0013.00)	0.023[c]
p value	0.000[c]	0.314[c]	
difference	-2.10±1.19 (-6.00 - 0.00)	-1.05±3.48 (-8.00 - 7.00)	0.077
PSV(cm/s)			
preoperation	11.55 (9.50-15.20)	10.27±3.45 (5.40-22.10)	0.001[c]
postoperation	11.16±1.52 (8.20-14.60)	8.62±3.35 (0.40-19.10)	0.000[b]
p value	0.022[c]	0.032	
difference	-1.07±2.40 (-5.50 - 5.10)	-1.66±2.95 (-8.50 - 4.50)	0.330
PI			
preoperation	1.48±0.29 (0.80-1.90)	2.28±2.14 (0.40-9.90)	0.024
postoperation	1.40±1.74 (0.70-12.00)	1.85±1.82 (0.40-8.60)	0.267
p value	0.782	0.334	
difference	-0.08±1.72 (-0.90 - 10.40)	-0.43±1.39 (-5.30 - 2.40)	0.313
RI			
preoperation	0.89±0.25 (0.45-1.30)	0.97±0.48 (0.20-2.30)	0.387[b]
postoperation	0.70 (0.40-0.90)	1.05 (0.40-6.00)	0.000[c]
p value	0.000[c]	0.074[c]	
difference	-0.25±0.28 (-0.90 - 0.20)	0.27±0.99 (-0.90 - 5.80)	0.002

Values are mean ± SD (range), median (range) or n (%); [a]pared-samples T test; [b]T' test; [c]Mann-Whitney U test

30.75±10.36 years in the laparoscopy group and 32.75±6.15 years in the V-NOTES group. The mean body mass index (BMI) was 22.05±2.82 and 23.18±2.93, respectively. There was no difference between the two groups concerning age and BMI. Regarding the delivery history, there were 15 (37.5%) nulliparae in the laparoscopy group versus 5 (12.5%) in the V-NOTES group (p<0.05). 17 patients (42.5%) had a history of abdominal surgery in the V-NOTES group (p<0.01). The maximum diameter of excised material in the laparoscopy group was larger than in the V-NOTES group, and the difference was significant (p<0.05).

The histopathological diagnoses are shown in Table 2. Teratoma accounted for 37.5% of women in the laparoscopy group and 72.5% in the V-NOTES group. Six patients in the laparoscopy group (15.0%) and 9 in the V-NOTES group (22.5%) had cystadenoma. In the laparoscopy group, 32.5% were diagnosed with a simple cyst and 15.0% were diagnosed with endometriosis cyst. The V-NOTES group had 1 case of follicular cyst (2.5%) and 1 case of luteal rupture and hemorrhage (2.5%). There was a significant difference in the pathologic diagnosis results between the two groups (p=0.000).

Clinical and efficiency outcomes of the two groups are presented in Table 3. The amount of blood loss in the V-NOTES group was significantly less than in the laparoscopy group (26.63±20.30 mL in the laparoscopy group and 18.13±6.57 mL in the V-NOTES group, p=0.015). Postoperative anal exhaust time between the two groups were similar (p>0.05). In terms of surgical efficiency outcomes, there were significant differences between the two groups. Overall operating time was 71.25±32.04 min (range 25 to 160 min) in the laparoscopy group and 50.88±18.67 min (range 25 to 95 min) in the V-NOTES group (p=0.001). The time of first ambulation after surgery was 18.03±7.46 h (range 6 to 36 h) in the laparoscopy group and 5.25±2.10 h (range 2 to 11) in the V-NOTES group (p=0.000).The mean length of postoperative hospital stay was 0.65±0.95 days (range 0 to 4) in the laparoscopy group and 3.80±1.09 days (range 2 to 6) in the V-NOTES group (p=0.000). Only 17.5% of the cases in the laparoscopy group used postoperative painkillers whereas none of the patients in the V-NOTES group take postoperative analgesics (p=0.012).

Variations of ovarian function in the two groups are listed in Table 4. After the operation, the hemoglobin (Hb) (p=0.000) and PSV (p=0.022 for laparoscopy group, p=0.032 for V-NOTES group) levels of the two groups were apparently reduced. PI of the two groups also decreased after surgery, but the differences were not significant (p>0.05, respectively). Similarly, the concentration of E2 in both groups decreased post-operation, and the decrease was notable only in the laparoscopy group (p = 0.016), but not in the V-NOTES group (p = 0.053). Antral follicle count (AFC) was apparently reduced after laparoscopic surgery (p=0.000) and basically unchanged after V-NOTE (p=0.314). In the laparoscopy group, both FSH and LH levels increased postoperatively, and LH changed significantly (p=0.030); RI levels decreased statistically after surgery (p=0.000). In contrast, the levels of FSH and LH in the V-NOTE group decreased after surgery, with an obvious change of FSH level (p=0.006) while RI levels increased.

Discussion

With the progress of technology, V-NOTES approach was gradually used in gynecologic surgery [19]. Little was found in the literature about the effect of V-NOTES and laparoscopic surgery on ovarian function in the treatment of benign ovarian tumors. Our main purpose of this study was to verify the safety and reliability of V-NOTES in the protection of ovarian function by comparing the effects of V-Notes and traditional laparoscopic surgery.

When V-NOTES approach was used to treat ovarian benign tumors, the clinical and efficiency outcomes were generally better than that of the laparoscopy group. It had better control over blood loss (p=0.015), operation time (p=0.001) and postoperative time of first ambulation (p=0.000) compared with laparoscopic surgery. The study of Housmans et al [20] also reported shorter operation time and less estimated blood loss. In addition, patients in V-NOTES group did not need analgesics after surgery (p=0.012), suggesting that V-NOTES could significantly reduce the pain of patients and facilitate postoperative recovery. This was consistent with that of Benhidjeb et al study [21], Puisungnoen et al [22] and Kale et al [23] who evaluated the mean postoperative visual analog scale (VAS) pain score. It may be own to the absence of abdominal wall incision during surgery that reduces postoperative pain and restores postoperative mobility earlier. We believe that these results were due to the minimally invasive nature of the V-NOTES approach. However, patients undergoing V-NOTES had a longer postoperative hospital stay than those undergoing laparoscopic surgery (p=0.000). This outcome was similar to that of Kaya et al study [24], but contrary to that of Yang et al [25] and Baekelandt et al [26]. There were several possible explanations for this result. On the one hand, more people had a history of abdominal surgery in V-NOTES group (p=0.007) compared to that in the

laparoscopy group. On the other hand, pathologic characteristics differed apparently between the two groups (p=0.000). Most of the patients in this group had teratomas (72.5%) and cystadenoma (22.5%), so a longer hospital stay was needed to observe the condition.

After operation, the change trends of Hb, E2, PSV and PI in the two groups were similar. However, the increase/decrease of FSH, LH and RI post-operation in the two groups showed opposite trends. Ovarian blood flow is closely related to ovarian reserve function [27]. In the laparoscopy group, with the continuous increase of ovarian blood flow (RI decreased), the ovarian function enhanced, and the number of ovarian internal follicles increased accompanied by high-ability to synthesize sex hormones in the ovary. So, the levels of FSH and LH increased after laparoscopic surgery.

After the operation, the levels of FSH, LH and E2 in V-NOTES group decreased. The imbalance of the hypothalamus-pituitary-ovary axis reduces the feedback mechanism of ovary and increases the secretion of gonadotropin in a feedback manner. In the V-NOTES group, RI was increased but not significantly, so the decline in LH and E2 levels was not apparent, and AFC was basically unchanged. V-NOTES group maintained lower FSH and LH levels and higher E2 levels, indicating that V-NOTES had little effect on the patient's endocrine function. Antral follicles are the precursors of mature follicles. Small antral follicles with a diameter of 2-6 mm are significantly related to basic FSH, LH etc. [28]. It can not only reflect the basic state and reserve capacity of the ovary, but also predict the overreaction of the ovary, and be alert to the occurrence of ovarian hyperstimulation syndrome. In our study, AFC decreased significantly in the laparoscopy group but kept the same quality in V-NOTES group. It indicated that the minimal invasive treatment of V-NOTES was beneficial to maintain the integrity of the ovary itself, and had no interference effect on many physiological processes such as ovarian follicle growth.

There are several limitations in our study. First of all, this study was a retrospective cohort study in a single centre with the possibility of selection bias. Blinding is needed in the trials although it is difficult. Secondly, the sample size of this study was small which compromises the validity of the results. We need and are conducting further large sample tests to support our conclusion. Finally, we should continue to monitor up and collect more information about the effect of V-NOTES on fertility and the living quality. It brought about much better intraoperative and postoperative outcomes, and a smaller effect on ovarian reserve compared to laparoscopic surgery.

Conclusions

In conclusion, our findings have important implications for developing V-NOTES application in gynecological operations. Considerably more work will need to be done to elucidate the advantages of this technique deeply, including cosmetic advantages, decreased postoperative pain, and high patient satisfaction.

Conflict of interests

The authors declare no conflict of interests.

References

1. Chen Y, Du H, Bao L, Liu W. Opportunistic salpingectomy at benign gynecological surgery for reducing ovarian cancer risk: a 10-year single centre experience from China and a literature review. J Cancer 2018;9:141-7.
2. Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F. Epidemiology and Risk Factors of Uterine Fibroids. Best Pract Res Clin Obstet Gynaecol 2018;46:3-11.
3. Missmer SA, Tu FF, Agarwal SK et al. Impact of Endometriosis on Life-Course Potential: A Narrative Review. Int J Gen Med 2021;14:9-25.
4. Wang J, Zhu M, Zhou X, Wang T, Zhang J. Changes in tumor markers, coagulation function and serum VEGF in patients with ovarian cancer and benign ovarian disease. JBUON 2020;25:2287-92.
5. Guleria S, Jensen A, Toender A, Kjaer SK. Risk of epithelial ovarian cancer among women with benign ovarian tumors: a follow-up study. Cancer Causes Control 2020;31:25-31.
6. Xu J, Shao H, Yang Y, Shi X, Tao M. Improvement and effect of stress responses and ovarian reserve function in patients with ovarian cysts after laparoscopic surgery. J Int Med Res 2019;47:3212-22.
7. Bedaiwy MA, Sheyn D, Eghdami L et al. Laparoendoscopic single-site surgery for benign ovarian cystectomies. Gynecol Obstet Invest 2015;79:179-83.
8. Yuen PM, Yu KM, Yip SK, Lau WC, Rogers MS, Chang A. A randomized prospective study of laparoscopy and laparotomy in the management of benign ovarian masses. Am J Obstet Gynecol 1997;177:109-14.
9. Jiang D, Nie X. Effect of endometrioma and its sur-

gical excision on fertility (Review). Exp Ther Med 2020;20:114.

10. Deckers P, Ribeiro SC, Simoes R, Miyahara C, Baracat EC. Systematic review and meta-analysis of the effect of bipolar electrocoagulation during laparoscopic ovarian endometrioma stripping on ovarian reserve. Int J Gynaecol Obstet 2018;140:11-7.
11. Sho T, Urabe R, Hachisuga T. Port-site metastasis after laparoscopic surgery for mature cystic teratoma. Eur J Gynaecol Oncol 2016;37:247-50.
12. Yiannakopoulou E, Nikiteas N, Perrea D, Tsigris C. Effect of laparoscopic surgery on oxidative stress response: systematic review. Surg Laparosc Endosc Percutan Tech 2013;23:101-8.
13. Baekelandt J, De Mulder PA, Le Roy I et al. HALON-hysterectomy by transabdominal laparoscopy or natural orifice transluminal endoscopic surgery: a randomised controlled trial (study protocol). BMJ Open 2016;6:e11546.
14. Jallad K, Walters MD. Natural Orifice Transluminal Endoscopic Surgery (NOTES) in Gynecology. Clin Obstet Gynecol 2017;60:324-9.
15. Baekelandt J. Transvaginal natural-orifice transluminal endoscopic surgery: a new approach to myomectomy. Fertil Steril 2018;109:179.
16. Chen X, Liu H, Sun D et al. Transvaginal Natural Orifice Transluminal Endoscopic Surgery for Tubal Pregnancy and a Device Innovation from Our Institution. J Minim Invasive Gynecol 2019;26:169-74.
17. Liu J, Lin Q, Blazek K, Liang B, Guan X. Transvaginal Natural Orifice Transluminal Endoscopic Surgery Myomectomy: A Novel Route for Uterine Myoma Removal. J Minim Invasive Gynecol 2018;25:959-60.
18. Yoshiki N. Review of transvaginal natural orifice transluminal endoscopic surgery in gynecology. Gynecol Minim Invasive Ther 2017;6:1-5.
19. Li CB, Hua KQ. Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) in gynecologic surgeries: A systematic review. Asian J Surg 2020;43:44-51.
20. Housmans S, Noori N, Kapurubandara S et al. Systematic Review and Meta-Analysis on Hysterectomy by Vaginal Natural Orifice Transluminal Endoscopic Surgery (vNOTES) Compared to Laparoscopic Hysterectomy for Benign Indications. J Clin Med 2020;9:3959.
21. Benhidjeb T, Kosmas IP, Hachem F, Mynbaev O, Stark M, Benhidjeb I. Laparoscopic cholecystectomy versus transvaginal natural orifice transluminal endoscopic surgery cholecystectomy: results of a prospective comparative single-center study. Gastrointest Endosc 2018;87:509-16.
22. Puisungnoen N, Yantapant A, Yanaranop M. Natural Orifice Transluminal Endoscopic Surgery-assisted Vaginal Hysterectomy versus Total Laparoscopic Hysterectomy: A Single-center Retrospective Study Using Propensity Score Analysis. Gynecol Minim Invasive Ther 2020;9:227-30.
23. Kale A, Sariibrahim B, Basol G. Hysterectomy and salphingoopherectomy by Transvaginal Natural Orifice Transluminal Endoscopic Surgery(NOTES): Turkish surgeons' initial experience. Int J Surg 2017;47:62-8.
24. Kaya C, Alay I, Cengiz H et al. Conventional Laparoscopy or Vaginally Assisted Natural Orifice Transluminal Endoscopic Surgery for Adnexal Pathologies: A Paired Sample Cross-Sectional Study. J Invest Surg 2020:1-6.
25. Yang YS, Kim SY, Hur MH, Oh KY. Natural orifice transluminal endoscopic surgery-assisted versus single-port laparoscopic-assisted vaginal hysterectomy: a case-matched study. J Minim Invasive Gynecol 2014;21:624-31.
26. Baekelandt JF, De Mulder PA, Le Roy I et al. Hysterectomy by transvaginal natural orifice transluminal endoscopic surgery versus laparoscopy as a day-care procedure: a randomised controlled trial. BJOG 2019;126:105-13.
27. Xiao J, Zhou J, Liang H, Liu F, Xu C, Liang L. Impact of hemostatic methods on ovarian reserve and fertility in laparoscopic ovarian cystectomy. Exp Ther Med 2019;17:2689-93.
28. Bosch E, Alviggi C, Lispi M et al. Reduced FSH and LH action: implications for medically assisted reproduction. Hum Reprod 2021;36:1469-80.