Heliyon 10 (2024) e24945

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Research article

Transvaginal natural orifice endoscopic surgery for tubal ectopic pregnancy: A more suitable surgical approach for enhanced recovery after surgery

Ying Liu [a,1], Xin Li [a,*], Tianjiao Liu [a,1], Aijie Xie [a], Xian Wu [a], Yujian Jia [a], Xiaoyan Liao [a], Wei Cheng [a], Hui Wang [a], Fangyuan Zhong [a], Lijuan Xu [a], Juan Huang [a], Siqin Xiu [a], Zhongzhi Li [b], Yalan Li [c], Xue Xiao [d,**], Yonghong Lin [a,***], Xiaoqin Gan [a,****]

[a] Department of Gynecology and Obstetrics, Chengdu Women's and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology of China, Chengdu, 611731, China
[b] Department of Gynecology and Obstetrics, Chongqing University Fuling Hospital, Chongqing, 408099, China
[c] Psychiatry Department, Psychosomatic Medical Center, The Fourth People's Hospital of Chengdu, Chengdu, 610036, China
[d] Department of Gynecology and Obstetrics, West China Second University Hospital, Sichuan University, Chengdu, 610041, China

ARTICLE INFO

Keywords:
Enhanced recovery after surgery
Salpingectomy
Salpingostomy
Laparoendoscopic
Transvaginal natural orifice endoscopic surgery
Tubal pregnancy

ABSTRACT

Objective: We aimed to determine the safety of Vaginal natural orifice transluminal endoscopic surgery (vNOTES) in terms of the Enhanced Recovery after Surgery (ERAS) concept for tubal pregnancy surgery and provide a detailed process of vNOTES for tubal pregnancy surgery, including experience and key points for surgeons performing this procedure.

Methods: The Longitudinal Vaginal Natural Orifice Transluminal Endoscopic Surgery Study (LovNOTESS), which was conducted in Chengdu, China. A total of 219 patients who underwent tubal ectopic pregnancy surgery between September 2021 and March 2022. The patients underwent salpingectomy or salpingostomy using transumbilical laparoendoscopic single-site surgery (LESS) or vNOTES, according to their preferences. This study prospectively collected perioperative and one-year follow-up data on tubal pregnancy outcomes after vNOTES and compared them with those after LESS.

Results: The vNOTES group showed a shorter surgical duration, hospitalization duration, and postoperative exhaust time and a lower analgesic medication usage rate, but it showed a higher surgical conversion rate. The vNOTES approach reduced the postoperative exhaust time by

* Corresponding author. Chengdu Women's and Children's Central Hospital, 1617 Riyue Avenue, Qingyang District, Chengdu, 611731, Sichuan, China.
** Corresponding author. West China Second University Hospital, Sichuan University, No. 20, Block 3, Renmin Road, Chengdu, 610041, China.
*** Corresponding author. Chengdu Women's and Children's Central Hospital, 1617 Riyue Avenue, Qingyang District, Chengdu, 611731, Sichuan, China.
**** Corresponding author. Chengdu Women's and Children's Central Hospital, 1617 Riyue Avenue, Qingyang District, Chengdu, 611731, Sichuan, China.
E-mail addresses: 554989333@qq.com (Y. Liu), xinlicwcch@163.com (X. Li), xiaoxuesc@aliyun.com (X. Xiao), linyhcd2011@163.com (Y. Lin), amandine2021@163.com (X. Gan).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.heliyon.2024.e24945
Received 18 October 2023; Received in revised form 13 January 2024; Accepted 17 January 2024
Available online 20 January 2024

approximately 9 h (95% confidence interval [CI]: −11.93, −5.57 h, p < .001) and the risk of postoperative analgesic drug use by 77% (odds ratio, 0.23; 95% CI: 0.10, 0.61, p = .023).
Conclusion: vNOTES can shorten the exhaust time and duration of hospitalization, reduce postoperative pain, and avoid surface surgical scars in tubal pregnancy surgeries, consistent with the ERAS concept. However, more comprehensive preoperative evaluation of patients who choose vNOTES is required to reduce the occurrence of intraoperative conversion.
Trial registration: ChiCTR2100053483.

1. Introduction

Ectopic pregnancy involves implantation of the zygote outside the uterine cavity, and tubal pregnancy is the most common form of ectopic pregnancy [1]. Although the incidence rate of tubal pregnancies is only approximately 0.5%–2.3% [2,3], it is the main cause of early pregnancy death [4,5]. Stable and ruptured tubal pregnancies are primarily treated using surgical procedures, which are divided into salpingostomies and salpingectomies [6,7].

Tubal pregnancy surgeries are routinely performed as daycare surgeries at our department because of the minor surgical damage. While the conventional surgical approach is transumbilical laparoendoscopic single-site surgery (LESS), vaginal natural orifice transluminal endoscopic surgery (vNOTES) has recently emerged as an option [8–11]. The growing relevance of the Enhanced Recovery after Surgery (ERAS) concept requires surgeons to continuously refine their surgical skills to ensure less surgery-related damage and pain, shorter hospital stays, and earlier return to normal life [12–14]. In comparison with LESS, vNOTES shows milder postoperative pain, faster anal exhaust, and complete absence of surface scars, consistent with the concept of ERAS [15–19]. Although the feasibility of vNOTES for tubal pregnancy surgery has been reported, data regarding its safety are limited [8]. Considering its anatomical specificity, this approach may cause damage to adjacent organs such as the bladder or rectum [16,20,21], indicating the need to investigate the safety of vNOTES in tubal pregnancy surgery in terms of the ERAS concept.

Therefore, this study prospectively collected and compared perioperative and one-year follow-up data on tubal pregnancies treated using vNOTES and LESS. Using these data, we aimed to determine the safety of vNOTES in terms of the ERAS concept for tubal pregnancy surgery and provide detailed insights regarding vNOTES for tubal pregnancy surgery, including important considerations for surgeons performing this procedure.

2. Materials and methods

2.1. Study design and participants

This study was based on the Longitudinal Vaginal Natural Orifice Transluminal Endoscopic Surgery Study (LovNOTESS), which was conducted in Chengdu, China (China Clinical Trials Registry ChiCTR2200059282), and was approved by the Institutional Review Board of Chengdu Women and Children's Central Hospital (No. 202130). This subgroup study prospectively collected perioperative and one-year follow-up data of patients with tubal pregnancy who were willing to undergo surgical treatment between September 2021 and March 2022. This study only recruited patients with stable vital signs, and patients suspected of significant abdominal bleeding or hemorrhagic shock underwent emergency surgery. Meanwhile, this study excluded patients with absolute or relative contraindications to vNOTES, such as suspected vaginal infections, severe pelvic adhesions, fallopian tube ovarian abscesses, endometriosis, malignancy, intrauterine pregnancy, potential interstitial ectopic pregnancy (through preoperative ultrasound examination [22]) or sacrouterine nodularity. After informing the patient in detail about the risks associated with the surgery and providing written informed consent, the patient underwent salpingectomy or salpingostomy using LESS or vNOTES according to their preferences. In tubal pregnancies, suspected vaginal infections, severe pelvic adhesions, or lesions located in the interstitial part of the fallopian tubes are contraindications for vNOTES.

2.2. Data collection

The patients' perioperative data were collected from the hospital's electronic medical record system, including data related to the patients' age, duration of amenorrhea, body mass index (BMI), fertility history, previous abdominal surgery, surgical method, surgical approach, maximum diameter of the mass, preoperative and postoperative blood human chorionic gonadotropin (HCG) levels, operation time, pelvic adhesions, surgical conversion, postoperative exhaust time, length of hospital stay, and perioperative complications. The operative time was measured from the time the incision was made to the end of suturing. Postoperative recovery data included the time from the end of the surgery to the first postoperative activity, urination, feeding, and exhaust. For salpingectomy, outpatient follow-up assessments were performed 1 week after surgery and 1 month thereafter; for salpingostomy, patients were required to undergo weekly blood HCG tests until they showed negative results.

2.3. Standard surgical procedures for transumbilical LESS and vNOTES under ERAS

For all patients, the routine procedure for ERAS was as follows: patients fasted for >8 h after consuming fried or fatty foods or

meats, >6 h after consuming light meals or milk, and >2 h after drinking water. Urinary catheters were not routinely placed during surgery. After waking up from anesthesia, the patient was asked to eat light food as soon as possible and get out of bed as soon as possible. For patients who experienced no specific discomfort, discharge was routinely performed on the same day or in the morning after surgery (within 24 h of admission). After discharge, patients were given a 24-h online phone number to contact the doctors in case of adverse events.

All surgeries were performed by the same qualified surgeons in accordance with the same surgical procedures. Patients emptied their bladder before surgery and received an intravenous infusion of 1-g cefazoline 30 min before surgery to prevent infection. The patient was assisted in the lithotomy position and administered general anesthesia. Before performing vNOTES, cervical forceps were used to pull the cervix to ensure good cervical and uterine activity. For vNOTES, the specific operating steps are as follows: 1) The vaginal retractor exposes the cervix, and 2 Allis forceps are used to pull the cervix outward and upward to expose the posterior vaginal fornix; 2. Make a 2 cm transverse incision at the midpoint of the posterior vaginal fornix, cut the whole thickness of the vaginal wall, and then use tissue scissors to separate the tissue to reach the peritoneum; 3) Cut the peritoneum and extend the incision toward 4 and 8 o'clock in the vagina; 4) A disposable double-ring multi-instrument access port (Beijing Aerospace Kadi Technology Development Institute, HK-TH-60.4TY) was inserted into the pelvic cavity through the incision. For the LESS procedure, an incision was made at the navel. The next steps were same in all groups and followed: Pneumoperitoneum was created up to 14 mmHg of CO2 insufflation and a 10-mm 30-degree rigid laparoscope (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) was used for visualization.

2.4. Standard surgical procedures for salpingostomy or salpingectomy

For salpingostomy, an incision was made on the opposite side of the fallopian tube mesentery, at the most prominent point of the pregnancy mass. Bipolar electrocoagulation was performed to create an electrocoagulation band along the long axis of the fallopian tube. The fallopian tube was placed inside a specimen bag to prevent the villi from flowing into the abdominal cavity. Electrocoagulation hooks or scissors were used to cut longitudinally along the long axis of the affected fallopian tube, with a slightly shorter incision length than the pregnancy mass. Non-invasive forceps were used to lift the incision edge of the fallopian tube wall, stretch into a 5-mm flushing suction device along the tube wall into the lumen, use water pressure to separate the villi and blood clots from the tube wall, and drive the villi and blood clots to completely discharge from the incision under water flow. If the villi and blood clots adhered tightly to the tube wall and could not be completely separated by water pressure, non-invasive grasping forceps were used to gently pull the villi tissue and continue to separate the villi from the base of the tube wall under water pressure. The lumen of the fallopian tube was rinsed repeatedly with an NaCl solution to ensure the absence of residual villous tissue. The wound surface of the Fallopian

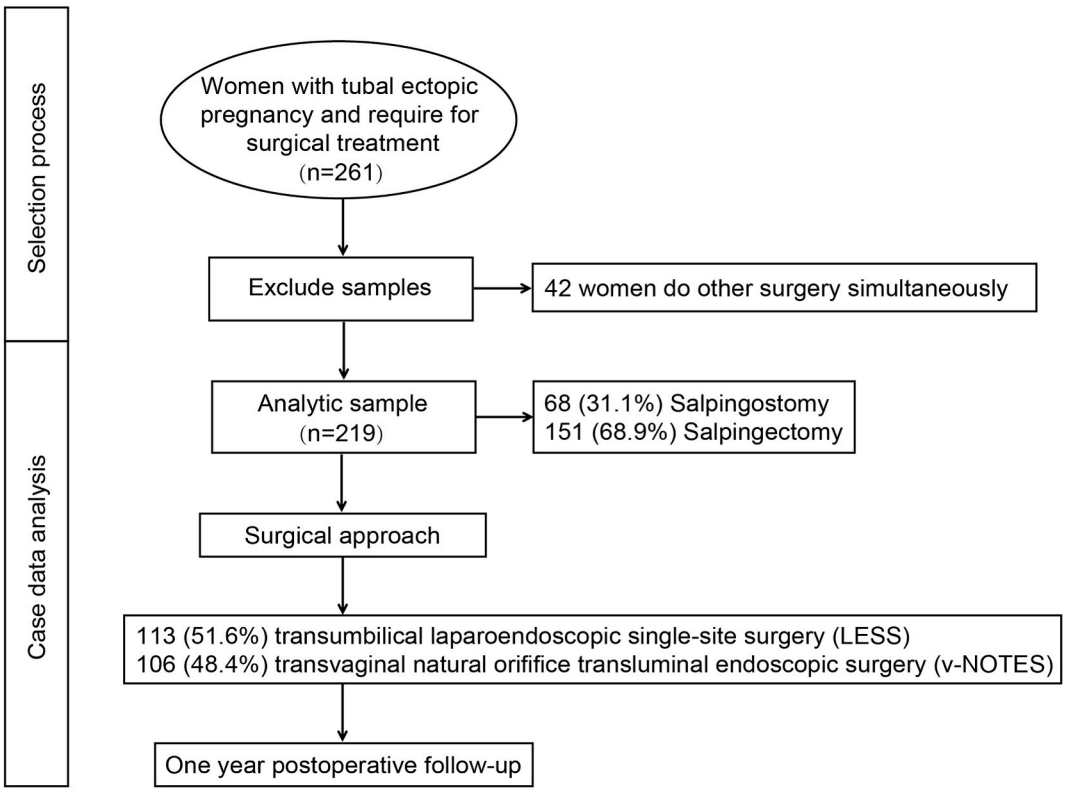

Fig. 1. Selection process for this study.

tube was opened or sutured discontinuously to the mucosal layer.

For salpingectomy, the fimbriated extremity of the fallopian gland was lifted with non-invasive forceps, the mesosalpinx was coagulated with bipolar electrocoagulation, and the mesosalpinx was gradually cut to the isthmus of the oviduct with scissors. After bipolar electrocoagulation of the interstitial part of the fallopian tube, scissors were used to cut the fallopian tube at the electrocoagulation site, and the wound was electrocoagulated to stop the bleeding.

All surgeons and surgical team members follow standardized operating procedures to complete the learning curve [23] and achieve proficiency. If intraoperative injury of large vessels, important organs or bleeding >800 ml, the surgical method will be changed. vNOTES is generally converted to transabdominal single-port laparoscopic surgery, and single-port laparoscopic surgery is converted to multi-ports surgery. Immediately convert to open surgery if there is a life-threatening vascular injury.

The abdominal and vaginal wound were closed with 2-0 absorbed suture and 2-0 barbed absorbable suture respectively. If the patient feels significant pain after surgery, 10 ml of ibuprofen will be given as a single oral analgesic. Use again after 4–6 h if necessary.

2.5. Statistical analysis

SPSS software (version 27.0; IBM Corp., Armonk, NY, USA) were used to perform the all statistical analyses. Fisher's exact or Chi-square tests were used to analyze categorical data, reporting as counts (percentages). The mean ± standard deviation values of continuous variables were evaluated via Student's t-test and least significant difference Student's t-test. Multivariate linear regression analysis was used to detect the factors influencing intraoperative bleeding, duration of surgery, and postoperative exhaust time. Binary logistic regression was used to analyze the associations between preoperative characteristics and postoperative analgesic medication usage. Covariates were selected according to the different variables in the univariate analysis and factors that were reported to affect the dependent variable in previous studies. All statistical significance was set at $P < .05$ with two-tailed tests.

3. Results

The selection process for the study population is illustrated in Fig. 1. Initially, 261 patients with tubal ectopic pregnancies who were willing to undergo surgical treatment were recruited for the study. After excluding patients who underwent other surgeries simultaneously, the final analysis included 219 patients, of whom 106 (48.4%) underwent vNOTES and 113 (51.6%) underwent LESS. The average age of the patients, duration of amenorrhea, and BMI at recruitment were 31.40 ± 5.45 years, 31.40 ± 5.45 days, and 21.28 ± 3.16 kg/m^2, respectively. Among these patients, 159 (72.6%) had a history of artificial dilation and curettage abortion, 115 (52.5%) had undergone abdominal surgery, and 30 (13.7%) had a previous ectopic pregnancy. Among the 219 patients, 68 (31.1%) chose salpingostomy and 151 (68.9%) chose salpingectomy **(Table 1)**.

No statistically significant differences were observed in the demographic characteristics of the patients in the LESS and vNOTES groups. Patients in the vNOTES group showed a shorter duration of surgery and hospitalization, a shorter postoperative exhaust time, and a lower analgesic medication use rate, but had a higher surgical conversion rate **(Table 2)**. The reasons for surgical conversion in four cases in the vNOTES group were as follows: the procedure was beyond the scope of the surgical instrument due to adhesion of the fallopian tube to the lateral wall of the pelvic cavity in one case; difficulty stopping bleeding due to the proximity of the mass to the uterine part in one case; and difficulty entering the pelvic cavity due to pelvic adhesions in two cases. All four of these patients were transferred to the LESS group. Perioperative complications in the LESS group included persistent ectopic pregnancy after surgery in one patient, poor incision healing in one patient, and postoperative fever and one patient had; in contrast, perioperative complications in the vNOTES group included persistent ectopic pregnancy after surgery in one patient, postoperative pelvic hemorrhage in one patient, and postoperative fever in two patients had. All patients recovered after undergoing conservative treatment and were discharged without re-surgery.

The volume of intraoperative bleeding can be indirectly used as an indicator of surgical injury, and was further analyzed using

Table 1
Description of the patients demographic characteristics and operation types.

Variables	Total
Patients	219
Age (year)	31.40 ± 5.45
BMI (kg/m^2)	21.28 ± 3.16
Duration of amenorrhea (day)	47.90 ± 10.45
History of abdominal surgery	115 (52.5%)
History of D & C artificial abortion	159 (72.6%)
History of ectopic pregnancy	30 (13.7%)
Surgical approach	
LESS	113 (51.6%)
v-NOTES	106 (48.4%)
Surgical type	
Salpingostomy	68 (31.1%)
Salpingectomy	151 (68.9%)

BMI: body mass index, v-NOTES: vaginal natural orifice transluminal endoscopic surgery, LESS: laparoendoscopic single-site surgery.

Table 2
Description of the patient characteristics by surgical approaches.

Variables	LESS	v-NOTES	P-value
Patients	N = 113	N = 106	
Age (year)	31.60 ± 4.98	31.24 ± 5.86	0.735[a]
BMI (kg/m^2)	21.38 ± 3.41	21.20 ± 2.97	0.769[a]
Duration of amenorrhea (day)	46.92 ± 7.95	48.67 ± 12.15	0.374[a]
History of abdominal surgery	60 (53.1%)	55 (51.9%)	0.756[b]
Max diameter of mass (cm)	2.94 ± 1.32	2.78 ± 1.19	0.493[a]
Preoperative HCG (mIU/ml)	2861.12 ± 5765.42	3004.95 ± 5647.45	0.897[a]
D&C artificial abortion	73 (64.6%)	86 (81.1%)	0.787[b]
History of ectopic pregnancy	17 (15.0%)	13 (12.2%)	0.293[b]
Emergency surgery	4 (3.5%)	5 (4.7%)	0.702[c]
Surgical type			0.215[b]
Salpingostomy	38 (33.6%)	30 (28.3%)	
Salpingectomy	75 (66.4%)	76 (71.7%)	
Operative information			
Duration of surgery (min)	59.53 ± 21.35	55.94 ± 17.06	0.230[a]
Bleeding volume (ml)	22.19 ± 31.01	18.02 ± 15.39	0.370[a]
Pelvic adhesion	35 (31.0%)	32 (30.2%)	0.846[b]
Surgical conversion	0 (0%)	4 (3.8%)	0.026[c]
Post-Operative information			
Hemoglobin difference (g/L)	15.65 ± 9.43	13.71 ± 9.23	0.387[a]
Hospital stay (day)	1.03 ± 0.18	0.60 ± 0.13	0.041[a]
Exhaust time (hour)	6.05 ± 4.89	4.84 ± 3.90	0.204[a]
Analgesic medication use	26 (23.9%)	8 (7.6%)	<0.001[b]
Perioperative complications	3 (2.7%)	4 (3.8%)	0.776[c]

BMI: body mass index, v-NOTES: vaginal natural orifice transluminal endoscopic surgery, LESS: laparoendoscopic single-site surgery, HCG: human chorionic gonadotropin, D&C: Dilation and Curettage.
[a] Average and standard deviation. Student's *t*-Test.
[b] Number (percentage). Chi-squared Test.
[c] Number (percentage). Fisher Exact Test.

multiple linear regression. The results showed that the amount of intraoperative bleeding was positively correlated with surgical conversion and pelvic adhesions. The bleeding volume increased by approximately 29 mL in cases involving surgical conversion (95% confidence interval [CI]: 17.56, 39.73 mL, p = .019) and 19 mL for each 1-grade increase in pelvic adhesion (95% CI: 7.08, 27.39 mL, p = .043) (**Table 3**).

The factors influencing operation time were further analyzed using multiple linear regression, and the results showed that operation duration was correlated with BMI, surgical type, surgical conversion, and pelvic adhesion (Fig. 2A). Salpingostomy, surgical conversion, and each grade of pelvic adhesion increased the operation duration by approximately 10 min (95% CI: 1.24, 18.22 min, p = .025), 32 min (95% CI: 16.83, 46.17 min, p = .037), and 9 min (95% CI:5.33, 13.39 min, p = .012), respectively (Fig. 2B). Interestingly, the operation duration also increased by approximately 1.4 min when BMI increased by 1 kg/m^2 (95% CI: 0.24, 2.59 min, p = .019).

Early postoperative anal exhaust indicates faster recovery of gastrointestinal function. Multiple linear regression analysis was conducted to investigate the factors influencing postoperative anal exhaust time, and the results showed that exhaust time was correlated with BMI, surgical approach, and pelvic adhesions (**Table 4**). A 1-kg/m^2 increase in BMI and an increase one 1 grade in

Table 3
Association between perioperative characteristics and volume of intraoperative bleeding.

Variables	Beta	95% CI	P-value	VIF
R^2 = 0.360				
Age (year)	0.09	(−0.87,1.06)	0.849	1.29
BMI (kg/m2)	−0.25	(−1.86,1.36)	0.760	1.21
Surgical approach (vNOTES)	−5.62	(−15.08,3.84)	0.242	1.04
Surgical type (Salpingostomy)	2.49	(−9.14,14.11)	0.672	1.36
Surgical transfer	28.64	(17.56,39.73)	0.019	1.13
History of abdominal surgery	−2.15	(−7.45,3.15)	0.423	1.15
Duration of amenorrhea	−0.02	(−0.51,0.46)	0.929	1.19
Max diameter of mass	−0.35	(−4.15,3.45)	0.855	1.04
Preoperative HCG	0.01	(0,0.02)	0.146	1.16
Emergency surgery	2.16	(−4.49,8.81)	0.588	1.06
Pelvic adhesion	19.24	(7.08,31.39)	0.043	1.10
Duration of surgery	0.19	(−0.08,0.46)	0.166	1.28
Surgeon	−3.60	(−11.39,4.19)	0.361	1.22

BMI: body mass index, v-NOTES: vaginal natural orifice transluminal endoscopic surgery, HCG: human chorionic gonadotropin.

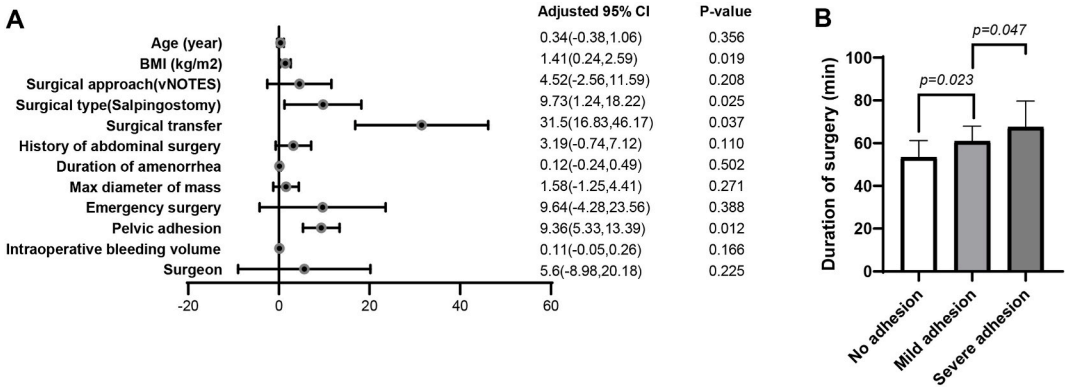

Fig. 2. The influence of surgical characteristics on the operation duration. (A) Multiple linear regression showed that the operation duration was correlated with BMI, surgical type, surgical conversion, and pelvic adhesion. Salpingostomy, surgical conversion, and each grade of pelvic adhesion increased the operation duration by approximately 10 min (95% confidence interval [CI]: 1.24, 18.22 min; p = .025), 32 min (95% CI: 16.83, 46.17 min; p = .037), and 9 min (95% CI: 5.33, 13.39 min; p = .012), respectively. Interestingly, the operation duration increased by approximately 1.4 min when BMI increased by 1 kg/m^2 (95% CI: 0.24, 2.59 min, p = .019). (B) The groups with no adhesions, mild adhesions, and severe adhesions showed significant differences in the duration of surgery.

pelvic adhesion increased the exhaust time by 0.6 h (95% CI: 0.26, 0.85 h, p = .027) and 6.7 h (95% CI: 2.90, 10.57 h, p = .019), respectively. Notably, the vNOTES approach reduced the postoperative exhaust time by approximately 9 h (95% CI: −11.93, −5.57 h, p < .001).

Analgesics are not routinely used after surgery, and patients actively requesting the use of analgesics may be experiencing greater pain and discomfort. The factors influencing postoperative analgesic drug use were analyzed using binary logistic regression, and the results showed that analgesic drug use was correlated with the surgical approach, surgical conversion, and duration of surgery (**Table 5**). Surgical conversion increased the risk of postoperative analgesic drug use by 102% (odds ratio [OR]: 2.02, 95% CI:1.34, 3.56, p = .025), while vNOTES decreased the risk by 77% (OR:0.23, 95% CI: 0.10, 0.61, p = .023). Moreover, the risk of postoperative analgesic drug use increased by 3% when the duration of surgery increased by 1 min (OR:1.03, 95% CI: 1.01, 1.12, p = .037).

The patient's fertility history was followed-up by phone one year after surgery. In the salpingostomy group, more patients chose contraception, mostly because of concerns regarding the recurrence of ectopic pregnancy. In this group, patients planning to conceive had a higher natural conception rate and risk of recurrent tubal pregnancy, and lower rates of infertility or conception through assisted reproductive technologies (**Supplementary Table 1**).

4. Discussion

Our results showed that vNOTES shortened the exhaust time and hospital stay, reduced postoperative pain, and helped avoid surface surgical scars, consistent with ERAS requirements. In this prospective study, we compared the perioperative characteristics of tubal pregnancy surgery using LESS and vNOTES in terms of the ERAS requirements and collected data on fertility one year after surgery. In addition, the advantages and disadvantages of vNOTES in relation to the ERAS requirements for tubal pregnancy surgery are discussed in detail, providing a theoretical basis for the further development of vNOTES.

The vNOTES and LESS approaches showed no significant differences in intraoperative bleeding, surgical duration, or postoperative

Table 4
Association between postoperative exhaust time and perioperative characteristics.

Variables	Beta	95% CI	P-value	VIF
$R^2 = 0.607$				
Age (year)	−0.01	(−0.33,0.32)	0.963	1.32
BMI (kg/m2)	0.56	(0.26,0.85)	0.027	1.14
Surgical approach (vNOTES)	−8.75	(−11.93,−5.57)	<0.001	1.07
Surgical type (Salpingostomy)	−2.19	(−5.92,1.55)	0.249	1.28
Surgical transfer	5.68	(−18.31,29.66)	0.201	1.21
History of abdominal surgery	1.31	(−0.64,3.25)	0.187	1.43
Max diameter of mass	0.63	(−0.63,1.88)	0.325	1.04
Emergency surgery	0.42	(−5.55,6.39)	0.889	1.35
Pelvic adhesion	6.73	(2.90,10.57)	0.019	1.16
Intraoperative bleeding volume	−0.03	(−0.09,0.04)	0.415	1.07
Duration of surgery	−0.02	(−0.10,0.07)	0.715	1.22
Surgeon	−0.45	(−1.60,0.71)	0.443	1.12

BMI: body mass index, v-NOTES: vaginal natural orifice transluminal endoscopic surgery.

Table 5
Association between postoperative analgesic medication use and perioperative characteristics.

Variables	Exp(B)	95% CI	P-value
Age (year)	0.94	(0.85,1.02)	0.177
BMI (kg/m2)	1.01	(0.86,1.18)	0.901
Surgical approach (vNOTES)	0.23	(0.10,0.61)	0.023
Surgical type (Salpingostomy)	1.02	(0.71,1.44)	0.916
Surgical transfer	2.02	(1.34,3.56)	0.025
History of abdominal surgery	0.68	(0.02,1.38)	0.826
Duration of amenorrhea	1.47	(0.89,2.43)	0.128
Max diameter of mass	0.97	(0.92,1.02)	0.255
Emergency surgery	1.29	(0.02,2.31)	0.256
Pelvic adhesion	0.56	(0.03,1.32)	0.545
Postoperative exhaust time	1.02	(0.97,1.06)	0.212
Intraoperative bleeding volume	1.00	(0.98,1.02)	0.791
Duration of surgery	1.03	(1.01,1.12)	0.037
Surgeon	1.45	(0.27,2.02)	0.109

BMI: body mass index, v-NOTES: vaginal natural orifice transluminal endoscopic surgery.

complication rates, indicating that the vNOTES approach is safe and feasible. However, the surgical conversion rate of 3.8% in the vNOTES group was much higher than that in the LESS group (0%). These conversions were primarily attributable to adhesions and the presence of the mass in the uterine part. In such cases, continued surgery under vNOTES may cause damage to neighboring organs; consequently, these patients were converted to LESS. Thus, surgeons should conduct a more comprehensive preoperative evaluation of the patients selected for vNOTES. A history of dysmenorrhea or previous pelvic surgery, difficult uterine activity, and tenderness of sacral ligament nodules may provide important clues for screening of severe pelvic adhesions [24,25]. In addition, vaginal ultrasound can be used for real-time assessment of the sliding of the uterus on the anterior wall of the rectum. If these evaluations indicate severe pelvic adhesions, the vNOTES approach should be avoided. Notably, the lesion was in the uterine part in one case. Due to failure to reach the uterine fundus, the patient underwent transumbilical single-port laparoscopy for hemostasis. This reflects the limitations of vNOTES that for lesions in the uterine fundus, vNOTES is difficult to perform surgery due to limitations in field of view and instrument range. We believe that a combination of these methods can effectively avoid the complications associated with inappropriate patient selection.

In this cohort, the incidence of complications was 3.2%, slightly higher than that associated with LESS in previous studies [21, 26–30]. Among the cases showing complications, two involved persistent ectopic pregnancies, accounting for 2.9% of salpingostomy cases, which was similar to the corresponding percentage reported in previous studies [31,32]. Both patients recovered and were discharged from the hospital after methotrexate administration following surgery, and neither patient required re-surgery. Moreover, the surgical duration in the vNOTES group was shorter than that in the LESS group, although the difference was not statistically significant. This may be due to the smaller chopstick effect caused by the lesion being closer to the platform [33–35]. Our experience suggests that salpingostomy and ovarian cystectomy are more convenient to perform using vNOTES because the lesion site is directly located in front of the approach [36,37].

The timing of postoperative anal exhaust as a part of the discharge evaluation criteria is crucial for evaluating the ERAS mode [38, 39]. In our cohort, the postoperative exhaust time was shorter in the vNOTES group than in the LESS group, which is consistent with previous studies [40]. The vNOTES procedure was performed in the pelvic area, and showed little effect on the upper abdomen. After entering the pelvis, the first step is to push the small intestine into the abdominal cavity, after which the intestine will not be touched again, thereby minimizing intestinal irritation. Additionally, because the vNOTES incision is made in the vaginal vault, this site is insensitive to cutting pain caused by visceral nerve innervation. Lighter postoperative pain encourages patients to get out of the bed early after surgery, which can also promote gastrointestinal recovery and facilitate earlier exhaust [41,42].

The ERAS concept requires less damage to patients, faster postoperative recovery, greater patient comfort, and an earlier return to normal life activities [43–45]. The findings of this study imply that vNOTES is not inferior to or is even more suitable than LESS in terms of the ERAS concept. Moreover, vNOTES offers the advantage of completely eliminating surface scars, making it aesthetically pleasing. However, in patients who choose vNOTES, a more comprehensive preoperative evaluation is required to reduce the occurrence of intraoperative conversion.

The follow-up assessments of the patients' fertility status one year after surgery yielded noteworthy findings. Among the patients who chose salpingostomy because of reproductive reasons, 61.8% chose continuous contraception because of concerns regarding another ectopic pregnancy. However, patients who undergo salpingectomy have fewer options for contraception because they don't have to worry about ectopic pregnancy happening again in the affected fallopian tubes. This situation may also be caused by informed notification from physicians during the perioperative period. As for patients who choose salpingostomy, physicians usually recommend strict contraception for 3–6 months and inform them that the affected fallopian tube will increases the risk of ectopic pregnancy again after surgery. This may increase the psychological pressure on patients, leading them to choose long-term contraception. Although patients undergoing salpingostomy have a slightly higher natural conception rate, they also have a 15.4% chance of recurrent tubal pregnancy. Therefore, further studies are needed to determine which surgical method is the best choice for women with reproductive needs.

The strengths of this study include its prospective design and professional participants. The patients were included on the basis of

strict inclusion and exclusion criteria and a surgical procedure, ensuring a high degree of consistency in demographic characteristics between the two groups. This study compared the perioperative characteristics of the two most advanced surgical methods for tubal pregnancy surgery and preliminarily confirmed the safety and effectiveness of vNOTES for this procedure. In addition, a relatively comprehensive experimental design was implemented by prospectively collecting follow-up data from patients at 1 week, 1 month, and 1 year after surgery.

This pilot study strengthened our understanding of the safety of vNOTES during tubal pregnancy. However, this study had some limitations. First, the sample size of this study was relatively smaller than that of similar studies using Multi-port and LESS. Second, the limitations of the vNOTES technique are the chopstick effect (lack of triangulation resulting from the use of the conventional equipment) and the limited experience of the surgeons. Before performing vNOTES surgery, we suggest that all surgeons and surgical team members should follow standardized operating procedures to complete the learning curve [23]. Third, although this study shows that vNOTES can promote ERAS in patients, it is necessary to grasp the indications of this approach to reduce the occurrence of complications and surgical conversions. Four, since this study is not a randomized clinical trial, we are unable to specify surgical procedures for patients. After fully informing the advantages and disadvantages of the two surgeries, the final decision is based on the patient's wishes. Therefore, in this process, some potential bias factors may be added, which may affect the choice of surgical methods for patients. Five, if there is a conventional surgical group as the control group, it can indeed better demonstrate the advantages of vNOTES. However, due to the fact that our hospital no longer performs routine open surgery and Multi-port laparoscopic surgery except for some large uterine fibroids or malignant tumor surgeries, we do not have enough data as a control. Six, vNOTES has been widely used in gynecology for only 5 years, and the patients in this study were followed-up for only 1 year. Longer follow-up periods with more patients can improve our understanding of the short- and long-term complications of vNOTES and their potential influence on sexual function and fertility. Therefore, large-scale multicenter studies involving more patients, longer time periods, and more types of surgery are needed to further promote the widespread use of vNOTES in the field of gynecology.

5. Conclusions

Our results indicated that vNOTES could shorten the exhaust time and hospital stay, reduce postoperative pain, and avoid surface surgical scars, consistent with the ERAS concept. Thus, vNOTES may be more suitable for ERAS than LESS. However, in patients who choose vNOTES, a more comprehensive preoperative evaluation is required to reduce the occurrence of intraoperative conversion. With the further popularization of minimally invasive and scar free surgery, vNOTES will inevitably achieve longer-term development. Therefore, more and higher quality research is needed to demonstrate its advantages and promote its rapid development.

Capsule

To reflect the safety of vaginal natural orifice transluminal endoscopic surgery (vNOTES) in terms of the Enhanced Recovery after Surgery (ERAS) concept for tubal pregnancy surgery and provide a detailed process of vNOTES for tubal pregnancy surgery, including experience and key points for surgeons performing this procedure.

Funding

Financial support for this study was provided by the Sichuan Provincial Department of Science and Technology (2023YFS0219 and 2023YFS0228), Chengdu Science and Technology Bureau (No: 2021-YF0500530-SN) and the Chengdu Municipal Health Commission (No: 2021074, 2022441, 2023261, 2023413 and 2023475). The funding agencies did not have any role in the design of the study; collection, analysis, and interpretation of data; or in writing the manuscript.

Attestation statement

The subjects in this trial have not concomitantly been involved in other randomized trials. Data regarding any of the subjects in the study has not been previously published unless specified. Data will be made available to the editors of the journal for review or query upon request.

IRB approval

This study was approved by the Institutional Review Board of Chengdu Women and Children's Central Hospital (No. 202130) on June 14, 2021.

Data availability

The datasets generated and analyzed during the current study are not publicly available because of our ongoing prospective study but are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Ying Liu: Writing – original draft. **Xin Li:** Writing – original draft. **Tianjiao Liu:** Writing – original draft. **Aijie Xie:** Writing – original draft. **Xian Wu:** Writing – original draft. **Yujian Jia:** Writing – original draft. **Xiaoyan Liao:** Writing – original draft. **Wei Cheng:** Writing – original draft. **Hui Wang:** Writing – original draft. **Fangyuan Zhong:** Writing – original draft. **Lijuan Xu:** Writing – original draft. **Juan Huang:** Writing – original draft. **Siqin Xiu:** Writing – original draft. **Zhongzhi Li:** Writing – original draft. **Yalan Li:** Writing – original draft. **Xue Xiao:** Writing – review & editing, Writing – original draft, Funding acquisition. **Yonghong Lin:** Writing – original draft. **Xiaoqin Gan:** Writing – original draft.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to thank all participants and researchers who contributed to this cohort study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e24945.

References

[1] Y.T. Shen, Y.Y. Yang, P.G. Zhang, L.M. He, R.H. Che, Z. Li, W. Lu, Tubal ectopic pregnancy: a retrospective cohort study on clinical characteristics, treatment options and reproductive outcomes within 5 years, Arch. Gynecol. Obstet. 306 (6) (2022) 2055–2062.
[2] K. Tamai, T. Koyama, K. Togashi, MR features of ectopic pregnancy, Eur. Radiol. 17 (12) (2007) 3236–3246.
[3] G. Oron, T. Tulandi, A pragmatic and evidence-based management of ectopic pregnancy, J. Minim. Invasive Gynecol. 20 (4) (2013) 446–454.
[4] P. Cheng, X.H. Yang, Preservation of the fallopian tube in ectopic tubal pregnancy. An analysis of the outcome of two laparoscopic surgical approaches, Ann. Ital. Chir. 93 (2022) 241–247.
[5] E. Nedopekina, S. Escura, T. Cobo, S.R. Hansson, J.M. Martinez, F. Figueras, M. Lopez, Conservative treatment in non-tubal ectopic pregnancy and predictors of treatment failure, Eur. J. Obstet. Gynecol. Reprod. Biol. 257 (2021) 6–10.
[6] E. Eghbali, M. Azari, A. Jafarizadeh, S. Alihosseini, Spontaneous bilateral tubal ectopic pregnancy preoperatively diagnosed by the ultrasound: a case report, BMC Pregnancy Childbirth 23 (1) (2023) 125.
[7] P. Torok, A. Naem, S. Csehely, V. Chiantera, Z. Sleiman, A.S. Lagana, Reproductive outcomes after expectant and surgical management for tubal pregnancy: a retrospective study, Minim Invasive Ther. Allied Technol. (2023) 1–9.
[8] B. Xu, Y. Liu, X. Ying, Z. Fan, Transvaginal endoscopic surgery for tubal ectopic pregnancy, J. Soc. Laparoendosc. Surg. 18 (1) (2014) 76–82.
[9] Y.W. Kim, B.J. Park, T.E. Kim, D.Y. Ro, Single-port laparoscopic salpingectomy for surgical treatment of tubal pregnancy: comparison with multi-port laparoscopic salpingectomy, Int. J. Med. Sci. 10 (8) (2013) 1073–1078.
[10] G. Ozceltik, D. Simsek, I. Hortu, A.O. Yeniel, I.M. Itil, Transvaginal natural orifice transluminal endoscopic surgery for ectopic pregnancy, J. Obstet. Gynaecol. Res. 48 (3) (2022) 843–849.
[11] G. Ozceltik, A.O. Yeniel, A.O. Atay, I.M. Itil, Transvaginal natural orifice transluminal endoscopic surgery for tubal stump pregnancy, J. Minim. Invasive Gynecol. 28 (4) (2021) 750–751.
[12] J. Ripolles-Melchor, A. Abad-Motos, M. Bruna-Esteban, M. Garcia-Nebreda, I. Otero-Martinez, O.A. Fernandez, M.P. Tormos-Perez, G. Paseiro-Crespo, R. Garcia-Alvarez, M Am-O, et al., Association between use of enhanced recovery after surgery protocols and postoperative complications after gastric surgery for cancer (POWER 4): a nationwide, prospective multicentre study, Cir. Esp. (Engl. Ed.) (2023).
[13] G. Nelson, C. Fotopoulou, J. Taylor, G. Glaser, J. Bakkum-Gamez, L.A. Meyer, R. Stone, G. Mena, K.M. Elias, A.D. Altman, et al., Enhanced recovery after surgery (ERAS(R)) society guidelines for gynecologic oncology: addressing implementation challenges - 2023 update, Gynecol. Oncol. 173 (2023) 58–67.
[14] J. Gillet, L. Morgado, A. Hamy, C. Casa, S. Mucci, F. Drissi, P. Le Naoures, J.F. Hamel, A. Venara, Does stoma modify compliance with enhanced recovery after surgery programs? Results of a cohort study, Int. J. Colorectal Dis. 38 (1) (2023) 100.
[15] J. Baekelandt, L. Matak, M. Merckx, S. Housmans, J. Deprest, T. Tollens, Posterior rectus fascia prolapse (PREFAP) repair: a new native tissue approach to pelvic organ prolapse via vaginal natural orifice transluminal endoscopic surgery, Arch. Gynecol. Obstet. (2023).
[16] L. Mereu, B. Pecorino, M. Ferrara, M. Siniscalchi, G. Garraffa, M.G. D'Agate, P. Scollo, Cumulative sum analysis of learning curve process for vaginal natural orifice transluminal endoscopic surgery (V-notes) hysterectomy, J. Minim. Invasive Gynecol. (2023).
[17] V.T. Lerner, G. May, C.B. Iglesia, Vaginal natural orifice transluminal endoscopic surgery revolution: the next frontier in gynecologic minimally invasive surgery, J. Soc. Laparoendosc. Surg. 27 (1) (2023).
[18] L. Huang, J. Yu, Y. Li, Z.L. Gong, D. Feng, L. He, Y.H. Lin, Transvaginal natural orifice transluminal endoscopic surgery versus conventional vaginal surgery for sacrospinous ligament fixation of apical compartment prolapse: a retrospective analysis, BMC Surg. 23 (1) (2023) 24.
[19] J. Jung, J.J. Noh, J. Jeon, C.S. Chang, T.J. Kim, Comparison of surgical outcomes of adnexectomy by vaginal natural orifice transluminal endoscopic surgery (vNOTES) versus single-port access (SPA) surgery, J. Personalized Med. 12 (12) (2022).
[20] J. Zhang, Y. Dai, J. Leng, L. Zhu, J. Lang, D. Sun, Hysterectomy and bilateral adnexectomy using transvaginal natural orifice transluminal endoscopic surgery: the role of multichannel abdominal PORT and vaginal support ring, J. Obstet. Gynaecol. Res. 47 (7) (2021) 2521–2528.
[21] M.S. Kim, J.J. Noh, T.J. Kim, Hysterectomy and adnexal procedures by vaginal natural orifice transluminal endoscopic surgery (VNH): initial findings from a Korean surgeon, Front. Med. (Lausanne) 7 (2020) 583147.
[22] M. Elsherbiny, E.T. Lim, K. Ma, Interstitial ectopic pregnancy: laparoscopic cornuostomy, J. Minim. Invasive Gynecol. 30 (6) (2023) 439–440.
[23] L. Huang, L. He, L. Huang, X. Gan, Y. Lin, Z. Xiong, Learning curve analysis of transvaginal natural orifice transluminal endoscopic hysterectomy combined under the standard operating procedure, Int. J. Gynaecol. Obstet. 159 (3) (2022) 689–695.
[24] M. Hui, C. Schwartzenburg, A. Bhalwal, Utility of vaginal natural orifice transluminal endoscopic surgery for permanent sterilization after failed attempt at bilateral tubal ligation at the time of previous cesarean section, J. Minim. Invasive Gynecol. 29 (10) (2022) 1138–1139.

[25] X. Guan, E. Bardawil, J. Liu, R. Kho, Transvaginal natural orifice transluminal endoscopic surgery as a rescue for total vaginal hysterectomy, J. Minim. Invasive Gynecol. 25 (7) (2018) 1135–1136.
[26] A. Kale, E. Mat, G. Basol, E.C. Gundogdu, Y. Aboalhasan, G. Yildiz, B. Kuru, E. Kale, T. Usta, M. Altintas, et al., A new and alternative route: transvaginal natural orifice transluminal endoscopic scarless surgery (vaginal natural orifice transluminal endoscopic surgery) for class 2 and class 3 obese patients suffering from benign and malignant gynecologic pathologies, Surg. Innovat. 29 (6) (2022) 730–741.
[27] I. Tavano, S. Housmans, J. Bosteels, J. Baekelandt, Pregnancy outcome after vaginal natural orifice transluminal endoscopic surgery, a first retrospective observational cohort study, Gynecol. Obstet. Invest. 86 (5) (2021) 432–437.
[28] K. Nulens, R. Kempenaers, J. Baekelandt, Hysterectomy via vaginal Natural Orifice Transluminal Endoscopic Surgery in virgin patients: a first feasibility study, J. Obstet. Gynaecol. 42 (1) (2022) 116–121.
[29] K. Nulens, I. Van Genechten, J. Baekelandt, Repeat vaginal natural orifice transluminal endoscopic surgery: a first feasibility study, Gynecol. Obstet. Invest. 86 (1–2) (2021) 117–122.
[30] L. Huang, Y.H. Lin, Y. Yang, Z.L. Gong, L. He, Comparative analysis of vaginal natural orifice transluminal endoscopic surgery versus transumbilical laparoendoscopic single-site surgery in ovarian cystectomy, J. Obstet. Gynaecol. Res. 47 (2) (2021) 757–764.
[31] E. Wall-Wieler, C.L. Shover, J.M. Hah, S.L. Carmichael, A.J. Butwick, Opioid prescription and persistent opioid use after ectopic pregnancy, Obstet. Gynecol. 136 (3) (2020) 548–555.
[32] S. Akira, Y. Negishi, T. Abe, M. Ichikawa, T. Takeshita, Prophylactic intratubal injection of methotrexate after linear salpingostomy for prevention of persistent ectopic pregnancy, J. Obstet. Gynaecol. Res. 34 (5) (2008) 885–889.
[33] T. Benhidjeb, I. Benhidjeb, M. Stark, S. Kreisel, M. Kruger, J. Pfitzenmaier, J. Schulte am Esch, Women's perception of transgastric and transvaginal natural orifice transluminal endoscopic surgery (NOTES) - impact of medical education, stage of life and cross-cultural aspects, Int. J. Womens Health 14 (2022) 1881–1895.
[34] M.L. Interdonato, P. Scollo, T. Bignardi, F. Massimello, M. Ferrara, G. Donatiello, M. Caretto, P. Mannella, B. Pecorino, M.G. Meroni, et al., Hysterectomy by transvaginal natural orifice transluminal endoscopic surgery: an Italian initial experience, Front. Med. (Lausanne) 9 (2022) 1018232.
[35] A.B. Tekin, M. Yassa, C. Kaya, D. Budak, P.B. Ilter, M.A. Mutlu, C. Usta, O.S. Gunkaya, E. Yavuz, N. Tug, Implementing the transvaginal natural orifice transluminal endoscopic surgery (vNOTES) "first" strategy in benign gynecological surgeries, Arch. Gynecol. Obstet. 307 (4) (2023) 1007–1013.
[36] Y. Jung, A. Rattanaburi, O. Kim, J.H. Park, K.H. Lee, A simple gasless direct suturing technique to achieve ovarian hemostasis during transvaginal natural orifice transluminal endoscopic surgery ovarian cystectomy, J. Laparoendosc. Adv. Surg. Tech. 31 (9) (2021) 1046–1050.
[37] C.B. Li, K.Q. Hua, Transvaginal natural orifice transluminal endoscopic surgery (vNOTES) in gynecologic surgeries: a systematic review, Asian J. Surg. 43 (1) (2020) 44–51.
[38] J. Chen, A.L. Luo, L. Yang, W. Wang, X. Zhou, M. Yang, Nutrition management by a multidisciplinary team for prevention of nutritional deficits and morbidity following esophagectomy, Braz. J. Med. Biol. Res. 56 (2023) e12421.
[39] Z. Wang, Q. Xia, A. Li, Q. Lv, Comparison of the effects of endoscopic submucosal dissection and laparoscopic distal radical surgery on the rehabilitation and quality of life of patients with early gastric cancer, Am. J. Transl. Res. 15 (3) (2023) 2183–2190.
[40] Q. Hou, X. Li, L. Huang, Y. Xiong, D. Feng, Q. Zhang, X. Zeng, Y. Yang, T. Liu, Y. Li, et al., Transvaginal natural orifice endoscopic surgery for myomectomy: can it be a conventional surgery? Front. Surg. 9 (2022) 1013918.
[41] X. Lv, C. Li, M. Tang, D. Yuan, Y. Zhong, Y. Xie, Study of the effect of pain on postoperative rehabilitation of patients with uterine malignant tumor, Front. Surg. 9 (2022) 1052800.
[42] N. Zhang, J. Miao, Q. Zheng, The effect of nursing intervention on patients with inguinal hernia and its influence on self-management ability, Contrast Media Mol. Imaging 2022 (2022) 4965709.
[43] Z. Lin, C. Yang, Y. Wang, M. Yan, H. Zheng, Comparison of prolonged postoperative ileus between laparoscopic right and left colectomy under enhanced recovery after surgery: a propensity score matching analysis, World J. Surg. Oncol. 20 (1) (2022) 68.
[44] N. Kugelman, O. Lavie, N. Cohen, M. Schmidt, A. Reuveni, L. Ostrovsky, H. Dabah, Y. Segev, Enhanced recovery after surgery is feasible and beneficial and should Be the standard in major gynecological surgeries, Isr. Med. Assoc. J. 23 (11) (2021) 725–730.
[45] O.I. Tkachenko, S.H. Chetverikov, O.V. Bondar, V.Y. Maksymovskyi, M. Chetverikov, V.V. Chetverikova-Ovchynnyk, Implementation of the enhanced recovery after surgery protocol for patients with peritoneal carcinomatosis undergoing cytoreductive surgery and hyperthermic intraperitoneal chemoperfusion, Contemp. Oncol. 25 (2) (2021) 133–139.