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Minimally invasive surgery in benign gynecological pathology

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Minimally invasive surgery in benign gynecological pathology

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Editorial: Minimally invasive surgery in benign gynecological pathology

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KEYWORDS

laparoscopy, gynecology, robotic surgery, hysteroscopy, minimally invasive surgery

Editorial on the Research Topic
Minimally invasive surgery in benign gynecological pathology

In the ever-evolving landscape of medical science, one particularly remarkable advancement has changed the surgical approach of the abdominal wall—minimally invasive surgery.

This revolutionary approach has transformed the field of gynecology by offering safer, less painful and more effective alternatives to traditional open surgery. In this editorial, we will explore the significance of minimally invasive surgery in treating benign gynecological conditions and the positive impact it has on patients' quality of life after complex surgery.

Traditionally, benign gynecological pathologies such as uterine fibroids, ovarian cysts, endometriosis and pelvic adhesions often required open abdominal surgeries, which involved large incisions, extended hospital stay and prolonged recovery periods. These procedures also implied a higher risk of complications, increased pain and emotional distress for patients.

The philosophy of minimally invasive surgery is performing complex surgery for various pathologies through small incisions. This can be achieved by laparoscopy, robotic and vaginal surgery. In the spirit of reducing the surgical related trauma the use of natural orifices such as the vagina to approach the pelvis is very effective. Xie et al. showed that surgery for ovarian cyst can be performed by transvaginal natural orifice endoscopic surgery as a day-care procedure. Mei et al. performed the comparison of gases and traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery in hysterectomy showing that there is still room for reducing the trauma associated to minimal invasive surgery.

One of the most common benign gynecological conditions treated using minimally invasive surgery is uterine fibroids. This represents the most common benign disease of the uterus, affecting up to 68.6% women (1) generating symptoms like heavy menstrual bleeding, pelvic pain, and infertility. Minimal invasive surgery can be used to perform either hysterectomy or myomectomy (1–6). Dumitrașcu et al. performed a review showing the importance of surgical technique when performing laparoscopic myomectomy. This approach is suitable for complex cases also, and techniques to minimize blood loss during surgery can be applied (7–13) Balulescu et al. presented the results of a clinical trial that investigated the efficiency of temporary occlusion of the hypogastric artery during laparoscopic myomectomy (9). Hertling et al. demonstrated the benefit of uterine artery embolisation before laparoscopic myomenucleation of large fibroids.

Pelvic floor disorders that require complex surgery can also be approached by minimal invasive surgery. Ciortea et al. performed a systematic review and meta-analysis investigating the best approach for the treatment of vaginal vault prolapse and showing the benefits of minimal invasive surgery.

Hysteroscopy is another form a minimal invasive surgery (14–18) and the spectrum of indication for this type of surgery is developing continuously. Teng et al. published their results with hysteroscopic curettage in the treatment of type II cesarean scar pregnancy. Liu et al. investigated the use of hysteroscopy vs. dilation and curettage for the assessment of the endometrium.

The advantages of minimally invasive surgery extend beyond the operating room. Patients experience shorter hospital stays, reduced postoperative pain, faster recovery, and improved cosmetic outcomes due to smaller incisions. Furthermore, the risk of postoperative complications, such as infection and blood loss, is significantly lower compared to traditional open surgeries (19–23). Xing et al. demonstrated that enhanced recovery after surgery alleviates neutrophil to lymphocyte ratio, correlates with lower pain score and faster recovery.

Hence, minimally invasive surgery leads to better overall patient satisfaction. Women who undergo these procedures report improved quality of life, as they can return to their daily activities sooner and with less discomfort. This is particularly crucial for those who are balancing their careers, families, and personal lives.

While *Minimally invasive surgery in benign gynecological pathology* has transformed the field, it is essential to acknowledge that these techniques require specialized training and experience. Surgeons must be skilled in the use of laparoscopic and robotic-assisted equipment to ensure optimal outcomes for patients. Therefore, continued investment in surgical education and technology is paramount to further advancing the field.

In conclusion, *Minimally invasive surgery in benign gynecological pathology* has ushered in a new era of patient-centered care. It has replaced the traditional open surgeries with less invasive, safer, and more effective options. Women facing conditions such as uterine fibroids, ovarian cysts, endometriosis, and pelvic adhesions can now benefit from quicker recoveries, shorter hospital stays, and improved overall wellbeing. As we continue to advance in the field of gynecology, the integration of minimally invasive techniques will undoubtedly play a pivotal role in empowering women to lead healthier, more fulfilling lives.

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Comparison of prognosis of patients with endometrial cancer after hysteroscopy versus dilatation and curettage: A multicenter retrospective study

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Introduction: Hysteroscopy is a useful procedure for diagnosing endometrial cancer. There is controversy regarding whether hysteroscopy affects the prognosis of endometrial cancer by prompting cancer cell into intraperitoneal dissemination. Our purpose was to confirm whether hysteroscopy could be a risk factor of the tumor stage, recurrence and survival rate of endometrial cancer.

Methods: This multicenter retrospective study included all consecutive patients who had endometrial carcinoma diagnosed preoperatively with hysteroscopy and directed endometrial biopsy (HSC, group A) and dilatation and curettage (D&C, group B) between February 2014 and December 2018 at the Fujian Provincial, China. We compared the demographic feature, clinical characteristics and prognosis between the two groups.

Results: A total of 429 patients were included in the study (Group A, n = 77; Group B, n = 352). There was no significant difference between their baseline characteristics [including age, BMI, histological type and International Federation of Gynecology and Obstetrics (FIGO) stage]. By comparing several pathological conditions that may affect prognosis, there were no significant differences between the two groups in the peritoneal cytology, depth of myometrial invasion, the positivity of lymph nodes, lymphovascular space invasion and paraaortic lymph node dissection. Finally, no significant difference was found between the two groups in overall survival (OS) (P = 0.189) or recurrence free survival (RFS) (P = 0.787).

Conclusion: Under certain inflation pressure and distension medium, hysteroscopic examination and lesion biopsy ensure the safety and have no adverse effects on prognosis compared to conventional curettage.

KEYWORDS

endometrial cancer, hysteroscopy, peritoneal cytology, prognosis, curettage

Introduction

Endometrial cancer, a tumor originating in the uterine endometrium, is one of the most common gynecological cancers, with its prevalence has increased worldwide in recent years (1). As the disease is frequently symptomatic at an early stage in the majority of patients, endometrial cancer is often diagnosed at stage I, which means the disease is confined to the uterus. The 5-year survival rates are as high as 74–91% in these stage I patients (1, 2). Therefore, it is important to diagnose endometrial cancer at an early stage. The current diagnosis of endometrial cancer is based on histological results of endometrial sampling by endometrial biopsy, uterine dilation and curettage (D&C), and hysteroscopy and directed endometrial biopsy (HSC). D&C is a common diagnostic procedure. The tools of D&C are more readily available, and the procedures are more mature and easily quality-controlled, thus facilitating the implementation of D&C in a wide range of primary care hospitals in China. Although D&C is a common diagnostic blind procedure for endometrial cancer in all institutions (3), it might lead to a high false negative rate in endometrial cancer (4). In contrast, visible HSC has increasing used to determine endometrial lesions, especially in minimal lesions, and performing biopsies. Considered HSC provides direct visualization of the endometrial cavity, hysteroscopy-guided biopsy has a high accuracy for the diagnosis of endometrial cancer (5).

Recently, hysteroscopy is considered to be a standard procedure for diagnosing endometrial cancer (4, 6–8). Especially, for young women who wants to preserve fertility, hysteroscopy can preserve the integrity of the endometrium to the greatest extent, offering the possibility of fertility for patients with early stage endometrial cancer and reducing the incidence of adverse pregnancies and deliveries (9, 10) and for postmenopausal women, the hysteroscopic visual appearance could detect morphological differences in endometrial cancer (11, 12). Hysteroscopy can also underly the advantages of performing hysteroscopy in the preoperative management of endometrial cancer, as it allows the distinction between endocervical mucosal infiltration and a protrusion into the endocervical canal, helping to inform the decision on therapeutic management. However, some studies have shown that hysteroscopy has the potential risk to cause the spread of cancerous cell (13) and manifest side effects in endometrial prognosis. Therefore, we conducted this retrospective study to compare the risk factors, recurrence and survival rate of women with endometrial cancer between HSC and D&C as the diagnostic procedure.

Patients and methods

Patients

This multicenter retrospective study included all consecutive patients who had endometrial carcinoma diagnosed preoperatively with either D&C or HSC between February 2014 and December 2018 at the Fujian Provincial, China. Patient stage of endometrial cancer was based on the International Federation of Gynecology and Obstetrics (FIGO) 2009 staging system. The patients were divided into two groups by the diagnostic procedure: HSC (Group A) versus D&C (Group B).

Women were excluded as follows: (1) had not undergone hysterectomy and bilateral salpingo-oophorectomy (HBSO) with washing for cytology; (2) had not undergone neither D&C or HSC before HBSO; (3) incomplete follow-up. The study was approved by our institution's ethics committee (2022KYLLR0343).

The clinical, surgical, and pathological results were retrieved from electronic dataset for analysis. A detailed analysis of tumor histopathological risk characteristics was performed, including histopathological type, tumor differentiation, the depth of myometrial invasion, lymph-vascular invasion and FIGO stage. Follow-up information were recorded by outpatient department and telephone. Our cohort of patients was followed every 3 months from the date of surgery until an event (recurrence, death from disease, or death) or the last follow-up up to December 2020.

Surgical procedure

HSC was performed under general anesthesia. A saline solution warmed to body temperature was used as the distension medium. In the procedure, the distension medium was installed into the pressure cuff, and the intrauterine pressure was set

between 20 and 23 kPa. Intrauterine pressure was controlled with a Vario Flow device (Olympus). We used hysteroscopy to examine the cervical canal, anterior and posterior walls, both sides of the wall, the fundus of the uterine cavity and suspicious lesions, all of which were sampled at multiple points. The sample technique is using a hysteroscopic 5Fr toothed grasping forceps to "plow" along with the suspicious tissue for about 0.5–1 cm. And then grasping forceps retrieved from the uterine cavity together along with the hysteroscope, without, retracting the tip of the forceps into the operating channel. D&C was also performed under general anesthesia. Curettage of the cervical canal and the uterine cavity was performed separately. Tissue samples for histological examination were obtained during both procedures.

During the comprehensive staging surgery for endometrial carcinoma, samples of peritoneal washings with saline solution was performed to obtain cytological examination in cases with no free fluid. The samples were inspected by an expert cytopathologist. In cases of small numbers of positive cells after immunostaining, peritoneal cytology was described as suspicious. We therefore included suspicious results in the analysis of positive peritoneal cytology.

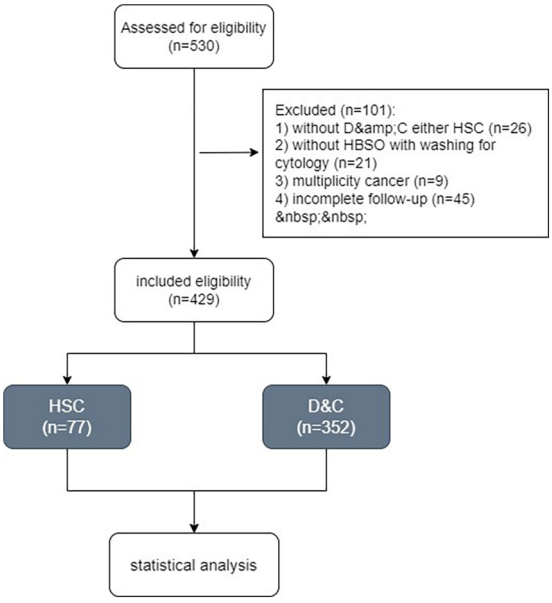

FIGURE 1
Patients collection flowchart.

Statistical analysis

Statistical analysis was performed with SPSS software version 22.0 (IBM, Armonk, NY, USA). Descriptive analysis, chi-square tests and t tests of independent samples were performed as applicable. A *p*-value of less than 0.05 was considered statistically significant. We conducted a series of survival analyses using Kaplan-Meier statistics. The significance of the difference in the unadjusted survival curves was assessed using the log-rank test.

Results

Baseline characteristics

Totally, 530 women with endometrial carcinoma were recorded between February 2013 and December 2018. Finally, 429 patients who met our criteria underwent HSC (Group A, $n = 77$) and D&C (Group B, $n = 352$) were included in the study (**Figure 1**).

The baseline characteristics of the two groups are presented in **Table 1**. The mean age was 52.36 years in Group A and 53.99 years in Group B, and the mean BMI was 24.74 kg/m^2 in Group A and 24.79 kg/m^2 in Group B. There was no significant difference between the two groups. In terms of postoperative pathology, endometrioid adenocarcinoma was predominant in both groups ($N = 371$; 86.5%). Among the endometrioid adenocarcinomas, differentiation was predominantly G1 and G2, and there was no significant difference between the two groups. According to 2009 FIGO staging system, early stage was predominant in both groups, and there was no significant difference.

HSC impact on prognostic high-risk factors for endometrial cancer

As mentioned in many studies, HSC can lead to positive peritoneal cytology; however, the correlation between positive peritoneal cytology and tumor progression is more controversial. And HSC may cause poor prognosis by myometrial invasion, lymph node metastasis, and lymph-vascular invasion for the inflation pressure (14, 15). Therefore, by comparing several results from HSC pathological risk conditions that may affect prognosis (13, 16–18), such as the depth of myometrial invasion, lymph node metastasis, and lymph-vascular invasion, there was no significant difference between the 2 groups (**Table 2**).

Analysis of cases of positive peritoneal cytology

Peritoneal dissemination is most likely to be influenced by HSC (7, 8, 15, 19). However, in our study, there was no significant difference between the two groups. Therefore, we would like to further explore the factors associated with peritoneal dissemination. Only a total of 12 patients in the two

TABLE 1 Baseline characteristics of HSC and D&C.

Baseline characteristics	Hysteroscopy *n* = 77 (%)	D&C *n* = 352 (%)	*P*-value
Age (years, mean ± S/D)	52.36 ± 7.51	53.99 ± 8.35	0.115
BMI (kg/m^2, mean ± S/D)	24.74 ± 3.52	24.79 ± 3.59	0.911
Histological type, *n* (%)			0.518
Endometroid adenocarcinoma	70 (90.9)	320 (90.9)	
Non-endometroid adenocarcinoma	7 (9.1)	32 (9.2)	
Histological grade			0.809
G1	34 (54.8)	172 (57)	
G2	22 (35.5)	108 (35.8)	
G3	6 (9.7)	22 (7.3)	
FIGO stage			0.435
Early stage (I–II)	71 (92.2)	321 (91.2)	
Advanced stage (III–IV)	6 (7.8)	29 (8.3)	

TABLE 2 Comparing pathological conditions that may affect the prognosis of EC between HSC and D&C.

High-risk factors	Hysteroscopy *n* = 77 (%)	D&C *n* = 352 (%)	*P*-value
Myometrial invasion			0.191
None	11 (14.3)	41 (11.8)	
Less than 1/2	44 (57.1)	237 (68.1)	
More than 1/2	22 (28.6)	70 (20.2)	
Positivity of lymph nodes	5 (6.5)	18 (5.1)	0.398
Pelvic lymph node	2 (2.6)	14 (4.0)	0.429
Para-aortic lymph node	3 (3.9)	4 (3.9)	0.113
Lymph node dissection			
Pelvic lymph node dissection	22 (28.6)	163 (46.3)	0.005
Para-aortic lymph node dissection	12 (15.6)	40 (11.4)	0.525
Lympho-vascular space invasion			0.459
Present	6 (7.8)	24 (6.8)	
Absent	71 (92.2)	328 (93.2)	
Peritoneal cytology			0.442
Positive or suspicious	3 (4.3)	9 (2.7)	
Negative	67 (95.7)	327 (97.3)	

groups showed positive or suspicious cytology in the peritoneal washings, and the detailed cases of the results are shown in Table 3.

Prognosis

Finally, we compared the OS and RFS of the two groups, and the mean follow-up time (months) of Group A was 53.605 months (CI: 48.843–58.367) and that of Group B was 58.158 months (CI: 55.956–60.367). There was no significant difference between the 2 groups (P_{os} = 0.189, P_{RFS} = 0.787) (Figures 2, 3).

Discussion

Our findings affirm that HSC as a diagnostic procedure is not associated with a worse pathological risk factors and prognosis, and may probably be safely used in patients with endometrial cancer. Therefore, HSC may be used as one of the standard procedures for the diagnosis of suspected endometrial

TABLE 3 Description of 12 patients with positive peritoneal cytology.

Study ID	Age	Method of diagnosis	Diagnosis	FIGO stage	Myometrial invasion	LVSI	Distant metastasis
54	61	D&C	Endometrioid carcinoma 70% mixed serous carcinoma 30%	IIIc1	>1/2	Y	Pelvic lymph node
63	61	D&C	Endometrioid carcinoma FIGO G2	IIIA	>1/2	N	Bilateral accessary
139	61	Hysteroscopy	Non-keratinized squamous cell carcinoma	IIIC2	>1/2	Y	Para-aortic lymph node
158	46	D&C	Endometrioid carcinoma FIGO G1	IA	<1/2	N	None
174	50	D&C	Endometrioid carcinoma FIGO G1	II	<1/2	N	Cervix
211	43	D&C	Endometrioid carcinoma FIGO G3 mixed clear cell carcinoma	IIIC1	>1/2	Y	Pelvic lymph node
240	41	D&C	Endometrioid carcinoma FIGO G1	IA	>1/2	N	None
243	61	D&C	Serous carcinoma	IVB	>1/2	Y	Peritoneal, Omental, and accessary (L)
289	52	Hysteroscopy	Mixed clear cell carcinoma 65%, Serous carcinoma 30% and Endometrioid carcinoma 5%	IVA	>1/2	N	Sigmoid colon
304	52	D&C	Endometrioid carcinoma FIGO G1	IA	>1/2	N	None
360	60	D&C	Endometrioid carcinoma FIGO G3	IVB	>1/2	N	Cervix, Parametrium, Omental, and bilateral accessary
429	54	Hysteroscopy	Endometrioid carcinoma FIGO G2	IA	>1/2	Y	None

cancer. Additionally, HSC is considered the gold standard for evaluating the uterine cavity in cases of abnormal uterine bleeding (20), especially increased the accuracy in the diagnosis of endometrial cancer.

Up to now, the safety of HSC used in endometrial cancer, especially its long-term prognosis, are controversial. One of the most controversial points is whether hysteroscopy worsens the stage and prognosis of endometrial cancer. Therefore, this study was conducted to investigate this point. According to the hypothesis, the main cause of the worse progression of endometrial cancer may be the hysteroscopic distension pressure, which includes two key factors, inflation pressure and distension medium (21), for the spread of cancer foci into the abdominal cavity through the distension medium or for the invasion of cancer foci to a deeper level. In the present study, the inflation pressure was 20-23 kPa, and the distension medium was saline solution. The final study found no significant difference in postoperative peritoneal cytology, pathological staging (including the depth of myometrial invasion and lymph node metastasis) or prognosis of endometrial cancer detected

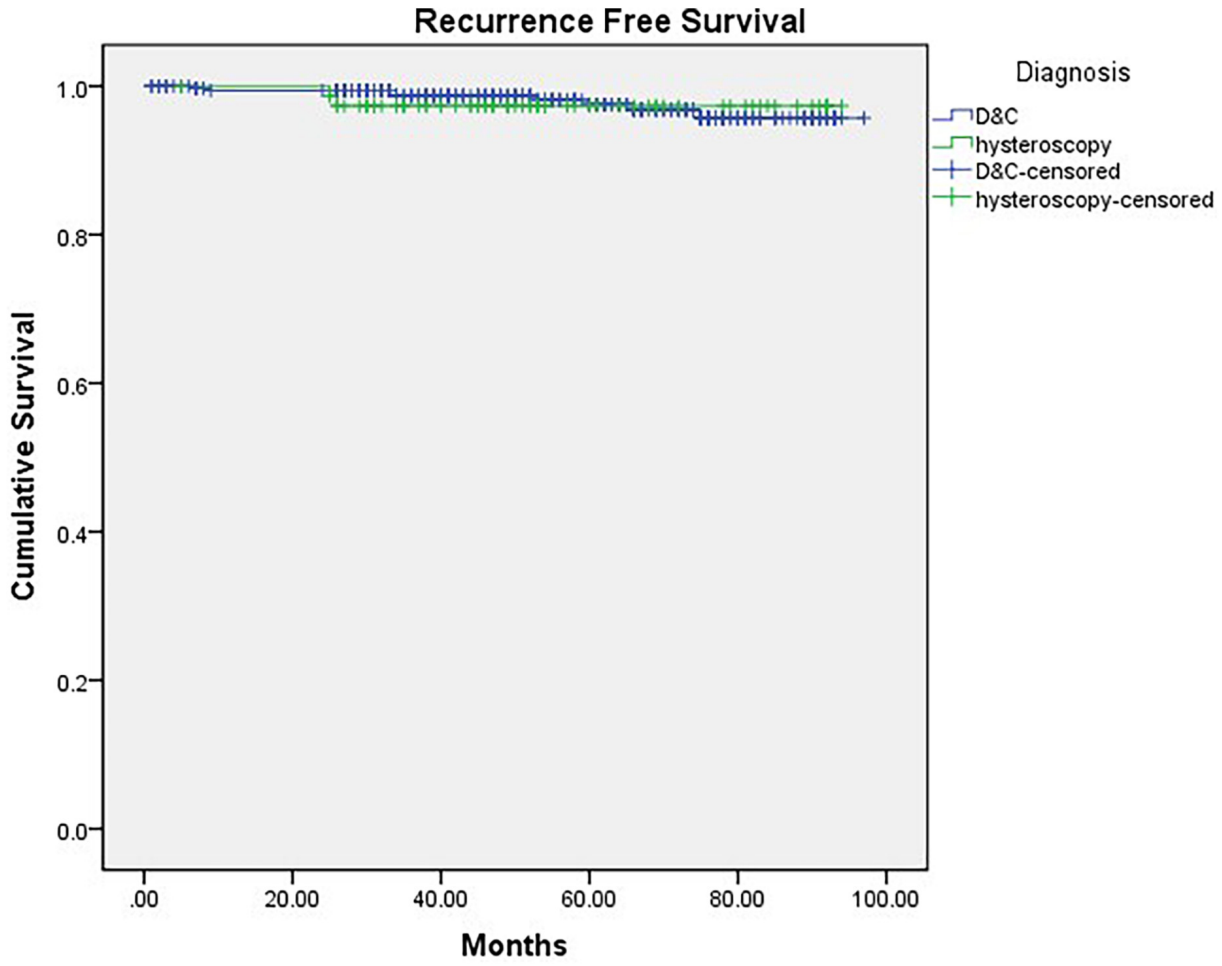

FIGURE 2
Kaplan-Meier curve of recurrence-free survival grouped by diagnostic procedure (p = 0.787).

by hysteroscopy compared with conventional curettage. It is reasonable to assume that hysteroscopic exploration and biopsy are safe, at least at the inflation pressure and distension medium used in this study. Studies in earlier years showed that hysteroscopy was associated with poor prognosis (22, 23), but in recent years studies have been more consistent with our findings whose hysteroscopic procedures with similarly inflation pressure and inflation media to ours (6, 7, 24, 25). Therefore, we consider that more standardized hysteroscopic practice was responsible for this change, as surgical techniques and equipment continue to improve. It is worth noting that general anesthesia was required for hysteroscopy in this study. In fact, this practice is also very common throughout China. On the one hand, anesthesia is relatively inexpensive in China, and on the other hand, human resources are limited to take a large number of patients to submitted to moderate parenteral sedation and a paracervical block (26). However, compared with the awake state, the patient's operative experience is more comfortable and the surgical cooperation is higher under general anesthesia, which facilitates better observation of the entire uterine cavity and cervical canal for lesion sites and removal of biopsies. There are studies to mention the office HSC was no differ from hospital HSC as for the prognosis of EC, but it is no system review or RCTs on it (11, 27).

However, some studies have also found a positive relationship between the time interval and positive ascites rate after including the length of time between hysteroscopy and the full staging procedure, which may be due to the time required for ectopic colonization and escape immunization of disseminated tumor cells (15, 19). In the present study, the gap of hysteroscopy and surgery were mostly between 1 to 3 weeks as well as D&C. And it was finally confirmed that hysteroscopy at this interval does not worsen the prognosis by our long-term follow-up.

It is worth mentioning that whether positive peritoneal cytology worsens the prognosis of the cancer is also a point of controversy. Though several studies have shown that positive peritoneal cytology has an impact on prognosis (17, 28, 29),

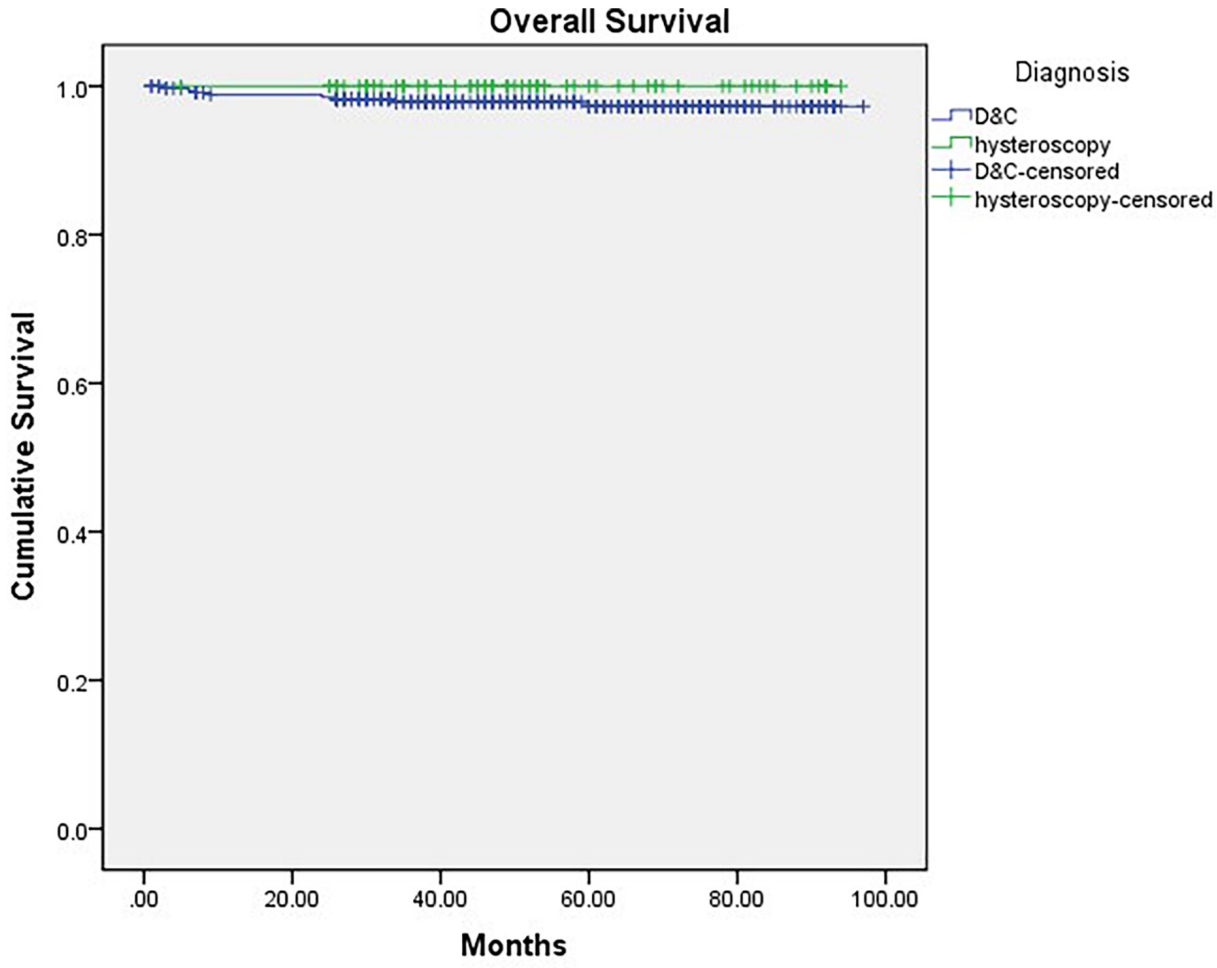

FIGURE 3
Kaplan-Meier curve of overall survival grouped by diagnostic procedure (P = 0.189).

the other studies have shown no significant correlation (30, 31), and then in the 2009 FIGO classification system, positive peritoneal cytology is not included in the grading criteria. The NCCN guidelines also do not use peritoneal cytology as an risk-factor of prognosis and adjustment of treatment options for endometrial cancer (32). However, up to now NCCN, FIGO, and AJCC still recommend to keep the step of retention of ascites or peritoneal irrigation fluid in full staging procedures of EC, on the one hand due to its still controversial prognostic impact. On the other hand, as the main way by which hysteroscopy may promote the possibility of tumor progression. And we think the retention of ascites or abdominal irrigation fluid is also a good way to assess and exclude this possibility, especially for specific types of endometrial cancer. In an era of sentinel node and molecular classification, tumor cells which enter the pelvis through the fallopian tubes is a potential risk factor to cause disseminated metastases in the pelvic and abdominal cavities. Moreover, hysteroscopy may also influence the lymphovascular space invasion and the depth of myometrial invasion, which are prognostic risk factor of EC. Therefore, hysteroscopy is a complementary tool to sentinel node and molecular classification to further refine diagnostic staging and guide treatment.

There are also near-term adverse effects of hysteroscopy, including water toxicity, uterine perforation, adjacent organ damage, bleeding, infection and air embolism, and long-term adverse effects of uterine adhesions (33). For near-term adverse reactions, our study found that only one patient had fever with vaginal bleeding 1 week after hysteroscopy, was considered to have a uterine infection and was discharged after 1 week of anti-infection treatment.

Finally, we found that in this study, there were 58 women of reproductive age (< 45 years), 13 of whom underwent hysteroscopy, which also included two stage IIIC patients. By the end of follow-up, none of these 58 women had experienced death or recurrence. Although they all underwent full staging procedure, it provides evidence that hysteroscopy does not increase the risk of distant metastases of endometrial cancer and

provides a basis for future studies of conservation therapy. This finding is consistent with current guidelines and other relevant studies recommending the use of hysteroscopic treatment for patients with early-stage endometrial cancer (3, 10).

As the largest referral hospital in Fujian Province, China, our multicenter data reflect the situation of hysteroscopic exploration and lesion biopsy for the population with endometrial cancer on the southeast coast of China. Moreover, the follow-up period of this study was up to 3 years, which can also reflect the true prognosis to some degree. Of course, there are some shortcomings in this study. For example, the sample size was still insufficient after screening. The association between duration of hysteroscopy, the time interval from hysteroscopy to full surgery and positive ascites was not further investigated due to ambiguous case data or follow-up. A retrospective case-control study showed that for patients with early endometrial cancer (FIGO I-II stage) the time between hysteroscopy and staging surgery was not statistically different between the positive and negative cytology groups (34). In the current study, we follow-up for 4 years, and no prognostic differences between the hysteroscopy and the controls. And our results showed no difference between endometrial and serous cancer.

As an obstetrics and gynecology referral hospital, we have been committed to bringing more accurate, convenient and comfortable treatment services to the local population. When we learned that pipelle sampling device, which can take with less training and less use of resources, has been shown to be as accurate as hysteroscopy (35, 36). Therefore, we are actively involved in a national clinical trial to facilitate the implementation of pipelle in China, particularly in a public health system that needs referral. Even though the trial is currently in its infancy and has a limited sample size and was not included in this study. However, we also look forward to exploring more new techniques to serve the public based on this study.

Conclusion

Under a certain inflation pressure between 20 and 23 kPa and distension medium like saline solution, hysteroscopic exploration and lesion biopsy, as a screening test for endometrial cancer, ensure safety and have no adverse effects on prognosis compared to conventional curettage.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by our Institution's Ethics Committee (2022KYLLR0343). The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

HY and XZ conceived the study. SL, YC, SZ, XHL, QY, and HL were responsible for clinical data collection. SL and HY analyzed the data. SL, XZ, and HY composed the first draft of the manuscript and edited it. LZ helped SZ complete the first and second revision of this article, including add reference, shape the manuscript, and so on during the most part of author went to the front line to participate in the fight against the epidemic in China. All authors approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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The comparison of gasless and traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery in hysterectomy

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Study objective: To describe the surgical technique and compare the operative outcomes of gasless and traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery (GR-vNOTES vs. TR-vNOTES) in hysterectomy.

Methods: The patients undergoing hysterectomy *via* GR-vNOTES or TR-vNOTES between February 2020 and January 2022 in our hospital were included. Clinical data regarding patient demographics, operative time, blood loss, complications, and postoperative hospital stays were collected and analyzed.

Results: Five cases underwent hysterectomy *via* GR-vNOTES, and nine cases *via* TR-vNOTES. The baseline demographics and operative outcomes were not significantly different in GR-vNOTES and TR-vNOTES groups. There was no conversion to multiport robotic laparoscopy, conventional laparoscopy or laparotomy. No complications were seen in both groups, except two cases had fever postoperatively in the TR-vNOTES group. For those with early stage cervical/endometrial cancer, no recurrence or metastasis was observed in the follow-up of six months.

Conclusion: Both GR-vNOTES and TR-vNOTES were feasible and safe for hysterectomy. GR-vNOTES was a promising alternative to TR-vNOTES in hysterectomy.

KEYWORDS

gasless technique, robot-assisted surgery, transvaginal natural orifice transluminal endoscopic surgery, hysterectomy, operative outcome

Introduction

Laparoscopy initiated the era of minimally invasive surgery. Natural orifice transluminal endoscopic surgery (NOTES) furtherly reduced the surgical trauma. The vagina is the most widely used natural channel because it provides safe access to the peritoneal cavity (1). According to the guideline of American College of Obstetricians and Gynecologists (ACOG), transvaginal surgery should be performed "whenever is feasible" (2, 3). Nowadays, transvaginal natural orifice transluminal endoscopic surgery (vNOTES) is successfully applied in adnexal surgery, hysterectomy, or lymphadenectomies (4). In recent years, robot-assisted laparoscopy has gained

popularity in transvaginal surgery, as it provides accurate and fine surgical procedures with its enhanced 3-dimensional visualization and"wrist-like" wide range device (5).

Laparoscopy is standardly performed by achieving pneumoperitoneum. However, pneumoperitoneum could bring many issues such as increased discomfort, longer recovery time, and the potential of tumor metastasis (6). Particularly, in the context of coronavirus disease 2019 (COVID-19) pandemics, pneumoperitoneum intensifies the risk of virus spread (7). Therefore, gasless technique was developed in laparoscopic surgery (8, 9). Here, we combined gasless technique, robot-assisted and vNOTES together in hysterectomy. As a novel procedure, the data to describe its implication in hysterectomy is limited. In addition, fewer studies comparing the effects of gasless robot-assisted transvaginal natural orifice transluminal endoscopic surgery (GR-vNOTES) and traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery (TR-vNOTES) exist. Therefore, this study was conducted to describe our technique and compare the operative outcomes between GR-vNOTES and TR-vNOTES groups in hysterectomy.

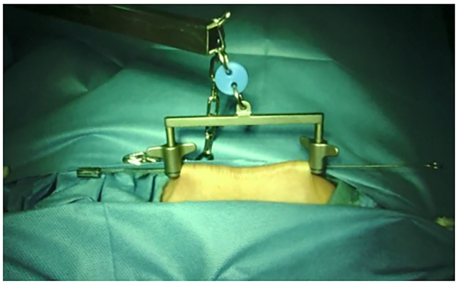

FIGURE 1
Presented the abdominal wall suspension skill with one steel.

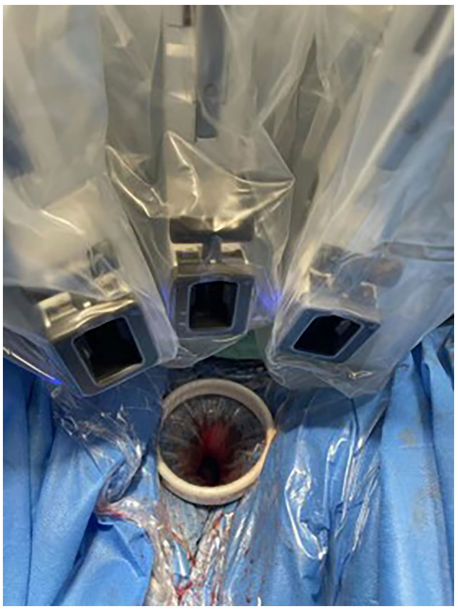

FIGURE 2
Presented the staggered triangular constructed by the endoscope and two robotic instruments.

Materials and methods

In this study, patients who underwent hysterectomy *via* GR-vNOTES and TR-vNOTES from May 2021 to July 2022 in our hospital were included. The operative approach was mainly based on the patients' choice, after they were informed of the pros and cons of "GR-vNOTES and TR-vNOTES." The exclusion criteria included patients with complete cul-de-sac obliteration, suspected severe endometriosis, late stage cervical/endometrial cancer， or a history of multiple prior open abdominal operations. Medical records were identified through our hospital's database. The baseline demographics and operative outcomes were compared between the two groups. The study was approved by the Ethics Committee of Chengdu Women and Children's Central Hospital (202315). All participants were given written informed consent.

Surgical technique

Patients were given the lithotomy position after administering general anesthesia. The cervical-vaginal junction was incised circumferentially and the posterior and anterior colpotomy was performed subsequently. For gasless surgery, one sterilized needle (1.2 mm) was inserted through the subcutaneous tissue 5 cm above symphysis pubis level, and lifted by abdominal wall retractors (Figure 1). If necessary, more sterilized needles would be inserted and lifted to expose surgical space. For traditional surgery, the GelPOINT Mini advanced access platform was established. Then, the da Vinci Si system was docked with the 8.5 mm cannula for the 30° robotic endoscope and two 8-mm cannulas for the endo-wristed rigid instruments in both groups. The endoscope and two working robotic instruments were constructed in a staggered triangular manner to ensure the widest range movement of the two working robotic instruments (Figure 2). The primary surgeon performed all tissue manipulation and dissection, while the assistant was responsible for the procedures such as suturing, suction, irrigation, morcellation, and tissue retraction (Supplementary Video S1). After complete removal of the detached uterus though the vagina, additional salpingo-oophorectomy or lymphadenectomy would be performed if necessary.

Data analysis

Statistical analysis was performed using SPSS 19.0 software. Categorical variables were assessed using the chi-square test, and continuous variables were evaluated by the Student's T-test or Mann–Whitney U test according to the data distribution. $p < 0.05$ was considered statistically significant.

Abbreviations: GR-vNOTES, gasless robot-assisted transvaginal natural orifice transluminal endoscopic surgery; TR-vNOTES, traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery; BMI, body mass index; VAS, visual analog score.

Results

Patient characteristics

Baseline patient characteristics such as age, menopause or not, body mass index (BMI), gravidity, parity, previous abdominal surgeries did not differ between the two groups (Table 1). There were two cases of early cervical cancer, one endometrial atypical hyperplasia, and two uterine myoma in the GR-vNOTES group. In the TR-vNOTES group, there were five cases of early cervical cancer, one endometrial atypical hyperplasia, two uterine myoma, one adenomyosis and one early endometrial carcinoma. All cases had hysterectomy and salpingectomy. Two cases had additional bilateral oophorectomy, and one case with early endometrial carcinoma underwent additional bilateral oophorectomy + pelvic lymphadenectomy + paraaortic lymph node sampling in the TR-vnotes group.

The operative time was not noticeably different in both groups (125 ± 20.9 *vs* 115 ± 23 min, $p = 0.421$). The amount of estimated blood loss (50 (50–75) vs. 50 (20–100) mL, $p = 0.594$), and postoperative hospital stays (3.7 ± 0.6 vs. 4 ± 1 min, $p = 0.643$) were also comparable in both groups. There was no significant difference in terms of VAS at operative day and postoperative days. And there was no conversion to multiport robotic surgery, conventional laparoscopy or laparotomy. Only two patients in the TR-vNOTES group developed a postoperative fever but recovered quickly after administering antibiotics. No patients experienced damage to adjacent organs, hematoma or re-operation. For those with early stage of cervical cancer or endometrial cancer, no recurrence or metastasis were observed in the follow-up of six months. The baseline characteristics and operative outcomes is shown in Table 1.

TABLE 1 The baseline data and operative outcomes in the GR-vNOTES and TR-vNOTES groups.

	GR-vNOTES	TR-vNOTES	*p*
Age	44.6 ± 6.5	48.5 ± 6.9	0.315
Menopause	20%	33.30%	0.68
BMI	21.4 ± 3.3	22.4 ± 1.6	0.522
Gravity	3 ± 1.6	3.3 ± 1.3	0.727
Parity	1 (1–2)	1 (1–2)	0.768
Previous abdominal surgeries	40%	20%	0.409
Estimated blood loss (mL)	50 (50–75)	50 (20–100)	0.594
Operative time (min)	125 ± 20.9	120 ± 14.9	0.421
VAS on the operative day	3 (3–3)	3 (3–3.25)	0.859
VAS 1 day postoperative	2 (2–3)	2 (2–3)	0.953
VAS 2 day postoperative	1 (1–2)	1 (1–2)	0.513
Complications	20%	0	0.283
Postoperative stay (Days)	3.2 ± 0.8	3.1 ± 0.9	0.836

GR-vNOTES, gasless robot-assisted transvaginal natural orifice transluminal endoscopic surgery; TR-vNOTES, traditional robot-assisted transvaginal natural orifice transluminal endoscopic surgery; BMI, Body Mass Index; VAS, visual analog score.

Discussion

In transvaginal approach, robot-assisted surgery could play to its strength. Our study revealed that robot-assisted hysterectomy could be successfully completed without conversion to laparotomy or traditional laparoscopy. This was in consistent with previous studies. In 2021, Guan reported one case with endometriosis who successfully underwent robotic v-NOTES for hysterectomy (10). Zhang (11) reported the operative outcomes of 33 cases patients with endometriosis who underwent hysterectomy *via* robotic v-NOTES. The average operative time was 141.93 ± 40.22 min, and the mean estimated blood loss was 52.25 ± 33.82 mL. Koythong (4) reported that robotic v-NOTES was a viable alternative to traditional v-NOTES for hysterectomy. The operative time and estimated blood loss in the robotic v-NOTES group were 157 (123–180) min and 50 (30–100) respectively. Liu (12) reported that the mean hysterectomy time was 77.27 ± 2.89 min, and the median additional operation time was 63 (8–206) min in 84 patients who underwent hysterectomy *via* robotic v-NOTES for benign gynecological disease. Furtherly, cancer related surgeries could also be completed by robot assisted v-NOTES. In our study, there were seven cases of early-stage cervical cancer and one case of early-stage endometrial cancer. In the case of early-stage endometrial cancer, additional pelvic lymph node biopsy and abdominal aortic lymph node sampling were successfully completed. To our knowledge, this may be the first case of endometrial cancer which was successfully completed *via* TR-vNOTES.

Furtherly, our study revealed that robotic v-NOTES hysterectomy could be successfully performed without pneumoperitoneum. The operative time was 125 ± 20.9 min and 50 (50–75) mL, respectively, in our study. According to our review, there appeared to be only one literature which reported the operative outcomes of 13 patients who had underwent gasless robotic V-notes for hysterectomy (13). And this study revealed that the median docking and operative time were 15 (5–25 min) and 135 (92–215 min) respectively, with estimated blood loss of 50 ml (20–450 mL). Moreover, our study revealed that GR-vNOTES had acquired similar operative outcomes with TR-vNOTES in hysterectomy. GR-vNOTES avoided the potential risk of CO2 pneumoperitoneum and it allowed for multiple laparoscopic instruments to be used simultaneously. In addition, air leakage and suction should no longer be considered. In cancer-related surgeries, gasless technique could also decrease the risk of cancer metastasis (13, 14). The literature review about GR-vNOTES or TR-vNOTES in hysterectomy is shown in Table 2.

Based on our knowledge, this is the first study to compare the operative outcomes of GR-vNOTES and TR-vNOTES in hysterectomy. The main limitation of our study was the small sample size which reduced its statistical power. Secondly, there was some difference in the disease type in both groups, which may bring some bias.

Conclusion

To summarize, GR-vNOTES and TR-vNOTES were both safe and effective in hysterectomy. Additionally, GR-vNOTES avoided the disadvantages of CO2 pneumoperitoneum and was a promising alternative to TR-vNOTES. However, to confirm the findings of this study, prospective studies with large sample sizes are required in the future.

TABLE 2 The literature review about GR-vNOTES or TR-vNOTES in hysterectomy.

Reference	Country	Research type	Year	Disease	Operation type	No	Operative time (min)	Estimated blood loss (ml)
Guan (10)	USA	Case	2021	Endometriosis	TR-vNOTES	1	200	-
Zhang (11)	USA	Case series	2021	Endometriosis	TR-vNOTES	33	141.93 ± 40.22	52.25 ± 33.82
Kakibuchi (15)	Japan	Case	2021	Early-stage endometrial cancer with massive uterine leiomyomas	TR-vNOTES	1	279	-
Yang (13)	China	Retrospective	2020	Benign uterine disease	GR-vNOTES	13	docking15 min (5–25) + operative 135 (92–215)	50 (20–450)
Liu (12)	USA	Retrospective	2022	Benign gynacological disease	TR-vNOTES	84	hysterectomy:77.27 ± 2.89 + extra:63 (8–206)	-
The present study	China	Retrospective	2022	Benign uterine disease, early cervical/ endometrial cancer	GR-vNOTES vs. TR-vNOTES	5 vs. 10	125 ± 20.9 vs. 115 ± 23, p = 0.421	50 (50-75)vs. 50 (20–100), p = 0.594

GR-vNOTES, gasless robot-assisted transvaginal natural orifice transluminal endoscopic surgery; TR-vNOTES, traditional robot-assisted transvaginal natural orifice transluminal.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Chengdu Women and Children's Central Hospital. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

YM drafted the manuscript and participated in data collection and analysis. LH participated in the design of the study. QZ, YC, and JZ participated in the data collection and analysis. YL participated in the design of the study and coordination. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fmed.2023.1117158/full#supplementary-material

SUPPLEMENTARY VIDEO S1
Transection of broad ligament, ovarian proper ligaments *via* GR-vNOTES.

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Laparoscopic myomectomy – The importance of surgical techniques

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Laparoscopy is a routine procedure for benign gynecological tumors. Although the laparoscopic approach for myomas is a common procedure, it can be challenging. To improve outcomes, research regarding port access, suture type, morcellation, and complication management remains ongoing. Myomectomy is the main surgical option for patients seeking uterus-sparing procedures to maintain future fertility. The laparoscopic technique is the most important in these cases, given that possible complications can impact fertility and pregnancy outcomes. Herein, we reviewed and collated the available data regarding different suture techniques, including advantages, difficulties, and possible long-term impacts.

KEYWORDS

laparoscopic myomectomy, suture, surgical technique, barbed suture, pregnancy outcome

1. Introduction

In a society where conception has been slowly shifting toward later life, gynecological pathology is more frequently encountered in females who desire to get pregnant. Uterine fibroids can be detected in 70–80% of females during their lifetime (1). In these cases, a decision must be reached regarding the treatment strategy, considering the symptomatology, characteristics of the fibroid nodule, impact on quality of life, and desire for pregnancy.

The treatment options for uterine myomas depend on the severity of the condition, the age and reproductive status of the patient, and the symptoms experienced. Based on FIGO (The International Federation of Gynecology and Obstetrics) staging, the management can start from observation (if the fibroids are small and asymptomatic) and up to surgical procedures like myomectomy or even hysterectomy in specific cases (2). The FIGO classification presents the uterine fibroids according to their localization which is correlated with specific symptoms and has a significant impact on the treatment options.

Treatment strategies for uterine leiomyoma can include medical options (such as oral contraceptives, progesterone, gonadotropin-releasing hormone agonist (GnRHa), selective progesterone receptor modulators, or the combination of relugolix-estradiol-norethisterone), surgical interventions (such as hysterectomy, laparoscopic myomectomy, and hysteroscopic myomectomy), and non-surgical options (uterine artery embolization) (3). Uterine artery embolization is a convenient method to spare the uterus if a patient experiences substantial bleeding (4). In addition to potential complications associated with uterine artery embolization,

the main concern is damage to the ovarian vascular supply (5). The symptomatology of uterine leiomyoma is one of the main factors determining the treatment protocol (6). The uterine-sparing surgery approach is addressed, especially in patients who desire reproductive options in the future. Therefore, surgical procedures should be selected considering that the uterus must be able to carry a pregnancy to term without major risk to the mother or fetus. Myomectomy is a medical procedure used to remove fibroid nodules and reconstruct uterine integrity. Moreover, myomectomy has been the elective fertility-sparing procedure for several years, remaining a top-ranking option owing to improved techniques (7–9).

Considering patients who desire to preserve fertility, approaches can differ depending on whether they wish to become pregnant in the immediate future or maintain this option (10). Female subjects who wish to get pregnant within a short duration can be subcategorized into two groups: those who can try getting pregnant despite the leiomyoma and those who need to address the leiomyoma to become pregnant (10). Moreover, some of these patients are diagnosed with uterine fibroid-related infertility. However, the precise mechanism through which leiomyomas alter fertility remains unclear. It has been suggested that a mechanical alteration occurs due to distortion of the uterine cavity, thereby affecting the cervical passage of the sperm and causing a tubal blockage (11). Fibroid nodules have been associated with increased inflammatory processes and vasoactive substances (12).

Even in the absence of infertility as a complication, leiomyomas during pregnancy can contribute to abortion, premature membrane rupture, premature birth, and labor complications (13). Recurrent pregnancy loss associated with leiomyomas can result from surgery prior to further pregnancy (14). Before laparoscopic myomectomy, one or two cycles of ulipristal acetate can be prescribed if the patient exhibits hypermenorrhoea-related anemia (10). The use of GnRHa prior to surgery has been associated with reduced blood loss and decreased uterine adhesion (15), although susceptibility to uterine fibroid recurrence has been documented (16).

Pregnancy outcomes after laparoscopic myomectomy have been discussed in several studies, which have reported improvements in pregnancy rates to various degrees (14). Uterine rupture is the most common pregnancy complication following myomectomy. Since the introduction of laparoscopic myomectomy as a routine procedure for intramural and subserous uterine nodules almost 30 years ago (17), the strength of the uterine scar has presented a major concern. To improve outcomes, an appropriate surgical technique must be used. The surgeon's experience is valuable, as he can correlate information regarding characteristics of the uterine fibroid and, consequently, adjust the port position, improve the ergonomics of the procedure, and precisely approach enucleation (18).

One, two, or three ports can be used to perform laparoscopic myomectomy. Typically, single-port laparoscopy results in a prolonged operative time (19, 20). Notably, the surgical port can influence the approach to the myoma in terms of traction, manipulation, enucleation, suturing, and morcellation (20–22). After enucleation, extraction of the uterine fibroid can be performed through one port site or colpotomy, followed by morcellation (23), recommending the in-bag strategy for contained morcellation (24).

In exceptional cases, a myomectomy can be performed during pregnancy (25). Considering leiomyoma refractive to conservative management, the laparoscopic approach has been associated with favorable outcomes and reduced complication rates (26).

Enucleation and closing techniques are the main determinants governing the success of laparoscopic myomectomy and subsequent obstetrical outcomes (27).

2. Types of sutures

The advantages of the laparoscopic approach for uterine fibroids have been well established. Compared with laparotomy, laparoscopy affords advantages such as a reduced hospitalization period, a minimal decline in hemoglobin levels, and low levels of postoperative pain (28); however, drawbacks such as blood loss and prolonged surgical time need to be addressed (29).

Bleeding control is one of the main challenges during this procedure, especially when it involves larger or more vascular fibroids. Before dissection, there are some techniques that can be used to help reduce blood loss. Placing a tourniquet at the base of the leiomyoma can significantly reduce the blood supply with the most effect on smaller fibroids (30). In case of a larger or more vascular nodule, the intermittent uterine artery clamping can be realized through laparoscopy (31). Intramyometrial injection of vasoconstriction agents (vasopressin, epinephrine) in the myometrium can be used successfully in reducing bleeding during laparoscopy but can lead to severe complications (32, 33). Hemostatic agents, such as fibrin glue, can be used to help control bleeding during laparoscopic myomectomy by promoting clot formation (34). In addition to these techniques, there are several other strategies that can be used to reduce bleeding during laparoscopic myomectomy. For example, ensuring adequate visualization of the surgical field, using a good surgical technique, and being mindful of tissue handling can all help to minimize bleeding. It's important to note that some bleeding is expected during any surgical procedure, and it's essential to have skilled and experienced surgical personnel to manage any complications that may arise.

Suturing remains the most important factor, even when employing methods such as ligation of the uterine artery, oxytocin, or vasoconstrictor agents (35, 36). The number of ports and type of suture are closely associated. Given the availability of instruments and suture devices, surgeons attempt to reduce the number of abdominal incisions without increasing operative time. For example, barbed suture devices are typically selected in single-port laparoscopy due to technical difficulties (37).

The first step in optimal suturing is the uterine incision. For posterior and anterior myomas, a vertical incision using a unipolar hook is preferred (38). After an incision is made, the pseudocapsule and myoma can be visualized. A high voltage is recommended for the initial cutting, although studies have suggested a low voltage to preserve the myometrium (39). Moreover, studies have recommended certain incisions for easier suturing: sagittal for posterior nodules, oblique for anterior nodules, and transverse or elliptical to avoid excessive myometrial tissue (39, 40).

Conventional sutures include an atraumatic needle with a fine resorbable suture. Sutures can be performed in a single plane when the stitch can pass through the entire thickness (39). If the incision runs deep or the cavity has been opened, the suture will be performed in multiple layers. Surgeons can perform separate or continuous stitches, depending on a case-to-case basis. Intracorporeal or extracorporeal knots can be used if tension is maintained. Preformed disposable endoscopic loops can be used if a progressive tie can

be realized (41). If enucleation is achieved, the endoloop is tied and offers mechanical hemostasis, as well as a good exposure of the cleavage plane. Studies have shown a reduction in diathermy, thus improving scar quality (41). The "bottom-up suture" technique was proposed for better suturing by elevating the bed of the myoma while still attached to the uterus (42); advantages of this technique include hemorrhage control and prevention of dead-space formation. The "baseball" suture technique has been described as an alternate option to the classical suture, affording advantages such as reduced suturing time, simple to perform, single-layer suture, reduced dead-space formation, and complete closure of the incision (43). In this technique, the needle is inserted initially into the bottom of the incision on each side leading to a final aspect similar to the stitches on a baseball.

Barbed sutures are among the most commonly used types of sutures. The major advantage is the ability to maintain tension by suturing and the lack of necessity for knots. This material is preferred for laparoscopic myomectomy, as multiple studies have shown the benefits of its use. Unidirectional barbed sutures with intracorporeal knots are associated with a shorter uterine wall repair time and significantly lower hemoglobin drop and blood loss than conventional sutures (44). One notable advantage is the ability to maintain the same tension of the uterine tissue during suturing, given the presence of barbs on the filament. These barbs create an equal distribution of force without the potential of tear- or laceration-induced damage around the knots. Collectively, these factors highlight a statistically significant reduction in surgical time ($p < 0.0001$) (40). Reduced technical difficulties related to suture characteristics and the learning curve have been reported (45, 46).

Nevertheless, laparoscopic blood loss remains a major challenge. Efficient hemostasis can be achieved by applying tension on the suture and suturing speed. Additional factors related to blood loss include the surgeon's experience, fibroid incision, number and size of nodules, and previous medical treatment to reduce uterine bleeding (47). A meta-analysis (45) has revealed a significant reduction in blood loss during surgery in patients who received barbed sutures ($p = 0.183$). Although this type of suture is expensive, the cost benefits favor barbed sutures (48). One complication of barbed sutures is increased adhesion. The current data showed similar postoperative adhesions in six-month second-look laparoscopy (49). Overall, barbed sutures are advantageous and have been associated with reduced technical difficulty, enhanced safety, decreased closure time, and minimal blood loss (50). To improve this suture, a bidirectional knotless barbed suture has been proposed (51), with the same benefits mentioned previously.

Overall, studies suggest that the modified extracorporeal knot-tying technique and the use of barbed sutures may be associated with shorter operation times and less blood loss during laparoscopic myomectomy. However, further research is needed to confirm these findings and determine the best suture technique for individual patients.

3. The impact of suturing technique on uterine vascularity and scar repair

A correlation has been suggested between the suture technique and uterine scar healing. This correlation has been studied extensively regarding cesarean sections, owing to its association with uterine rupture.

The first step that can alter the healing process is the extensive application of bipolar coagulation, which leads to thermal tissue damage (52). It is recommended that electrosurgery must be limited as much as possible (53). In addition, excessive electrosurgery to control bleeding after suturing has been associated with the weakening of the suture material (54). The type of suture realized is related to scar healing and subsequent complications. Studies have evaluated the closing technique in cesarean sections, revealing that although single-layer closure has a shorter operative time (55), it can be associated with a higher risk of complications, such as scar defects (56). Compared with interrupted sutures, continuous sutures were associated with a high risk of uterine rupture (57) and placenta accreta (58).

Studies have compared different suturing techniques for laparoscopic myomectomy scar healing. Although the wound completely healed in approximately 3 to 6 months (59), the continuous suture scar failed to recover completely, accompanied by altered vascularity (60). Compared with interrupted sutures 3 months post-surgery, currently used continuous sutures in laparoscopic myomectomy were associated with excessive myometrial ischemia, delayed post-surgery vascularization, and persistent avascular areas at 6 months post-surgery (60).

Although uterine hemostasis is well achieved, long-term wound healing with continuous barbed sutures needs to be established when compared with that of interrupted sutures. Double-layered sutures are reportedly associated with fewer complications than single-layer sutures.

4. Impact of sutures type on fertility and pregnancy outcomes

Fertility preservation remains one of the main purposes of laparoscopic myomectomy. Reproductive outcomes must be considered when evaluating the advantages or disadvantages of the procedure. Uterine rupture and abnormal placentation are two of the most undesirable complications, and precise suturing is critical to avoid these complications (17, 45). The two main aspects of uterine repair are represented by the type of suture performed and the layers of suturing depending on the depth of the fibroid nodule.

A meta-analysis made by Gardella et al. evaluated the importance of barbed sutures on the fertility outcome and concluded that is not sufficient information regarding the long-term outcome (45). As the authors concluded, the available data regards patients with previous barbed suture, lacking information about fertility outcomes in control groups. Considering barbed suture outcomes, pregnancy rates of 71% have been reported (61), similar to other studies that evaluated laparoscopic myomectomy without differentiation (17, 62). Cesarean sections were performed frequently, and the reported complications included preterm birth, abnormal placentation, hypertensive disorders, growth restriction, and myoma degeneration (18 of 110 pregnancies) (61).

The degree of myometrial penetration during myomectomy has been correlated with scar formation but not with uterine rupture during pregnancy (63). Multiple-layer suturing of the uterine fibroid bed has been associated with better reproductive outcomes (64). Additionally, studies have reported similar outcomes between single- and multiple-layer suturing techniques (65). Abdominal myomectomy has been associated with higher cesarean section rates than laparoscopic myomectomy (42.1% vs. 89.5, $p < 0.001$) (66).

Minimally invasive procedures can treat most of the fibroids, but they can also lead to irreversible infertility (67). Pre-operative medical treatments can be used to minimize the specific complications and to optimize the results (68). Even though there are important risks related with this procedures, the presence of uterine leiomyomas during pregnancy influences the evolution and outcomes (69, 70). With or without surgery, uterine fibroids represent an risk for infertility that needs to be proper addressed (71).

5. Conclusion

Laparoscopic myomectomy can be a valuable strategy for patients who desire fertility preservation. With advantages such as minimal postoperative pain, rapid recovery, esthetic outcomes, and good reproductive outcomes, the laparoscopic approach is considered the leading surgical approach in this field. Nevertheless, there is still a need for large-scale multicenter studies comparing different surgical techniques and suture methods in females throughout pregnancy.

Author contributions

MD, C-GN, and A-EN designed the study. MC, A-EN, and FȘ reviewed the literature and drafted the manuscript. MD, MC, AC, C-GN, and AN substantially contributed to the conception of the study and revised and edited the final manuscript. All authors have read and approved the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Corrigendum: Laparoscopic myomectomy – The importance of surgical techniques

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The authors apologize for this error and state that this does not change the scientific conclusions of the article in any way. The original article has been updated.

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Validation of uterine artery embolization before surgical laparoscopic myomenucleation compared to single surgical laparoscopic myomenucleation for the treatment of large fibroids and uterus myomatosus

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Aim: To determine the efficacy of preoperative uterine artery embolization (uterine artery embolization; UAE) prior to elective laparoscopic fibroid removal compared to single laparoscopic fibroid removal in women with large uterine fibroids and women with uterus myomatosus.

Material and methods: A total of 202 women with symptomatic uterine fibroids who were scheduled for elective fibroid enucleation were included in this retrospective, monocentric, non-randomized study. Two procedures were compared: women who received percutaneous UAE 24 h prior to elective laparoscopic fibroid eviction for large uterine fibroids (>6 cm) and uterus myomatosus. And women who received laparoscopic fibroid enucleation alone for large uterine fibroids and uterus myomatosus. Outcome parameters for effectiveness were the hospital stay, the operating time and the intraoperative blood loss.

Results: Women who underwent preoperative percutaneous embolization of the uterine arteries, both for large fibroids and uterus myomatosus, had significantly less blood loss, shorter hospital stays, and shorter operating times.

Conclusions: Especially women with large uterine fibroids and women with uterus myomatosus after having children can benefit from the combination therapy of preoperative percutaneous uterine embolization with subsequent laparoscopic myoma enucleation.

KEYWORDS

uterus, uterus myomatosus, big uterine fibroids, uterine embolization, laparoscopic myoma enucleation

Introduction

"The only definitive therapy for symptomatic uterine myomatosus is hysterectomy" (1).

This statement no longer corresponds to current treatment recommendations and surgical practice in surgical gynecology. More and more patients explicitly want the uterus to be preserved. Several national and international studies reflect this trend (2, 3). Uterine transplants are among the modern surgical procedures. The first living donation was made in

2013. Until a few years ago, such an operation was unthinkable. Only a very limited number of successful uterine transplants can be found in the literature. This shows how important it is to establish modern surgical procedures and how important uterine-preserving surgical measures are (4). From a health economic point, fibroids cause high treatment costs. A study from the USA estimates health costs in the amount of several billions of US dollars per year and, together with absenteeism and obstetric complications, the costs add up to several tens of billions per year in women's health (5). Therefore, the development of effective treatment options for the most common benign disease in women over 35 years of age (6) is important. The combination of uterine artery embolization (UAE) and conservative myomectomy is an established treatment option in the surgical treatment of fibroids. By reducing intraoperative blood loss, UAE facilitates surgery and improves the chances of surgical myoma enucleation. This provides a better starting point for performing a uterine-preserving surgical myomectomy. Reconstruction of the uterus is simplified (7). In large or multiple uterine fibroids, this treatment strategy is rarely used, especially in women who want to undergo uterine-preserving surgery (8). UAE can be a useful addition to surgery in women with massive fibroids (9). There are no studies on the use of preoperative UAE in combination with laparoscopic myoma enucleation in uterus myomatosus. The aim of the study was therefore to investigate the influence of the use of UAE before surgical laparoscopic myomectomy on the diagnosis of the uterus myomatosus and whether this combination therapy can meet the patient's desire for a uterine-preserving myomectomy.

Materials and methods

Data collection

The study is a retrospective, non-randomized, comparable clinical monocentric study with two comparison groups. A total of 202 patients were included. Of these, 101 patients who underwent surgery between February 1st, 2014 and March 31st, 2019 in the Clinic and Polyclinic for Gynecology and Reproductive Medicine at Jena University Hospital with the ICD-10 diagnosis of uterus myomatosus after preoperative uterine artery embolization (UAE) (first group). The comparison group also consists of 101 patients who underwent surgery between 2018 and 2020 in the Clinic and Polyclinic for Gynecology and Reproductive Medicine at Jena University Hospital with the ICD-10 diagnosis of uterus myomatosus without UAE (second group/control group). Local Ethics Committee approval is available (Reg. No.: 2021-2096 dates).

Data management

All patient-related data was recorded in an anonymous form using assigned patient identification numbers. The study data was protected from unauthorized access and only employees of the study were allowed to access it.

Statistical evaluation

The data were recorded in an Excel spreadsheet (Excel Version 2020. Microsoft, Redmod, USA). Then transferred to the statistical evaluation software SPSS (IBM SPSS Statistics Version 26, Chicago, Illinois, USA). Test-independent samples were used and p-values < 0.05 were considered statistically significant. The Welch t-test was used.

Study hypotheses

The hypotheses of this study are: In the case of operative laparoscopic myomectomy in the uterus myomatosus, PUAE can shorten the duration of the operation, the hospital stay and the transfusion of blood supplies, increase the postoperative outcome and the overall satisfaction of the treated patients.

Inclusion and exclusion criteria

Inclusion criteria

Age between 21 and 50, diagnosis of uterus myomatosus confirmed clinically, sonographically and with MRI. Symptomatic (bleeding disorders, pain symptoms) and asymptomatic fibroids in sterile patients for whom laparoscopic myomectomy has been indicated. As well as non-pedunculated submucosal, intramural, transmural, subserosal fibroids.

Exclusion criteria

Age below 20 and above 50 years, coagulation disorders, coagulopathies and vascular diseases, psychiatric illness that make study participation and follow-up questionable. Taking blood thinners, suspected sarcoma or malignancy, pedunculated subserous fibroids, pedunculated submucosal fibroids, intraligamentous fibroids. Localization outside the uterus, current pregnancy, myoma larger than 15 cm, infections in the urogenital tract, contrast medium allergy, hyperthyroidism.

All patients in the PUAE group received the following measures in addition to the normal course of inpatient admission: a preoperative 3 Tesla MRI of the pelvis in the radiology department of the University Hospital Jena (MAGNETOM Sola device from Siemens Healthineers Germany, Erlangen, Germany 2018), followed by an epidural anesthesia by the anesthetist, followed by embolization using Gelaspon under X-ray fluoroscopy with contrast medium 4 to 6 h before the elective laparoscopic fibroid enucleation by interventional radiologists from the Institute for Diagnostic and Interventional Radiology (IDIR).

In addition to epidemiological data, the following parameters were collected: symptoms (bleeding disorder, pain symptoms, feeling of pressure, sterility), gravida status, para status, menarche (year), BMI, secondary diagnoses, cycle length (days), duration of bleeding (days), bleeding intensity, pill intake, Previous therapy attempts, previous operations, size of the fibroids per cm (or the largest fibroid) measured by ultrasound and MRI, preoperative hemoglobin value (mmol/l), number of fibroids

removed, location of the fibroids (submucosal, intramural, transmural, subserous, intraligamentous), operation date, operation duration (in minutes), postoperative hemoglobin level (mmol/l), intraoperative complications, postoperative hemoglobin level (mmol/l), postoperative complications, postoperative length of stay (days).

Surgical therapy

The surgical therapy was carried out by qualified specialists in gynecology and obstetrics, certified by specialist societies and who have many years of experience in laparoscopy. The operative technique and the operative instruments were identical in both comparison groups. The patients were clinically examined by a specialist in a special consultation for fibroids and the indication for surgery was indicated by a specialist.

Expiry of the UAE

The indication for preoperative myoma embolization took place in an interdisciplinary manner in cooperation with radiology and the clinic and polyclinic for gynecology and reproductive medicine in the myoma center of the University Hospital Jena. An inserted intrauterine device (IUD) had to be removed prior to UAE. On the day of admission, blood was taken, a peripheral intravenous indwelling cannula was installed, a urinary catheter was inserted and the peridural catheter was explained. The day after admission, the UAE was performed with PDK in the radiology angiography department. Under local anesthesia, the interventional radiologist places a five French catheter (Roberts uterine curve) in the right femoral artery, probing the left internal iliac artery and then the uterine artery using a microcatheter directed cranially. Advance the catheter into the artery supplying the uterus under constant X-ray control. Performing a selective angiography to illuminate the anatomy using an iodinated contrast medium. Then "free-flow" flushing (embolization) using 10–15 ml of Gelaspon by Bausch and Lomb, cut into 1 mm pieces, and dissolved in isotonic saline solution 0.9% Bc and contrast medium until hemostasis of the blood supply in the ascending responsible (ascending part of the uterus) segment of the left uterine artery. The catheter is then removed from the inguinal artery and a pressure bandage is applied to the patient, which remains in place for up to 6 h after the intervention. The patient underwent laparoscopic myomectomy 4 to 6 h later.

Results

A total of 89 patients were included in the first group and 77 patients in the second group according to the exclusion and inclusion criteria listed in the Material and methods section. In the first group, the following intra- and postoperative complications were noted: a single intraoperative bowel injury and a single laparotomy. Here, an intraoperative conversion from a laparoscopic myomectomy to a laparotomy in suspected malignancy had to be made. This patient had to be excluded from the study. Thus, the complication rate in our study group was 1.12 % (1 of 89 patients) and corresponds to current statistical information on intraoperative complication rates (Danilyants 2020). In the second group, the following intra- and postoperative complications were noted. UAE-related complications (direct and indirect) were found in three patients. With the formation of a spur aneurysm of the femoral artery, one patient developed a post-puncture syndrome because of the epidural anesthesia and one patient suffered postoperative deep vein thrombosis. There were also non-UAE-related complications in the form of general surgical complications. A postoperative ileus due to an a.e. intraoperatively caused bowel injury. Thus, the overall surgical complication rate was 0.77 % (1/77 patients), as in the first group. The UAE-related complication rate was 3/77 patients, i.e., 2.31 %. No patient in either group underwent a hysterectomy intraoperatively or during the hospital stay.

Analysis of the epidemiological/preoperative data

The mean age of the treated patients from the first group was 38.98 ± 6.045 years (mean ± standard deviation) and in the second group was 40.56 years ± SD of 6.269. No significant difference was found here.

The mean age at menarche in the first group was 12.82 ± SD of 1.395 years and in the second group 12.85 ± SD of 1.306 years. No significant difference was found here.

The mean number of fibroids in the first group was 2.33 ± SD of 2.194 fibroids and in the second group 2.70 ± SD of 2.189 fibroids. No significant difference was found here.

The average myoma size of the largest myoma to be measured preoperatively in the treated patients from the first group was 6.68 ± SD of 2.239 cm and in the second group 6.69 ± SD of 2.499 cm. No significant difference was found here. No significant differences were found in the distribution of the clinical symptoms in the two groups (lower abdominal pain, hypermenorrhea, anemia, feeling of pressure, height progression and desire to have children).

Pelvic pain

30% in the first group reported this symptom (27 out of 89 patients) and in the second group 40% (31 out of 77 patients). There were no significant differences at $p = 0.181$.

Hypermenorrhea

49% of the patients in the first group (44 out of 89 patients) and in the second group 64.9% (50 out of 77 patients) suffered from this symptom. There were no significant differences at $p = 0.045$.

Feeling of pressure

44.9% of the patients in the first group (40 out of 89 patients) and 36.3% of the patients in the second group (28 out of 77 patients) reported this symptom. There were no significant differences at $p = 0.262$.

Size progression of the fibroids

19.1% of the patients in the first group (17 of 89 patients) and 11.6% in the second group 11.6% (9 of 77 patients) reported a size progression. There were no significant differences at $p = 0.190$.

Presence of preoperative anemia

7.8% of the patients in the first group (7 of 89 patients) and 12.9% in the second group (10 of 77 patients) had laboratory tests for anemia of grade 1 or higher. There were no significant differences at $p = 0.278$.

The mean BMI of the first group was 25.00 ± SD 4.858. The mean BMI of the second group was 24.50 ± SD 4.580. There were no significant differences.

In the first group, the intramural or transmural location of the fibroid was found in 57 of 89 patients, and in the second group, this location was found in 67 of 77 patients. There was no statistical significance at $p = 0.251$.

Outcome analyses

The average operating time in minutes for the first group was 167.11 min. The mean operating time in minutes for the second group was 141.23 min. Thus, the operation lasted on average 25.88 min longer in patients who did not receive UAE prior to fibroid enucleation than in patients who previously received UAE. This results in a statistical significance of $p = 0.0478$ for the performance of the UAE before myomectomy in relation to the total duration of the surgery.

The average postoperative Hb value in the first group was 6.1 mmol/l. The average postoperative Hb value in the second group was 7.8 mmol/l. Thus, the mean postoperative Hb value of the first groups without a previous UAE intervention was 1.7 Hb points lower than in the patients who received a previous UAE intervention. A statistical significance with $p = 0.0470$ is shown in relation to the postoperative Hb value in favor of the second group, which received a UAE intervention.

A significant difference with $p = 0.012$ was found for the mean length of stay. On average, the length of stay was 0.5 days longer for patients in the first group compared to patients in the second group. The average length of stay of the treated patients in the first group was 5.21 ± SD of 1.458 days and in the second group 5.7 ± SD of 0.988 days.

To deepen the analysis, the patients were subgrouped within both comparison groups.

Fibroid size over 6 cm

On average, 50.57% of patients (45 out of 89) in the first group had a fibroid size > 6 cm, and in the subgroup of the second group, 52.95% of patients (40 out of 77) had a fibroid size > 6 cm.

Surgery time

The average operating time of the patients in the first group without UAE was 189.99 min. The mean operating time of the patients in the second group was 151.97 min. All patients had a fibroid ≥6 cm. On average, the operating time for the patients in the first group was 38.02 min longer than for the patients in the second group who had previously received a UAE and had a fibroid larger than or equal to 6 cm. A statistical significance is shown in favor of the second group with $p = 0.0482$. Thus, the preceding UAE prior to fibroid enucleation shows a direct benefit in terms of surgical time. A preceding UAE significantly reduces the operating time in the presence of large fibroids.

Blood-loss

The average blood loss of the patients in the first group, who had no UAE and a fibroid larger than or equal to 6 cm, was 3.21 mmol/l. The average blood loss of the patients in the second group with UAE and a fibroid ≥6 cm was 0.02 mmol/l. Thus, a patient who did not receive UAE before fibroid nucleation and has a fibroid at least 6 cm in size has a 3.18 mmol/l higher Hb loss than a patient in the second group. This results in a statistical significance of $p = 0.0471$ in favor of the patients who received a UAE before fibroid nucleation and have a fibroid at least 6 cm in size.

Discussion

When selecting the patients based on the exclusion and inclusion criteria, a total of 89 patients in the first group and 77 patients in the second group were included. No technical failure of the embolism was noted. No patient in either group underwent a hysterectomy. The following complications were observed in the patients of the first group. One patient in this group required a blood transfusion. The following intraoperative and postoperative complications were observed in the patients in the second group. In addition, UAE-related complications (direct and indirect) were found in this group: aneurysm spurium, post-puncture syndrome because of (PDA) epidural anesthesia. Deep vein thrombosis. General surgical complications of a postoperative thin closure due to an intraoperative bowel injury. In both groups, the surgical techniques and surgical instruments used were identical. In our study, complications in the overall context occur more frequently in UAE patients. The embolization-related complications described above as well as the general surgical complications. However, the inpatient stay of the UAE group was not longer than that of the non-UAE group. On the contrary, the UAE group showed a significantly shorter hospital stay of 0.5 days. So, it can be assumed that the complications that occurred in connection with UAE are to be rated as moderate and have no influence on the inpatient course. There were no significant differences between the two groups in terms of preoperative hemoglobin level and the number and weight of removed fibroids. In the study group, there was an average hemoglobin decrease of 1.4 g/dl postoperatively compared with 1.7 g/dl in the control group ($p = 0.055$). Blood transfusions were not performed in

any case. The average duration of the operation was 136 and 120 min in the control group. Pathological changes in the pulsatility and resistance indices and complications that could clearly be attributed to the study intervention did not occur. There was a correlation between the weight and number of removed fibroids and the intraoperative blood loss. No significant difference in the hemoglobin drop, the intraoperative blood loss and the transfusion rate could be detected. This study was necessary to evaluate whether a significant difference in blood loss could be achieved in the comparison groups with uterus myomatosus (10). Like our study, a retrospective American study by Goldman et al. (11) also concluded that a UAE immediately before a laparoscopic fibroid eruption facilitates the surgical intervention, especially in the case of larger fibroids or large uteri. However, this study did not show a significant reduction in the duration of the procedure and could not minimize the intraoperative blood loss. The study evaluated data from 26 laparoscopic fibroid enucleations performed by the same surgeon between 2004 and 2010. Twelve patients were treated by UAE followed by laparoscopic myomectomy. The 14 patients in the control group were examined for age, calendar year, surgeon and number of fibroids removed. Surgical outcomes included preoperative clinical measurable uterine size, operative time, operative blood loss, and postoperative fibroid specimen weight. The data were analyzed using a 2-tailed *t*-test. The fourteen control patients underwent laparoscopic myomectomy alone. The UAE group had a larger mean preoperative clinical uterine size and a larger mean fibroid specimen weight measured postoperatively (595.3 vs. 153.6 g, $P < 0.05$) (11). In a study by David et al. (12), the use of UAE was presented in a very small number of cases. A total of three patients with a diagnosis of fibroids and a very large uterus weighing at least 1,100 g were included. The patient collective benefited from the combination therapy. A shorter inpatient stay as well as a shorter operation time and a significant reduction in intraoperative blood loss compared to the single implementation of conventional fibroid enucleation could be demonstrated (12). In 2018, Schnapauff et al. (13) the results of David et al. (12) with a larger patient collective of 21 patients. Patients who wish to preserve the uterus and suffer from large fibroids can benefit from this combination therapy c. The fibroid size of the patients in the study by Schnapauff et al. (13) was on average 12.7 cm. In one of the 21 patients, the administration of blood supplies was necessary. Another patient received a complete removal of the uterus (hysterectomy) intraoperatively despite the UAE. Eleven of the 21 patients could be examined postoperatively. Ten patients reported an improvement in their symptoms. Nine of the eleven patients would choose the treatment method again (13). Both studies included patients with a high uterine weight and/or large fibroids. The clinical picture of the uterus myomatosus was not included in either study. Current scientific findings on the use of combination therapy for UAE with conventional myomectomy are pending. The aim of this work was therefore to close this knowledge gap and to investigate the use of the combination therapy of UAE and conventional myomectomy in the ICD diagnosis of uterus myomatosus using the study designs described in detail in the Material and Methods chapter. The studies by David et al. (12) and Schnappauf et al. (30) served as the basis for this study. In contrast to these two studies mentioned, a higher number of patients were included in our study and compared with a comparison group with the same ICD-10 diagnosis using various parameters. In particular, the questions of intraoperative blood loss, operating times, length of stay in hospital and the postoperative patient outcome were examined. The working hypotheses of our study were detailed in the introductory chapter. In principle, we hypothesize that women who wish to have a uterus-preserving fibroid enucleation with the clinical picture of uterus myomatosus benefit from a combination therapy of UAE and conventional fibroid nucleation in that the intraoperative blood loss is less, the operation time is shorter, and the length of hospital stay is shorter compared to patients who receive a uterus-sparing fibroid enucleation without prior UAE.

To establish a new procedure in everyday clinical practice, various requirements must be met: the effectiveness and safety of the new method compared to previous methods, the additional costs and time required for the new method, as well as the availability of the experience of the hospital staff and the Quality of interdisciplinary collaboration between interventional radiologists and gynecologists (14–18). UAE requires several additional medical procedures, such as pelvic MRI, placement of epidurals, and performance of angiography, that are not performed with conventional laparoscopic fibroid enucleation (19). The experience of the radiologists and the availability of this method and the necessary equipment cannot be guaranteed in every hospital (20–23). The interdisciplinary myoma treatment in this way is demanding but can offer the option of having a positive influence on the surgical results if the indication is precise. Previous study results indicate that the combination therapy of UAE and myomectomy can be carried out easily in everyday clinical practice if the human and technical capacities are already available for this (24–28). In addition, the combination therapy of UAE and laparoscopic myomectomy represents a modern gynecological treatment method, which can demonstrably increase patient satisfaction and the postoperative outcome (29). In addition, this combined therapy method can in principle expand the spectrum of minimally invasive therapy in surgical gynecology for (very) large myomas, a high number of myomas and the clinical picture of the uterus myomatosus. The current trend toward minimally invasive and gentle surgical therapy methods, which are increasingly preferred by patients, can be strengthened with this combination therapy (30).

Other factors have expanded the established surgical method for removing fibroids in recent years. Such as the intraoperative use of tourniquet placing or administering tranexamic acid before surgery (14–16). What all methods have in common is the goal of reducing intraoperative blood loss during fibroid removal (17).

In addition to this fundamental trend development, with the combination therapy, the patient's desire for a uterus-preserving procedure in relation to fibroid therapy, even in the presence of large fibroids and/or many fibroids and the clinical picture of the uterus myomatosus can be promised and the statement by Scholz et al. (1) that the only therapy for uterine myomatosus is hysterectomy must be critically questioned.

Conclusion

In summary, the study showed that the combination therapy of UAE with subsequent minimally invasive myoma nucleation

can be a therapeutic option for the treatment of large myoma or the condition of uterus myomatosus, especially in patients who wish to have myoma removed after completion of the child wish due to possible complications in the medium and long term. By reducing intraoperative blood loss and shortening the surgery time, the UAE can improve the operating conditions and thus optimize the reconstructive capacity of the uterus from the surgeon's point of view. To date, very few studies have been established with many enrolled patients and a large number and size of fibroids. This study provides first findings in the field of minimally invasive myoma therapy in the treatment of large fibroids as well as in the clinical picture of the uterus myomatus in organ preservation procedures. It must be clearly mentioned that enormous costs and structural prerequisites must be met and that there are already optimized and common surgical treatment standards.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by University Jena. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

Author contributions

SH conceived and planned the experiments and performed the analysis. IG and ES provided critical feedback and helped to shape the research, analysis, and manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Enhanced recovery after surgery program alleviates neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in patients undergoing gynecological surgery

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Background: To evaluate the efficacy of the enhanced recovery after surgery (ERAS) programs on the systemic inflammatory response (SIR) of patients following gynecological surgery, a randomized controlled trial was performed to compare the ERAS programs with the conventional perioperative care programs. Furthermore, novel SIR markers could be identified to evaluate the ERAS programs of gynecological surgery.

Methods: Patients undergoing gynecological surgery were randomly allocated to either the ERAS group or the conventional group. The correlations between the elements of ERAS protocols and SIR markers following gynecological surgery were evaluated.

Results: A total of 340 patients who underwent gynecological surgery were enrolled (ERAS=170; conventional=170). First, we identified whether the ERAS programs after gynecological surgery reduced the perioperative difference between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR). Interestingly, first flatus time postoperatively, visual analog scale (VAS) score of patients was positively correlated with the perioperative difference NLR or PLR. Moreover, we discovered that the perioperative difference NLR or PLR was correlated with elements of ERAS protocol, including first sips of water, first semifluid diet postoperatively, pelvic drain duration, and out-of-bed time of patients.

Conclusion: We originally reveal that certain elements of ERAS programs alleviated SIR to operation. The implementation of ERAS programs enhances postoperative recovery after gynecological surgery *via* improving system inflammatory status. NLR or PLR could be the novel and inexpensive marker to assess ERAS programs in gynecological surgery.

Clinical trial registration: ClinicalTrials.gov, identifier, NCT03629626.

KEYWORDS

ERAS, gynecological surgery, platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio, systemic inflammatory response

Background

Enhanced recovery after surgery (ERAS) is a multimodal perioperative protocol. Its feasibility and benefits on perioperative care have been widely reported in patients undergoing colorectal surgery, gastrointestinal surgery, urological surgery, lung surgery, hepatobiliary, pancreatic surgery, and gynecological surgery (1–7). It has been reported that ERAS can result in shorter recovery times, including better patient outcomes, less opioid utilization, less postoperative nausea and vomiting (PONV), and shorter hospital stays for gynecological surgery (8–12). Nevertheless, the ERAS impact on the systemic inflammatory response (SIR) to surgery has not yet been clearly understood (13). Neutrophils and macrophages of the innate immune system are activated by releasing proinflammatory factors such as interleukin-1 and interleukin-6 and tumor necrosis factor alpha following the cell response to surgical injury. Meanwhile, the levels of circulating acute-phase proteins, including C-reactive protein, albumin, ferritin, transferrin, and fibrinogen, are modulated by proinflammatory factors (14). The SIR features changes in relative levels of circulating white blood cells (WBCs), neutrophils, and relative lymphocytes (15). As a direct consequence of tissue trauma, interleukin-6 is synthesized locally and stimulates C-reactive protein and the fibrinogen synthesis in scar tissue growth (16). However, the blood subtype is more common and less expensive, which could be used as a clinical marker of gynecological surgical trauma in patients (17). Thus, the SIR to surgical trauma also can be easily monitored through the analyses of blood subtypes in the bloodstream, such as neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), or monocyte-to-lymphocyte ratio (MLR) (18). The neutrophil-to-lymphocyte ratio (NLR) is related to clinical outcomes in patients with acute cerebral hemorrhage (19). Otherwise, a high neutrophil-to-lymphocyte ratio (NLR) or platelet-to-lymphocyte ratio (PLR) is associated with an adverse overall survival in many solid tumors (20–26). Available evidence does not show whether ERAS programs allow a measurable systemic inflammatory response (SIR) reduction in gynecological surgery. Thus, we investigated the application of ERAS principles to gynecological surgery in a prospective randomized control trial, in order to better understand the effectiveness of ERAS programs in minimizing the systemic inflammatory response, which would finally lead to shorter recovery time for patients and shorter hospital stays.

We assumed that ERAS programs would have a role in attenuating systemic inflammatory response (SIR) after gynecologic surgery. First, we demonstrated a measurable marker of SIR for ERAS following gynecological surgery, which could be a novel marker to estimate the implementation of an ERAS program after gynecologic surgery.

Methods

After obtaining informed consent, patients who were diagnosed with gynecological benign diseases, including myoma, adenomyosis, endometrial dysplasia, or benign ovarian tumors, were eligible for enrollment. Exclusion criteria were history of constipation and American Society of Anesthesiologists risk ≥4 (27). A total of 340 patients were required to evaluate surgical procedures and perioperative care. This study was designed as a prospective, randomized control trial with a follow-up period of 6 months. Patients were randomly assigned using block randomization on a 1:1 basis to either the ERAS or the conventional group. The study was approved by the institutional research board committee of the institution in line with the STROCSS criteria (28). The trial was registered on ClinicalTrials.gov (NCT03629626).

TABLE 1 Enhanced recovery pathway.

Groups	ERAS
Before admission	Preoperative education operative risk assessment
Preoperative	Eliminate bowel preparation
	1–3 days fluid diet before surgery
	Fasting up to 6 h before surgery; Oral carbohydrate solution (500 mL, Carbohydrate 2.5%) up to 2 h before surgery
Intraoperative	Insertion of Foley catheter
	Antiembolic stockings
	Maintain intraoperative euvolemia: Decrease crystalloid administration
	Opioid IV at discretion of anesthesiologist supplemented with fentanyl, After incision closure: injection with bupivacaine in transabdominal surgery
Postoperative	Evening of surgery: out of bed greater than 20 min; Day after surgery and until discharge: out of bed greater than 2 h
	Patient encouraged to start drink water 2 h after surgery; Semifluid diet in POD1; general diet in POD2
	Chewing gum 24 h after surgery
	Fluid restriction (1–2 l) after surgery in POD0
	LMWH injection and antiembolic stockings
	Foley removal as early as possible
	Drain removal as early as possible
	NSAIDs for analgesia

LMWH, low-molecular-weight heparin; POD, postoperative day; IV PCA, intravenous patient-controlled analgesia.

Enhanced recovery after surgery programs are given in Table 1. Before admission, the ERAS patients were given comprehensive preoperative education. Instead of bowel preparation, a clear liquid diet was followed for 1–3 days before surgery. Meanwhile, ERAS patients were also allowed to fast up to 6 h before surgery and intake of oral carbohydrate solution (500 mL, carbohydrate 2.5%) up to 2 h before surgery. Intraoperatively, opioid IV at the discretion of an anesthesiologist was supplemented with fentanyl. After incision closure, bupivacaine was injected in transabdominal surgery. Non-steroidal anti-inflammatory drugs (NSAIDs) (50 mg intravenous flurbiprofen axetil b.i.d. for 3 days) on the day of surgery and postoperative days (POD) 1–2. The conventional group was given intravenous patient-controlled analgesia (IV PCA) mostly composed

of opioid analgesics, such as fentanyl and morphine. Low-molecular-weight heparin (LMWH) and compression stockings are used as thromboprophylaxis in an ERAS setting.

Patients in the ERAS group were encouraged to start drinking water 2 h after surgery, chew gum 24 h after surgery, begin a semifluid diet in POD1, and returned to the general diet in POD2. Out of bed time greater than 20 min was encouraged on the day of surgery for the ERAS group and out of bed time greater than 2 h each day was encouraged after surgery until discharge. Foley and drain removal are recommended in patients in the ERAS groups as early as possible. The ERAS principles of maintenance of euvolemia and prophylactic antithrombotic were emphasized in the perioperative period. The systemic inflammatory response (SIR), hospital stay, and hospital cost were investigated. Surgical field exposure, the day of first flatus, postoperative nausea and vomiting (PONV), maximum pain score by the visual analog scale (VAS), postoperative complication, readmission rate, and re-operation rate also were demonstrated.

Patient baseline data, along with perioperative characteristics, are shown in Table 2. The time from the beginning to the end of the operation (operative time) was calculated. Gynecologic benign diseases including myoma, adenomyosis, endometrial dysplasia, and benign ovarian tumor were identified. Surgical procedure types including hysteromyomectomy, adenomyomectomy, resection of benign ovarian tumor, and hysterectomy were stated. Both laparoscopy cases and open cases are included since laparoscopic surgery is not appropriate in some circumstances, such as hyperuteri and oversize ovarian mass. To investigate the impact of ERAS on the surgical procedure, surgical field exposure was calculated as good (without intestinal distension), medium (with mild intestinal distension), and bad (with severe intestinal distension). Two experienced surgeons were involved in this study.

Peripheral complete blood samples were collected preoperatively and postoperatively. Different subtypes between postoperative and preoperative, including white blood cell (WBC), platelet, neutrophil, monocyte, lymphocyte, NLR, PLR, and MLR, were assessed. NLR was provided by the ratio between the absolute count of neutrophils and the absolute count of lymphocytes. PLR was calculated by dividing the absolute number of platelets by the absolute number of lymphocytes. MLR was calculated by dividing the absolute number of monocytes by the absolute number of lymphocytes.

Statistical analyses were performed using SPSS 25.0 and GraphPad Prism. Univariate analysis was used to compare the patient baseline data and operative characteristics between the two cohorts. For continuous variables, *t*-test or Mann–Whitney U-test was used, and for categorical variables, *t*-test or Fischer's exact test was performed. Linear regression and scatter diagram showed the correlation between the first flatus or VAS and SIR. Pearson's correlation coefficient for normally distributed data and Spearman's correlation coefficient for non-normally distributed data were calculated between elements of the ERAS program and SIR. A value of p of <0.05 was considered statistically significant for all statistical comparisons.

TABLE 2 Patient baseline data and perioperative characteristics.

	ERAS (*n*=170)	Conventional (*n*=170)	*p* value
Demographics			
Age	43.55 ± 11.04	45.51 ± 11.82	0.155
BMI (kg/m^2)	24.91 ± 4.51	24.53 ± 4.08	0.186
Diabetes	19 (11.2)	20 (11.8)	0.236
Hypertension	7 (4.1)	9 (5.3)	0.712
Semifluid diet before surgery (days)	1.05 ± 0.37	/	
Operative data			
Operative time (min)	74.74 ± 28.34	79.15 ± 31.09	0.179
Laparoscopy cases	124 (72.9)	122 (71.8)	0.219
Gynecologic disease			0.529
Myoma	73 (42.94)	76 (44.71)	
Adenomyosis	25 (14.71)	18 (10.59)	
Endometrial dysplasia	15 (8.82)	20 (11.76)	
Benign ovarian tumor	57 (33.53)	56 (32.94)	
Surgical procedure			0.531
Hysteromyomectomy /adenomyomectomy	35 (20.59)	26 (15.29)	
Resection of benign ovarian tumor	34 (20)	34 (20)	
Hysterectomy	101 (59.41)	110 (64.71)	
Postoperative course			
sips of water (hours)	5.66 ± 1.25	16.24 ± 5.75	0.001
Semifluid diet (hours)	23.86 ± 1.29	38.54 ± 11.76	0.001
General diet (hours)	63.25 ± 12.16	88.80 ± 11.03	0.001
IV fluid administration in POD0 (mL)	1694.18 ± 519.25	2592.68 ± 743.21	0.001
IV fluid administration in POD1 (mL)	1161.76 ± 305.97	2163.79 ± 417.81	0.001
IV fluid administration in POD2 (mL)	703.53 ± 482.06	1628.18 ± 555.48	0.001
Out of bed time in POD0 (min)	30.65 ± 5.54	1.89 ± 5.22	0.001
Out of bed time in POD1 (min)	138.35 ± 14.46	30.47 ± 18.03	0.001
Urinary catheter duration (days)	1.75 ± 1.49	2.68 ± 0.46	0.032
Pelvic drain duration (days)	0.44 ± 0.49	2.92 ± 0.27	0.021
Complications			0.165
Ileus	1 (0.6)	1 (0.6)	
Wound infection	0 (0)	1 (0.6)	
Re-operation (%)	0 (0)	0 (0)	0.998
Readmission (%)	2 (1.2)	3 (1.8)	0.469

Data are *n* (%) or mean ± standard deviation; IV, intravenous; POD, postoperative day.

Results

Patients undergoing gynecological surgery from September 2018 to September 2019 were included in this study. Ten patients were excluded because of constipation and ASA status, and six patients refused to proceed with the study. Finally, 170 patients were divided

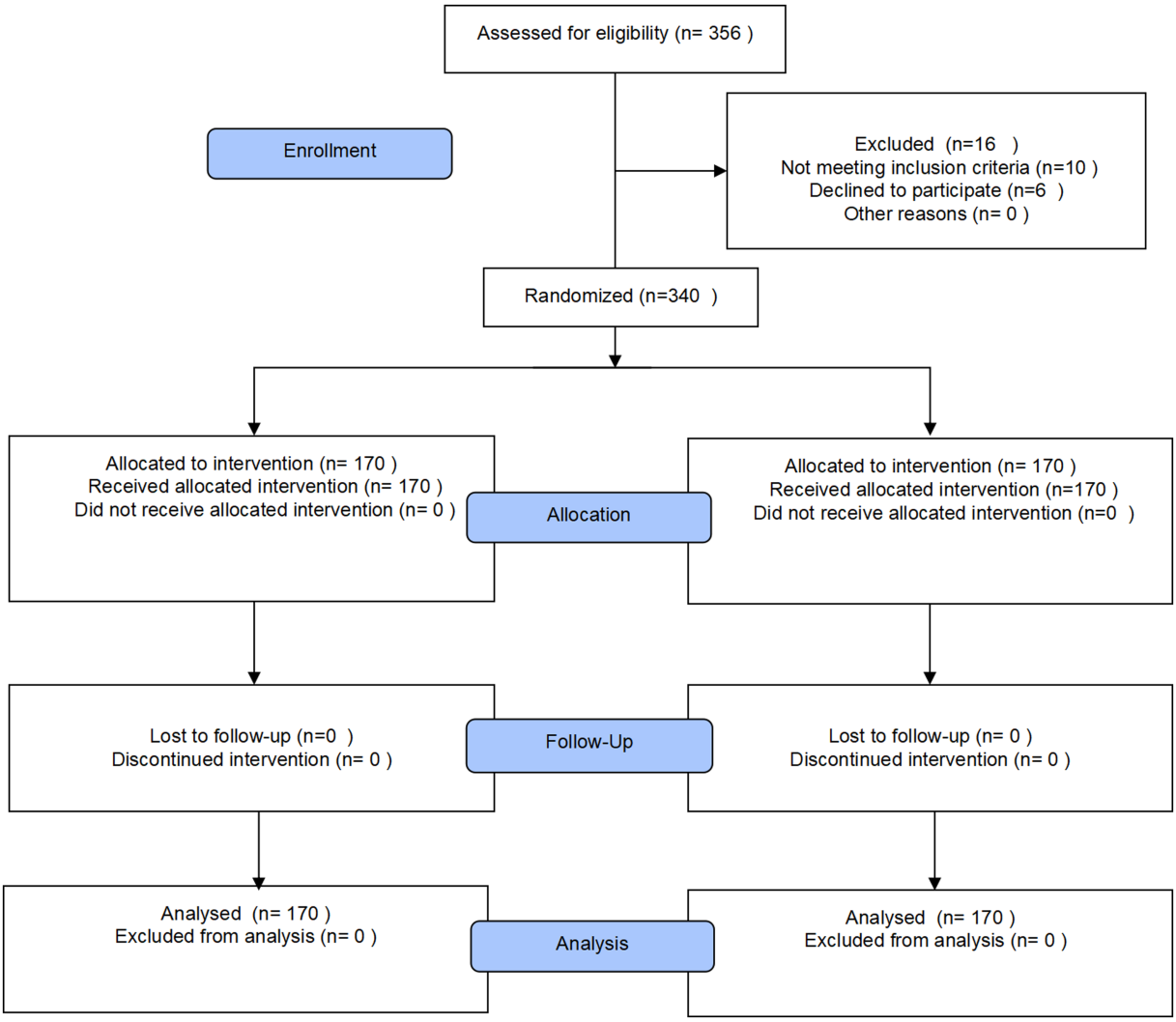

FIGURE 1
CONSORT flow diagram.

into the ERAS group, and 170 patients were divided into the conventional group (Figure 1). All patients were followed up postoperatively for up to 6 months. There was no statistical difference in the demographic characteristics of patients including age, body mass index (BMI), diabetes, hypertension rate, types of gynecologic disease, and surgical procedure, showing well randomization between the two groups (Table 2). The mean operative time was 74.74 ± 28.34 min in the ERAS group and 79.15 ± 31.09 min in the conventional group ($p = 0.179$, Table 2). No significant difference was shown in the laparoscopy rate between the two groups ($p = 0.219$, Table 2). The data of first sips of water, semifluid diet, and general diet were all significantly higher, while fluid administration was smaller and out-of-bed time was longer in the ERAS groups in accordance with the given protocol (Table 2). Urinary catheter and pelvic drain duration significantly reduced as required (Table 2).

According to our observation, the ERAS protocol did not affect the surgical field exposure ($p = 0.322$, Figure 2A). Thus, the ERAS pathway had no impact on the surgical procedure, which certain surgeons worried about that, especially by eliminating bowel preparation and short fasting time. ERAS protocol may reduce the intestinal wall edema and affect the status of bowel recovery and then lead to earlier flatus postoperatively. As expected, the day of the first flatus postoperatively was faster in the ERAS group compared with the conventional group ($p = 0.0001$, Figure 2B). Moreover, patients in the ERAS group experienced significantly less postoperative nausea and vomiting (PONV) (74.71% in the conventional group compared with 31.76% in ERAS group, $p = 0.021$, Figure 2C). Despite a significant reduction in opioid, there was no change in pain scores on an operative day between the two groups ($p = 0.612$, Figure 2D). However, maximum pain score obtained by the VAS scale in ERAS group was significantly lower from postoperative day 1 to postoperative day 2 ($p = 0.001$, Figure 2D).

Patients obviously benefited from ERAS protocols; furthermore, 30-day rates of complications and re-operation did not differ between the two groups (Table 2). The postoperative readmission rate for 6 months after discharge was not different between groups (Table 2).

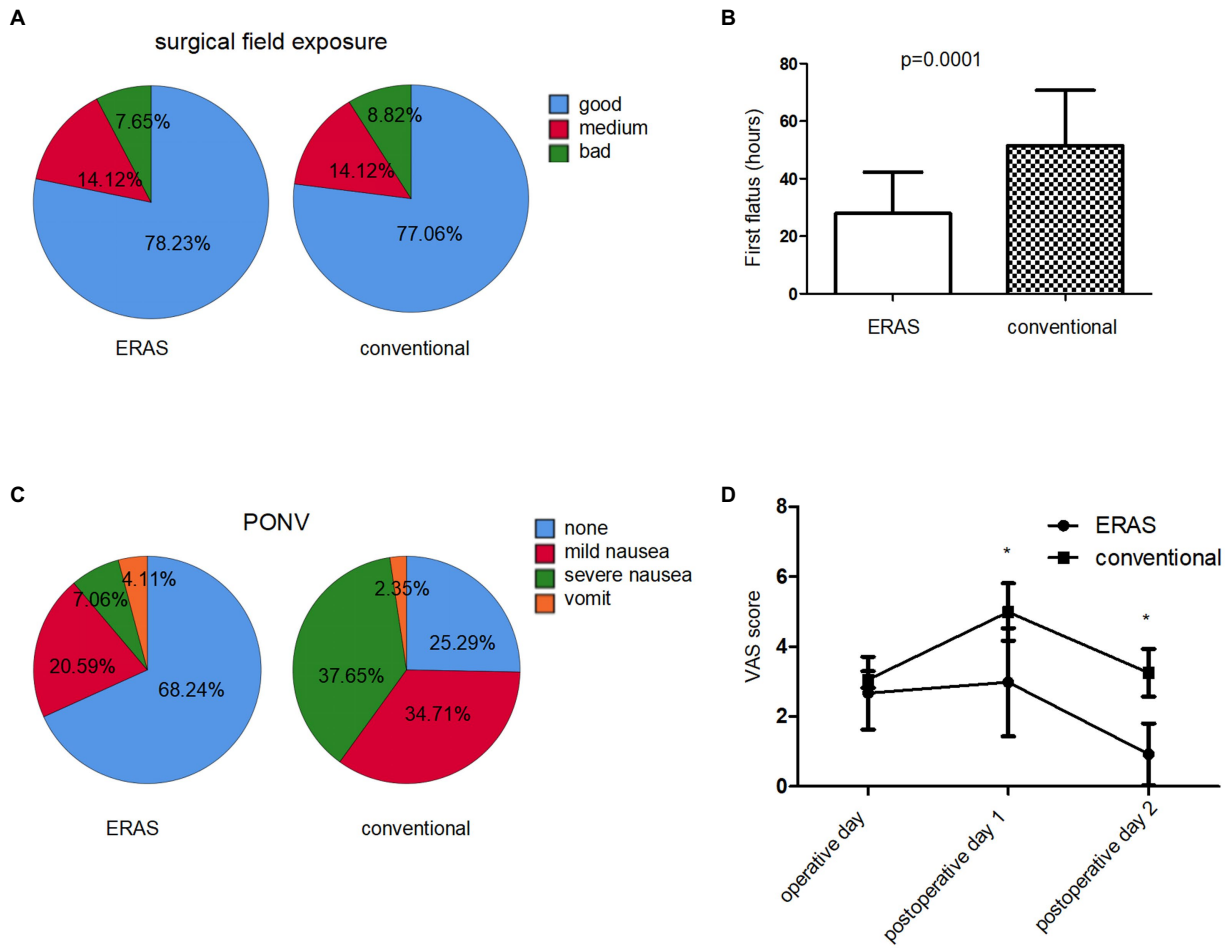

FIGURE 2
Postoperative results in ERAS and conventional group. **(A)** Surgical field exposure. **(B)** First flatus time postoperatively (hours). **(C)** Postoperative nausea and vomiting (PONV) rate after surgery. **(D)** Maximum pain (VAS) score on operative and postoperative days.

Unsurprisingly, among hysterectomy, resection of ovarian tumors, or hysteromyomectomy/adenomyomectomy, ERAS resulted in a reduction in the total length of stay and postoperative length of stay compared with the conventional group ($p = 0.0001$, Table 3). The reduction in length of stay was accompanied by total hospital cost savings of 2000RMB per patient ($p = 0.0001$, Table 3).

We evaluated that the modulation of the ERAS pathway on the systemic inflammatory response (SIR), including the perioperative difference in the composite of blood, was evaluated, including WBC, neutrophils, lymphocytes, monocytes and platelets, NLR, PLR, and MLR in the ERAS and conventional groups. We identified that the difference between NLR and PLR preoperatively and postoperatively in enhanced recovery pathway patients significantly decreased compared to the conventional group (Figure 3). Moreover, linear regression analysis and scatter diagram shows that first flatus time postoperatively, VAS score in POD0, POD1, and POD2 of patients following gynecologic surgery is positively correlated to perioperative difference neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) (Table 4; Figure 4). There is no association between PONV and SIR ($p = 0.108$, 0.539, Table 4). Next, in order to figure out which element of the ERAS protocol has an impact on SIR, we evaluated each element of the ERAS protocol and identified that the perioperative difference between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) is positively correlated with first sips of water time postoperatively, first semifluid diet time postoperatively, pelvic drain duration, and negatively correlated with out-of-bed time in PDO0 of patients following gynecologic surgery, not with elimination bowel preparation, IV fluid administration in POD0, and urinary catheter duration (Table 5).

Discussion

Enhanced recovery after surgery programs, which typically focus on minimizing preoperative stress and improving the response to postoperative stress, have grown substantially in modern surgical care. The systemic inflammatory response (SIR) is the direct manifestation of surgical stress. Although ERAS generates a reduced PONV, less pain, and shorter bowel recovery following gynecological surgery (29), evidence of the effect of ERAS protocols on SIR to the gynecological

TABLE 3 Recovery time and cost between ERAS and conventional cases.

	ERAS	Conventional	value of *p*
Hysteromyomectomy/ Adenomyomectomy	(*n* = 35)	(*n* = 26)	
Postoperative length of stay	4.43 ± 1.17	4.96 ± 1.82	0.0001
Total length of stay	7.20 ± 1.55	7.92 ± 2.61	0.0001
Total hospital cost	23105.26 ± 3840.93	24589.28 ± 6398.83	0.0001
Resection of ovarian tumor	(*n* = 34)	(*n* = 34)	
Postoperative length of stay	3.18 ± 0.87	3.97 ± 1.38	0.0001
Total length of stay	5.44 ± 1.11	6.67 ± 1.97	0.0001
Total hospital cost	19437.24 ± 3033.73	20948.84 ± 3974.27	0.0001
Hysterectomy	(*n* = 101)	(*n* = 110)	
Postoperative length of stay	4.14 ± 1.21	5.02 ± 1.75	0.0001
Total length of stay	7.09 ± 1.41	8.92 ± 3.05	0.0001
Total hospital cost	25716.27 ± 5500.35	27480.13 ± 5727.56	0.0001
Total	(*n* = 170)	(*n* = 170)	
Postoperative length of stay	4.01 ± 1.21	4.80 ± 1.73	0.0001
Total length of stay	6.78 ± 1.53	8.31 ± 2.93	0.0001
Total hospital cost	23922.90 ± 5364.27	25731.74 ± 6090.33	0.0001

TABLE 4 Correlation analysis between PONV, first flatus time postoperatively, VAS score in postoperative days POD0, POD1, and POD2 of patients following gynecologic surgery and the perioperative difference between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).

SIR		PONV	First flatus	VAS POD0	VAS POD1	VAS POD2
Difference NLR	*r*	0.087	0.454	0.318	0.344	0.356
	p	0.108	0.000	0.000	0.000	0.000
Difference PLR	*r*	0.033	0.224	0.152	0.184	0.213
	p	0.539	0.000	0.005	0.001	0.000

surgery is limited. No studies examined the impact of ERAS programs versus conventional perioperative care on the systemic inflammatory response (SIR) in gynecological surgery, making the interpretation of the inflammatory impact of ERAS protocols difficult. Instead of focusing on the length of hospital stay of patients and remarkable economic benefit, we instead focused on the modulation of ERAS protocols for the systemic inflammatory response to surgery. Consistent with our previous data in gynecological oncology surgery (30), here we first identified that ERAS protocols decrease the perioperative difference between PLR and NLR, alleviating the excessive inflammatory response status in patients with gynecological benign disease surgery.

Moreover, we found out NLR or PLR is positively correlated to pain score and first flatus time. The NLR or PLR has become a marker for gynecological surgical patients since it may directly affect pain and the return to normal bowel function. Analgesic regimens that minimize opioid demand, which may cause vomiting and intestinal dysfunction, are therefore key components of ERAS programs. It has been reported that local anesthesia techniques such as the transversus abdominis plane block (TAP) are successful in multiple surgical specialties and procedures (31, 32). Postoperative use of non-steroidal anti-inflammatory drugs (NSAIDs) has a good effect, which allows for more intense postoperative physical therapy and early mobilization, and results in lower pain scores (33, 34). Better pain control promotes more exercise, which stimulates faster bowel function recovery. Both faster bowel function recovery and less pain were seen in patients undergoing ERAS, and this is a consequence of a shorter systemic inflammatory status. Thus, here, we first demonstrate that the NLR or PLR could be used to assess the anesthetic effect and faster recovery of intestinal function.

Adherence to ERAS protocol improves SIR in patients undergoing gynecological surgery. Nevertheless, there is a lack of studies investigating a single ERAS item on systemic inflammatory responses. We needed to determine which individual interventions from ERAS contributed the most to the modulating systemic inflammatory response (SIR) markers. We demonstrated that the ERAS program, including early feeding, early ambulation after surgery, and shorter pelvic drain duration, was related to the perioperative difference between NLR and PLR. Early postoperative drinking and eating following gynecological surgery can reduce the systemic inflammatory response as part of an ERAS protocol. Meanwhile, within an enhanced recovery program following gynecological surgery, the more mobilization on postoperative day 0, the lower the NLR or PLR. The routine use of pelvic drains following gynecological surgery increases NLR and PLR. Therefore, early removal of pelvic drains can reduce the systemic inflammatory response as part of an ERAS protocol. In fact, enhanced protocols including early oral feeding and more mobilization lead to reduce SIR.

Although avoiding mechanical bowel preparation (MBP) has no adverse effect on postoperative complication rates, certain doctors and patients still feel anxious. Good education is necessary; Instead of bowel preparation, a clear liquid diet followed before surgery alleviates the anxiety of patients and doctors. There was no impact on surgical exposure by avoiding MBP following gynecological surgery. First, we identified that an MBP was not associated with the systemic inflammatory response as part of the ERAS protocol. Previous studies have shown that postoperative serum interleukin-6 is significantly lower following goal-directed therapy compared with conventional fluid management in colorectal surgery. However, our study found that NLR or PLR was not affected by intravenous (IV) fluid restriction in gynecological surgery. This finding raises the possibility that some of the components of ERAS programs provide little additional benefit to the SIR. In fact, postoperative C-reactive protein (CRP) in colorectal surgery was reported to be lower in laparoscopic surgery than in the open surgery group, regardless of perioperative care regimens (15, 35). However, there are limited data regarding clinical trials of individual components of ERAS protocols, which can lead to a reduction in the stress response following gynecological surgery.

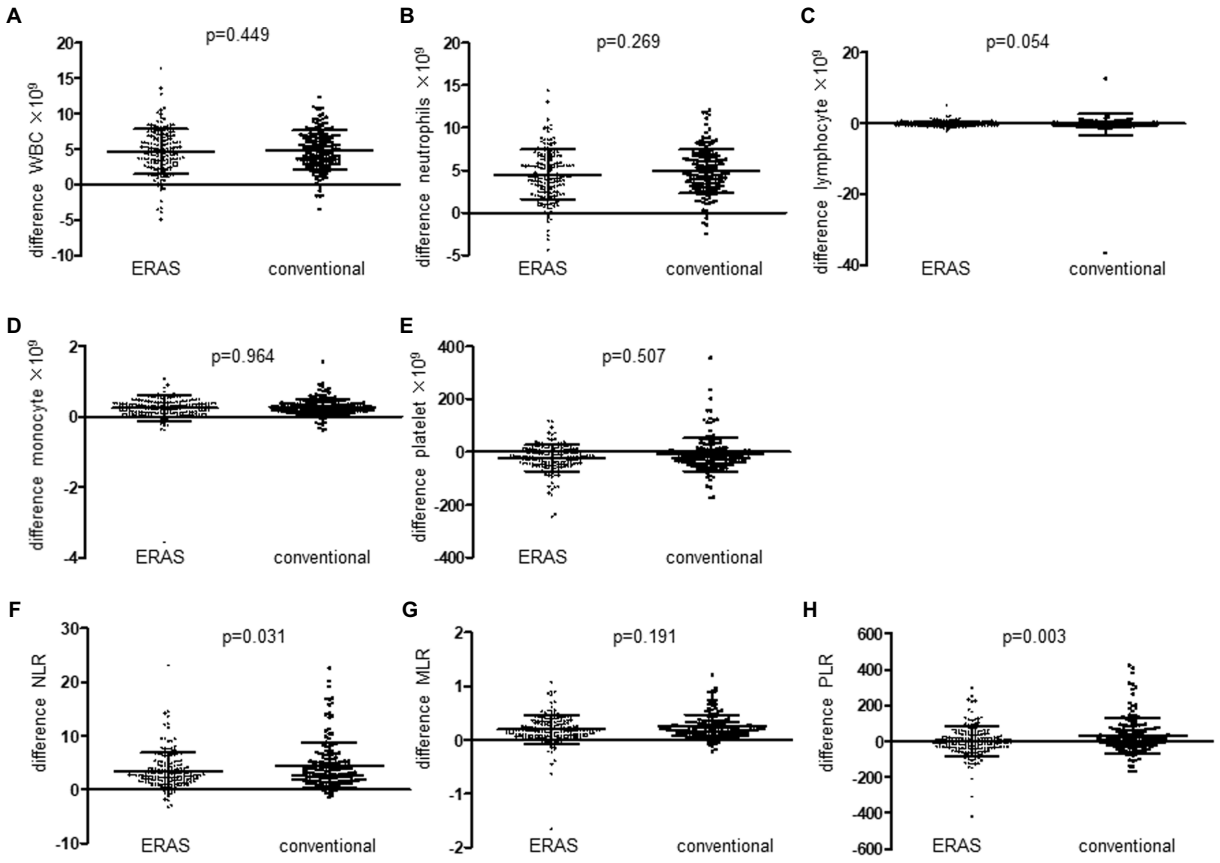

FIGURE 3
Comparison of patients following gynecologic surgery with ERAS programs and patients with conventional programs, in terms of the difference between preoperative and postoperative systemic inflammation response marker, WBC counts **(A)**, neutrophil counts **(B)**, lymphocyte counts **(C)**, monocyte counts **(D)**, platelet counts **(E)**, neutrophil-to-lymphocyte ratio (NLR) **(F)**, monocyte-to-lymphocyte ratio (MLR) **(G)**, and platelet-to-lymphocyte ratio (PLR) **(H)**.

Therefore, we demonstrated certain ERAS items, including early feeding postoperatively, early ambulation after surgery, and shorter pelvic drain duration, may attenuate system inflammation response, leading to a faster recovery of patients following gynecological surgery.

The strength of our study is the first clinical trial revealing the relationship between the component of the ERAS program and systemic inflammatory response in gynecological surgery. This study could help clinicians understand the effectiveness of enhanced recovery protocols in the modulating systemic inflammatory response. The benefits of an attenuated systemic inflammatory response could be a key to enhancing recovery and can be a protective feature for patients. Meanwhile, the limitation of this study is that more objective indicators are needed to reflect the effects of ERAS, and more research needs to be carried out in the future for a better evaluation of the molecular mechanism of ERAS on the systemic inflammatory response.

Conclusion

The enhanced recovery after surgery protocol provides faster recovery, less postoperative pain, decreased incidence of postoperative nausea and vomiting, and shorter hospital stays after gynecological surgery, which is a consequence of improved inflammatory status. Indeed, alleviated NLR or PLR could be a systemic inflammatory response predictor of ERAS programs' success in gynecological surgery. Moreover, we identified that certain ERAS items, including early feeding postoperatively, early ambulation after surgery, and shorter pelvic drain duration, applied to different types of gynecological surgery have a role in alleviating systemic inflammatory response.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of Qilu Hospital (scientific research review N0.2018-141). The patients/participants provided their written informed consent to participate in this study.

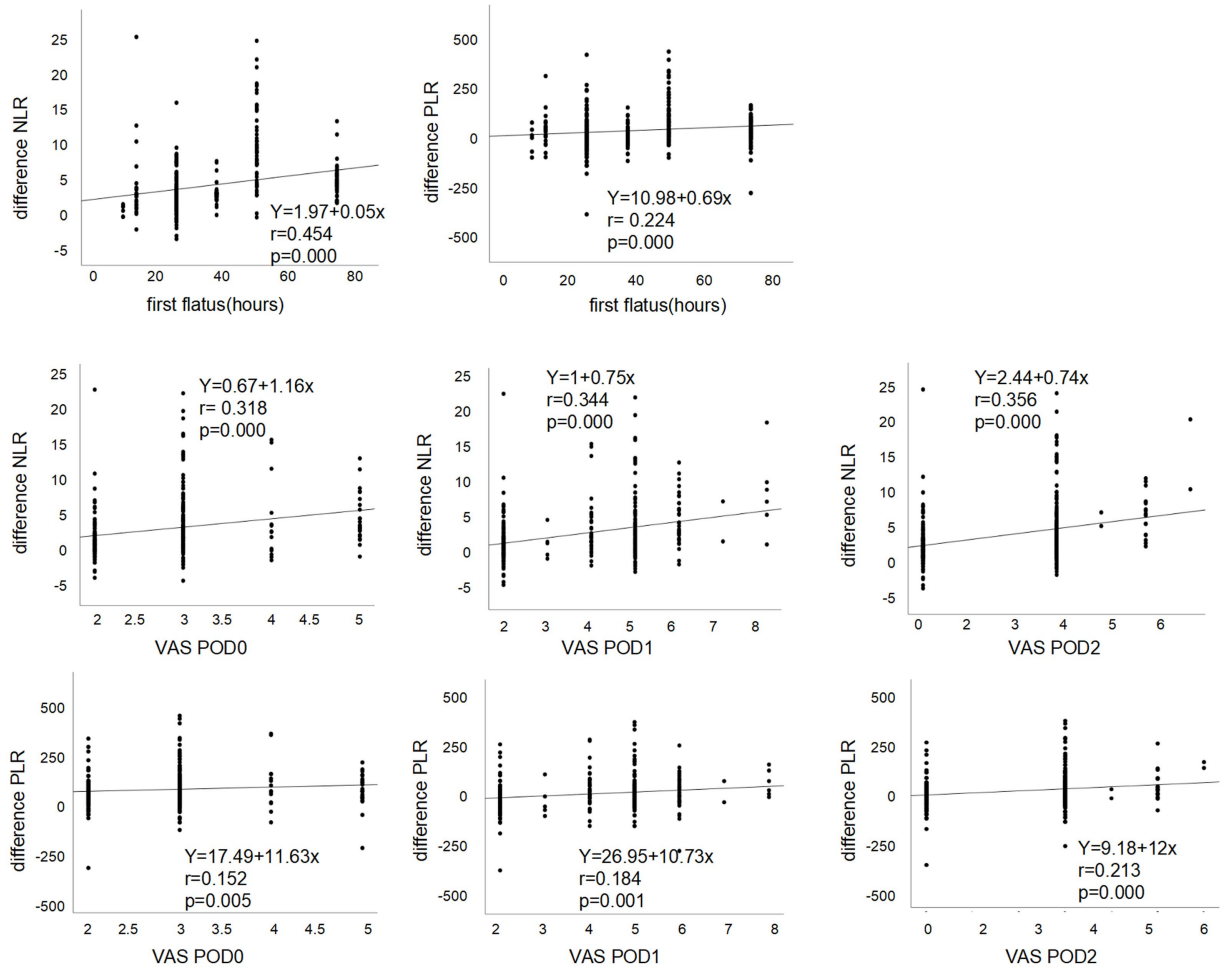

FIGURE 4
Linear regression and scatter diagram between first flatus time postoperatively, VAS score in POD0, POD1, and POD2 of patients following gynecologic surgery and the perioperative difference between neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR).

TABLE 5 Correlation analysis between perioperative difference between neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and elements of ERAS protocol, including elimination bowel preparation time, IV fluid administration volume in postoperative day POD 0, first sips of water time postoperatively, first semifluid diet time postoperatively, urinary catheter duration, pelvic drain duration, and out of bed time in POD 0 of patients following gynecologic surgery.

Elements of ERAS protocol		Eliminate bowel preparation	IV fluid administration volume in POD0	First sips of water time postoperatively	First semifluid diet time postoperatively	Urinary catheter duration	Pelvic drain duration	Out of bed time in POD0
Difference NLR	*r*	−0.099	0.102	0.170	0.147	0.097	0.121	−0.100
	p	0.069	0.059	0.002	0.007	0.074	0.025	0.047
Difference PLR	*r*	−0.064	0.093	0.199	0.173	0.104	0.138	−0.150
	p	0.241	0.088	0.000	0.001	0.056	0.011	0.006

Author contributions

NX and JP carried out the study, analyzed the data, and wrote the manuscript. YH and HW were involved in the study design, data management, and study analysis. All authors have made a great contribution to the manuscript, read, and approved the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Transvaginal natural orifice endoscopic surgery for ovarian cystectomy: a more suitable surgical approach for the day-care procedure

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Introduction: Although previous studies have shown that vaginal natural orifice transluminal endoscopic surgery (vNOTES) has the advantages of causing less pain, faster recovery, and better concealment of surgical incisions, which aligns with the concept of the day-care procedure, this approach poses a greater risk of damaging adjacent organs (i. e., rectum and bladder) due to its anatomical specificity. Moreover, the day-care procedure may lead to relatively less preoperative evaluation and postoperative care. Hence, it is necessary to explore the safety and effectiveness of vNOTES for ovarian cystectomy in the day-care procedure, to provide a theoretical basis for the wider development of vNOTES surgery.

Materials and methods: This retrospective study included 131 patients at our hospital who underwent ovarian cystectomy from September 2021 to October 2022. Based on the surgical approach, patients were classified into transumbilical laparoendoscopic single-site surgery (LESS) and vNOTES groups. The patients' demographic characteristics and follow-up data were collected during the perioperative period and 1-month postoperatively.

Results: Vaginal natural orifice transluminal endoscopic surgery has less postoperative exhaust time, a lower postoperative 6-hour pain score, and a lower incidence of analgesic drug use, with higher surgical conversion incidence. Multiple linear regression analysis showed that the surgical conversion, chocolate cyst, bilateral cyst, and pelvic adhesion increased the operation duration by ~43 (95% CI: 10.309, 68.152, $p < 0.001$), 15 (95% CI: 6.342, 45.961, $p = 0.036$), 10 (95% CI: 3.07, 40.166, $p = 0.019$), and 8 (95% CI: 4.555, 26.779, $p = 0.035$) min, respectively. Interestingly, vNOTES decreased the operation duration by ~8.5 min (95% CI: −18.313, −2.699, $p = 0.033$).

Conclusion: Vaginal natural orifice transluminal endoscopic surgery was equally safe and effective for ovarian cystectomy compared to LESS. vNOTES aligned with

the concept of the day-care procedure due to its reduced postoperative pain, shorter exhaust time, and absence of scarring. However, surgeons should conduct a comprehensive preoperative evaluation and exclude patients suspected to have severe pelvic adhesions.

KEYWORDS

transvaginal natural orifice endoscopic surgery, ovarian cystectomy, ovarian cyst, transumbilical laparoendoscopic single-site surgery, day-care procedure

Introduction

An ovarian cyst, a common tumor of the female reproductive system, is caused by an abnormal endocrine system or genetic factors (1, 2). It has an incidence rate of 1.3–24.0%, with more than 90% being benign tumors (3, 4). Physiological ovarian cysts generally have no specific symptoms, except for complications, such as torsion and rupture, and do not require any special treatment (5–7). Ovarian cystectomy is often the recommended treatment for symptomatic physiological or pathological ovarian cysts.

With the development of medical devices and the popularization of minimally invasive concepts, patients prefer surgeries that offer better esthetic outcomes, including those that inflict no or smaller scar (8, 9), such as needleoscopic and percutaneous-assisted surgery (10, 11). Currently, the minimally invasive approaches for ovarian cystectomy are vaginal natural orifice transluminal endoscopic surgery (vNOTES) and transumbilical laparoendoscopic single-site surgery (TU-LESS) (12, 13). Meanwhile, enhanced recovery after surgery (ERAS) has developed rapidly, which optimizes the clinical path of perioperative treatment, reduces the stress response of surgical trauma, shortens hospital stay, and promotes rapid recovery of patients (14–16). Based on the ERAS concept, the day-care procedure further optimizes the disease diagnosis and treatment process, which allows patients to be admitted, operated, and discharged within 24 h (17–19). In the two approaches mentioned above, the incisions are hidden in the belly button with no postoperative scar in the vaginal area; thus, they are suitable for the day-care surgery because of their small trauma and quick recovery.

However, although previous studies have shown that vNOTES has the advantages of causing less pain, faster recovery, and better concealment of surgical incisions, this approach poses a greater risk of damaging adjacent organs (i.e., rectum and bladder) due to its anatomical specificity (20–22). Moreover, the day-care procedure may lead to relatively less preoperative evaluation and postoperative care (17, 19). Hence, it is necessary to explore the safety and effectiveness of vNOTES for ovarian cystectomy in the day-care procedure.

Therefore, we investigate the perioperative data of vNOTES for ovarian cystectomy in the day-care procedure and compare them with single-port laparoscopic surgery. The purpose of this study is to explore the safety and effectiveness of vNOTES for ovarian cystectomy in the day-care surgery. In addition, we provide the complete process of the day-care procedure and key points of vNOTES for ovarian cystectomy.

Materials and methods

Study design and participants

This study is part of a Longitudinal Vaginal Natural Orifice Transluminal Endoscopic Surgery Study (LovNOTESS) conducted in Chengdu (China Clinical Trials Registry ChiCTR2100053483) and approved by the Ethics Committee of Chengdu Women and Children's Central Hospital (No. 202130). This subgroup study only included the retrospective clinical data of patients with ovarian cysts (i.e., pathological or symptomatic physiological ovarian cysts, with a max diameter of the cyst being >5 cm) who sought surgical treatment in our hospital between September 2021 and October 2022. Ovarian cysts suspected before the operation or confirmed by postoperative pathology as malignant were excluded, and vaginal infection was a contraindication for vNOTES. TU-LESS or vNOTES was performed according to the patient's wishes. Each patient who chooses vNOTES should be evaluated in detail before the operation, and the vNOTES approach should be avoided in one of the following cases (23, 24): suspected as malignant tumor before the operation, vaginal infection, highly suspected of severe pelvic adhesions, and the lesion location beyond the scope of the instrument of vNOTES. The exclusion criteria of malignant tumors are systematically based on physical signs, imaging, and serum blood tests, which are mainly according to some international expert consensuses (25, 26). Before the surgery, each patient was informed of the surgical risks (i.e., bladder, ureter, and rectum injuries) and benefits, and then signed written informed consent.

Data collection

Information on all patients was collected from hospital databases, including patient age, body mass index (BMI), the maximum diameter of the cyst, previous pregnancy and abdominal surgery, surgical location, the total time to surgery (i.e., from cutaneous incision to closure), blood loss quantified by subjective visual quantification (27, 28), simultaneously conducting other surgeries, intraoperative complications (i.e., bladder, bowel, and vascular injury), conversion to another surgical procedure, perioperative decrease in serum hemoglobin, postoperative exhaust time, postoperative fever (i.e., any oral temperature≥ occurrence of 38.0°C ≥24 h postoperatively), hospital stay, and postoperative complications. All patients underwent an outpatient review 1 month postoperative to assess postoperative recovery and clinical data.

Standard operating procedures for vNOTES and TU-LESS

Preoperation

All surgeries were performed under general anesthesia, and the patient is placed in the bladder lithotomy position. To prevent infection, 1 g of cefmetazole is administered intravenously 30 min before the procedure. The vaginal and perineal areas are repeatedly disinfected with iodophor, and Foley catheters are inserted for all patients.

Intraoperation

In the TU-LESS group, an incision is made 2 cm at the umbilicus. Then, multiple instrument access ports are inserted through the incision (Beijing Aerospace Cardi Technology Development Institute, HK-TH-60.4TY). In the vNOTES group, an incision was made 1.5 cm at the posterior cervical vault. The operating platform is still built with multiple instrument access ports.

The following steps are the same for both groups. Pneumoperitoneum was generated by CO_2 blowing up to 14 mmHg and visualized using a 10 mm 30-degree rigid laparoscope (Karl Storz GmbH & Co. KG, Tuttlingen, Germany). After separating the ovarian cyst from the surrounding tissue, part of the cortex along the long axis of the cyst was cut off using scissors to separate the cortex from the cyst wall. Once the cyst was removed, the remaining ovarian tissue was sutured with an absorbable thread, and an oophoroplasty was performed.

In the following situations, for example intraoperative damage to large vessels or important organs, bleeding volume $>$ 500 ml, change the surgical method; vNOTES was converted to transabdominal single-port laparoscopic surgery, while single-port laparoscopic surgery was converted to multiport surgery. In the event of any life-threatening vascular injury, open surgery was performed.

Peritoneal adhesions were assessed and classified according to the Nair scoring system. Adhesions are divided into four degrees according to the degree of adhesion between the two viscera and viscera and abdominal wall. Abdominal and vaginal wounds are closed with 2–0 absorbent sutures and 2–0 barbed absorbable sutures, respectively. In the TU-LESS and vNOTES groups, drainage tubes were not routinely placed.

Standard day-care procedure

Preadmission

Selection of suitable patients for the day-care surgery in the outpatient clinic. Exclude those who are suspected of severe pelvic adhesions, malignant tumors, or are not suitable for the day-care surgery.

Conduct preoperative testing in the outpatient setting (including blood examination, tumor markers, pretransfusion antibody screen, coagulation function, urination and leucorrhea routine, human chorionic gonadotropin, electrocardiogram, chest radiograph, and gynecological, abdominal, and urological ultrasounds).

Conduct preoperative evaluation, including the patient's general condition and anesthesia evaluation.

Inform patients of the specific admission time and precautions, such as 8-h fasting and water deprivation before admission, and the complete day-care procedure.

Hospitalization

The surgery was performed after completing the preoperative evaluation of the patient. After the surgery, the catheter is pulled out immediately, and regular postoperative nursing is carried out.

Post-discharge

Assess whether the patient meets the discharge criteria (i.e., usually discharged the morning after surgery). If there are any postoperative complications, such as fever, nausea, or vomiting, the patient is discharged on the third day after treatment and observation.

Ensure that patients and their families understand postoperative care and provide written precautions and follow-up arrangements.

Provide postoperative support and perform regular postoperative follow-ups (i.e., on the 7th day and 1 month after surgery).

Statistical analysis

All statistical analyses were performed using SPSS version 25.0 (IBM, Armonk, NY, USA). Continuous variables are expressed as means and standard deviations and analyzed using the Student's *t*-test, the corrected Student's t-test, one-way ANOVA, or a non-parametric test. Categorical variables are expressed as counts and percentages and analyzed using either the chi-square or Fisher's exact test. Multivariable linear regression analysis was used to assess the influencing factor of intraoperative bleeding, operative time, exhaust time, and postoperative 6-h pain score. Covariates were selected according to the different variables in the univariate analysis and factors reported in previous studies that would affect the dependent variable. All tests were double-tailed; a p-value of <0.05 was considered statistically significant.

Results

The selection process of the study population is shown in Figure 1. A total of 182 patients with ovarian cysts from our hospital were initially recruited. After excluding patients who had simultaneous surgery and malignant tumor, the final analysis included 131 patients; of which, 82 (62.6%) underwent LESS and 49 (37.4%) underwent vNOTES. Noteworthy, four patients were excluded due to final malign pathology. The characteristics of the

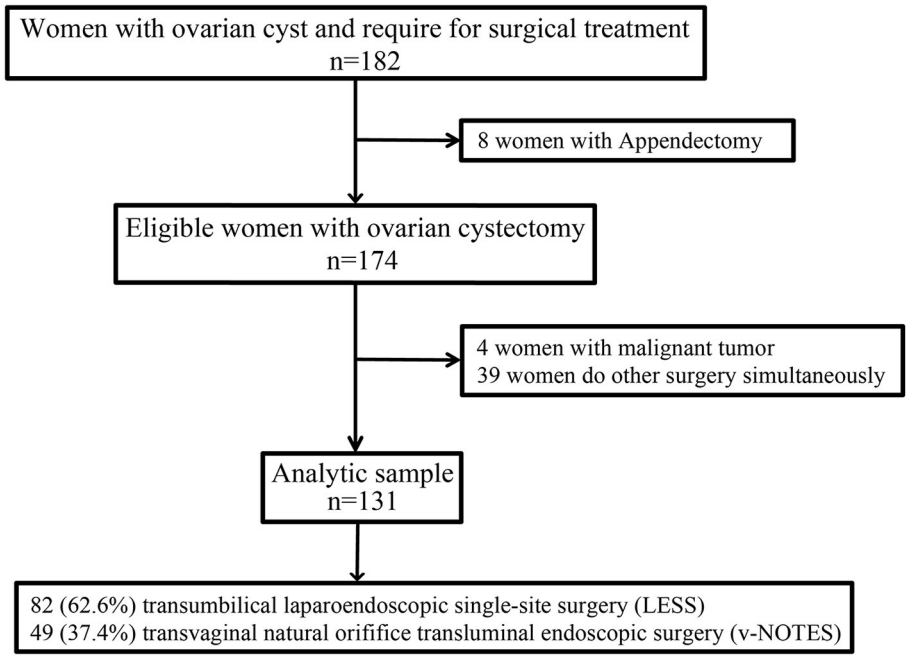

FIGURE 1
Selection process for this study.

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

Variables	Total
Patients	131
Age	32.54 ± 7.00
BMI (kg/m^2)	21.59 ± 2.94
Max diameter of cyst (cm)	5.19 ± 1.80
History of abdominal surgery	53(40.5%)
D & C artificial abortion	0.67 ± 1.08
Cyst type	
Simple cyst	48 (36.6%)
Chocolate cyst	52 (39.7%)
Teratoma	31 (23.7%)
Bilateral ovarian cyst	7 (5.3%)
Myomectomy type	
Laparoendoscopic single-site surgery (LESS)	82 (62.6%)
V-NOTES	49 (37.4%)

patients are presented in Table 1. The average age of patients at recruitment, BMI, and a maximum diameter of cysts was 32.54 ± 7.00 years, 21.59 ± 2.94 kg/m^2, and 5.19 ± 1.80 cm, respectively. Among these patients, 53 (40.5%) had undergone abdominal surgery, 7 (5.3%) had undergone bilateral ovarian cysts, and 52 (39.7%) had undergone chocolate cysts.

Further analysis of perioperative data showed that there were no significant differences between the two groups for age, BMI, abdominal surgery history, maximum cyst diameter, operation time, intraoperative bleeding, hospital stay, and postoperative complications. In vNOTES, this group had less postoperative exhaust time, a lower postoperative 6-hour pain score, and a lower incidence of analgesic drug use, with a higher surgical conversion incidence. During the postoperative follow-up (1 week and 1 month after surgery), four patients were found to have complications: one patient with febrile, one patient with anemia and transfusion, and one patient with poor wound healing in the LESS group, while one patient with febrile in the vNOTES group. All four complications occurred within 1 week after surgery and were cured in the outpatient department without re-operation (Table 2).

The operation duration reflects the effectiveness of the surgery. The multiple linear regression analysis showed that the operation duration was correlated with the operation approach, surgical conversion, chocolate cyst, bilateral cyst, and pelvic adhesion. The surgical conversion, chocolate cyst, bilateral cyst, and pelvic adhesion increased the operation duration by ~43 (95% confidence interval [CI]: 10.309, 68.152, $p < 0.001$), 15 (95% CI: 6.342, 45.961, $p = 0.036$), 10 (95% CI: 3.07, 40.166, $p = 0.019$), and 8 (95% CI: 4.555, 26.779, $p = 0.035$) min, respectively. Interestingly, vNOTES decreased the operation duration by ~8.5 min (95% CI: −18.313, −2.699, $p = 0.033$) (Figure 2).

Intraoperative blood loss is an important measure of the safety of surgery. The multiple linear regression analysis showed that the amount of intraoperative bleeding was positively correlated with surgical conversion, chocolate cyst, bilateral cyst, pelvic adhesion, and operation time. The surgical conversion, chocolate cyst, and bilateral cyst increased intraoperative bleeding volume by ~40 (95% CI: 25.023, 85.039, $p = 0.027$), 26 (95% CI: 5.013, 47.678, $p = 0.016$), and 33 (95% CI: 10.276,76.816, $p = 0.023$) ml, respectively.

Meanwhile, the bleeding volume increased by ~1.7 ml when the duration of surgery increased by 1 min (95% CI: 0.452, 2.856, $p < 0.001$) and 17 ml when pelvic adhesion increased by 1 grade (95% CI: 11.236, 22.716, $p = 0.014$) (Table 3).

TABLE 2 Description of the patient characteristics by cystectomy types.

Variables	LESS	v-NOTES	*p*-value
Patients	$N = 82$	$N = 49$	
Age (year)	32.74 ± 7.31	32.20 ± 6.51	0.671[a]
BMI (kg/m^2)	21.36 ± 2.99	21.95 ± 2.85	0.285[a]
History of abdominal surgery	33(40.2%)	20 (40.8%)	0.948[b]
Max diameter of cyst (cm)	6.62 ± 1.59	6.44 ± 1.46	0.065[a]
Pelvic adhesion	9(11.0%)	5(10.2%)	0.838[c]
Bilateral ovarian cyst	3(3.7%)	3(3.7%)	0.424[c]
D&C artificial abortion	0.71 ± 1.13	0.61 ± 1.01	0.629[a]
Operative information			
Procedure time (min)	95.47 ± 37.48	86.95 ± 52.03	0.239[a]
Bleeding volume (ml)	40.25 ± 58.24	35.20 ± 42.15	0.425[a]
Surgical conversion	0 (0%)	4 (8.9%)	0.013[c]
Post-operative information			
Hemoglobin difference (g/L)	13.71 ± 9.23	15.65 ± 9.43	0.281[a]
Hospital stay (day)	1.05 ± 0.31	1.04 ± 0.20	0.873[a]
Exhaust time (hour)	9.01 ± 7.52	7.14 ± 7.75	0.043[a]
Pain scores (6 h after surgery)	1.41 ± 0.74	1.06 ± 0.91	0.026[a]
Complications	3 (3.7%)	1 (2.0%)	1.000[c]
Pain medications	24 (29.3%)	3 (6.1%)	0.009[c]

[a]Average and standard deviation. Student's *t*-Test.
[b]Number (percentage). Chi-squared Test.
[c]Number (percentage). Fisher Exact Test.

In the vNOTES group, the postoperative exhaust time was significantly shorter than that of the LESS group. The multiple linear regression analysis revealed that the postoperative exhaust time was correlated with surgical approach and duration. vNOTES reduced the postoperative exhaust time by ~85 min (95% CI: −60.320, −110.462, $p = 0.012$), while the exhaust time increased by ~7 min when the duration of surgery increased by 1 min (95% CI: 4.768, 8.462, $p = 0.041$) (Table 4).

Further multivariate linear regression revealed that the 6-h postoperative pain score was correlated with the operation approach and abdominal surgery history. vNOTES reduced the 6-h postoperative pain score by ~0.9 (95% CI: −1.697, −0.008, $p = 0.047$) and previous abdominal surgery history reduced the score by ~0.6 (95% CI: −1.037, −0.175, $p = 0.012$) (Table 5).

Discussion

Vaginal natural orifice transluminal endoscopic surgery has advantages, such as reduced postoperative pain, shorter exhaust time and hospital stay, and absence of postoperative scar, which aligns with the concept of the day-care surgery (12, 29). In this retrospective preliminary study, we compared the perioperative data of vNOTES for ovarian cystectomy in the day-care procedure with those of single-port laparoscopic surgery. We also outlined the advantages and disadvantages of LESS and vNOTES for ovarian cystectomy in the day-care procedure, which could lay a theoretical basis for future vNOTES surgery in a wider area.

In our cohort, there was no significant difference between the vNOTES and LESS groups in terms of intraoperative bleeding volume, operation time, and incidence of postoperative complications, which suggested that ovarian cystectomy *via* vNOTES in the day-care procedure has the same safety threshold as LESS. However, the conversion rate of surgery, which indicates the effectiveness of surgery, was significantly different between the

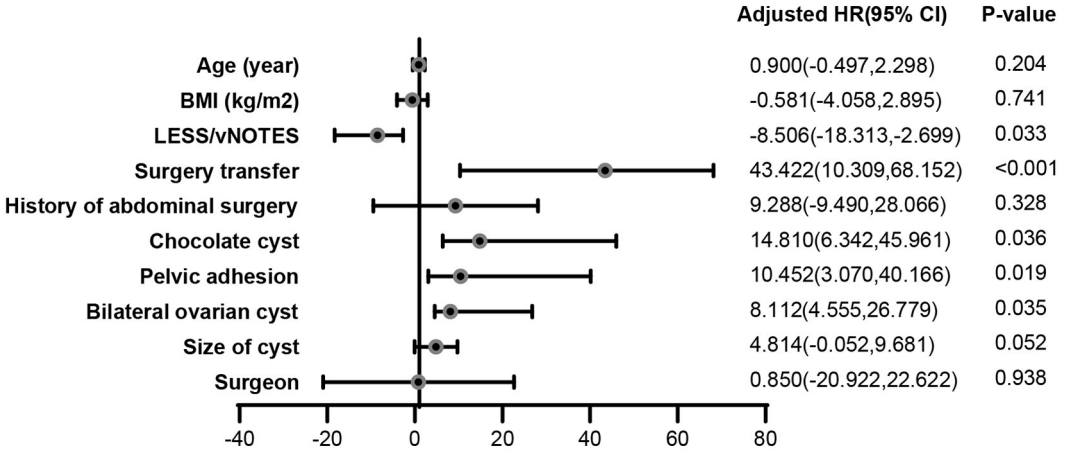

FIGURE 2
Impact of surgical characteristics on operation duration. The multiple linear regression analysis showed that the operation duration was correlated with the operation approach, surgical conversion, chocolate cyst, bilateral cyst, and pelvic adhesion. The surgical conversion, chocolate cyst, bilateral cyst, and pelvic adhesion increased the operation duration by ~43 (95% confidence interval [CI]: 10.309, 68.152, $p < 0.001$), 15 (95% CI: 6.342, 45.961, $p = 0.036$), 10 (95% CI: 3.07, 40.166, $p = 0.019$), and 8 (95% CI: 4.555, 26.779, $p = 0.035$) min, respectively. Interestingly, vNOTES decreased the operation duration by ~8.5 min (95% CI: −18.313, −2.699, $p = 0.033$).

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

Variables	Beta	95% CI	*P*-value	VIF
$R^2 = 0.393$				
Age (year)	−0.066	(−1.453, 1.322)	0.925	1.225
BMI (kg/m^2)	0.072	(−3.318, 3.462)	0.966	1.182
Surgical approach	2.481	(−19.092, 24.054)	0.820	1.602
Surgery transfer	40.031	(25.023, 85.039)	0.027	1.130
History of abdominal surgery	−2.036	(−20.773, 16.702)	0.830	1.200
Chocolate cyst	26.345	(5.013, 47.678)	0.016	1.528
Pelvic adhesion	16.976	(11.236, 22.716)	0.014	1.096
Bilateral ovarian cyst	33.546	(10.276, 76.816)	0.023	1.076
Duration of surgery	1.654	(0.452, 2.856)	<0.001	1.154
Size of cyst	−1.176	(−6.011, 3.660)	0.630	1.152
Surgeon	−3.598	(−11.390, 4.193)	0.361	1.229
Preoperative hemoglobin	−0.028	(−0.558, 0.503)	0.918	1.172

BMI, body mass index.

TABLE 4 Association between postoperative exhaust time and perioperative characteristics.

Variables	Beta	95% CI	*P*-value	VIF
$R^2 = 0.207$				
Age (year)	−14.501	(−31.433, 2.430)	0.092	1.262
BMI (kg/m^2)	−17.237	(−58.756, 24.282)	0.411	1.211
Surgical approach	−85.391	(−60.320, −110.462)	0.012	1.683
Surgery transfer	75.849	(−572.222, 723.92)	0.817	1.184
D&C artificial abortion	55.331	(−50.422, 162.084)	0.301	1.195
History of abdominal surgery	185.128	(−44.659, 414.915)	0.113	1.254
Chocolate cyst	242.828	(−16.322, 501.988)	0.066	1.581
Bilateral ovarian cyst	76.089	(−394.306, 546.484)	0.749	1.210
Pelvic adhesion	−268.048	(−1,345.821, 809.724)	0.622	1.114
Duration of surgery	6.615	(4.768, 8.462)	0.041	1.705
Intraoperative bleeding	−0.209	(−2.931, 2.513)	0.879	1.770
Size of cyst	23.759	(−34.445, 81.962)	0.419	1.162
surgeon	−23.324	(−119.937, 73.288)	0.632	1.289
Pain score (6 h at surgery)	98.552	(−10.880, 207.984)	0.077	1.195
Pain medications	124.715	(−118.924, 368.953)	0.312	1.141
Postoperative complications	239.915	(−362.779, 842.610)	0.431	1.352

BMI, body mass index.

two groups. In the vNOTES group, the surgical conversion rate was higher than that previously reported, which was attributed to the presence of pelvic adhesions. It was difficult to penetrate the pelvic cavity during the surgery. If vNOTES was continued, there is a risk of damage to adjacent organs; thus, it was switched to LESS. During LESS, the posterior wall of the uterus was tightly adhered to the pelvis, sealing the pelvis. Notably, the four patients had chocolate cysts. Due to the timely transit during surgery, no damage to the adjacent organs occurred, and there was no significant difference in the complication rate between the two groups. Therefore, surgeons should conduct a more comprehensive preoperative evaluation on patients who choose to undergo vNOTES, such as those with multiple abdominal surgeries and chocolate cysts (23, 30). Our study also included careful inquiry of dysmenorrhea history and gynecological physical examination to assess uterine activity and tenderness of the surface nodules of the sacral ligaments (24, 31). Moreover, multi-parameter scores for ovarian tumors (such as ESGO/ISUOG/IOTA/ESGE) (32) may be used to evaluate

TABLE 5 Association between 6-h pain score postoperatively and perioperative characteristics.

Variables	Beta	95% CI	*P*-value	VIF
$R^2 = 0.187$				
Age (year)	0.014	(−0.019, 0.047)	0.392	1.292
BMI (kg/m^2)	0.031	(−0.050, 0.111)	0.451	1.212
Surgical approach	−0.902	(− 1.697, −0.008)	0.047	1.588
Surgery transfer	−0.254	(−1.498, 0.989)	0.685	1.170
D & C artificial abortion	−0.103	(−0.307, 0.101)	0.318	1.195
History of abdominal surgery	−0.606	(−1.307, −0.175)	0.012	1.184
Chocolate cyst	−0.190	(−0.697, 0.316)	0.457	1.618
Bilateral ovarian cyst	−0.101	(−1.009, 0.807)	0.825	1.210
Pelvic adhesion	−0.555	(−2.602, 1.491)	0.591	1.078
Duration of surgery	0.002	(−0.004, 0.007)	0.582	1.722
Intraoperative bleeding	0.001	(−0.005, 0.006)	0.829	1.764
Surgeon	−0.113	(−0.298, 0.072)	0.230	1.271
Postoperative exhaust time	−0.004	(−0.029, 0.009)	0.059	1.196
Postoperative complications	−0.738	(−1.869, 0.392)	0.197	1.275

BMI, body mass index.

endometriosis to find severe adhesion before surgery. In addition, vaginal ultrasound can also be used to evaluate the sliding of the uterus on the anterior wall of the rectum in real-time. If severe pelvic adhesion is suspected after evaluations, vNOTES should be avoided (13, 33–35).

The difficulty of vNOTES lies in the establishment process (i.e., the approach and lesion exposure processes). The previous study showed that the operation duration is longer in vNOTES than that in LESS (36–38). However, in this cohort, the vNOTES group had a shorter operating duration, which may be due to the advantage of the visual field. Ovarian cysts, especially teratomas, can be directly assessed *via* the incision of vNOTES; therefore, we consider that vNOTES has an advantage over LESS for ovarian cystectomy. Consistent with the study of Giovanni Buzzaccarini et al., the new target of clinical trials should be to assess the appropriateness of vNOTES in selected populations, with the aim of maximizing the potential benefits of this technique compared to other approaches (39). For obese women and/or for women with large uteri, vNOTES may be particularly effective and safe (40). Moreover, for giant teratoma, specimen retrieval still represents an issue. Vaginal muscles have better ductility, making it easier to take out some large specimens, which may be another advantage of vNOTES (41, 42).

Consistent with previous studies, we also found that the vNOTES group had shorter postoperative exhaust times than that of the LESS group (43, 44), which may be due to the following reasons. First, vNOTES surgery is performed in the pelvis and has little effect on the upper abdomen. Second, before surgery, the small intestine is pushed to the true pelvic level. Therefore, the surgical instruments do not repeatedly contact the intestine, reducing irritation to the intestine. In addition, blood collects between the endoscopic body and the target area due to the upward viewing angle of surgery. Furthermore, the blood is constantly washed during the procedure to ensure clear vision. The postoperative residual blood volume in the abdominal cavity is significantly reduced, chemical irritation and inflammatory factors are reduced, and bowel function recovers faster (45–47).

Moreover, the vNOTES group experienced milder postoperative pain than that of the LESS group (33, 48, 49), which may be due to the vaginal fornix being innervated by visceral nerves and is not sensitive to pain. vNOTES also avoids damaging the abdominal wall, which occurs in LESS due to trocar puncture. Furthermore, the operation time of vNOTES was relatively shorter than that of LESS for ovarian cystectomy, which reduced the stimulation of the diaphragm by abdominal gas. Milder postoperative pain allows patients to get out of bed earlier, which promotes the recovery of gastrointestinal function after surgery, resulting in earlier postoperative exhaust.

Based on the ERAS concept, the day-care procedure requires surgeons to choose a surgical approach that is less damaging to the patient to ensure less postoperative pain, shorter exhaust time, faster recovery, and safer discharge within 24 h. Moreover, scarless surgery is the current trend of gynecological surgery; the vNOTES approach conceals the incision, avoids abdominal damage, and reduces the occurrence of incision hernia, which invokes psychologically minimal invasive effects and allows for the rapid recovery of patients.

The strength of this study is that it specifically studies the population and standard operating procedures for vNOTES. Participants were screened using rigorous inclusion and exclusion criteria. Patients who had other surgeries simultaneously or malignant ovarian cysts were excluded. This study compared the comprehensive perioperative data of the two latest surgical methods, LESS and vNOTES, for ovarian cystectomy, and preliminarily confirmed the effectiveness and safety of vNOTES. In addition, all patients underwent an outpatient review 1-month

postoperatively to assess postoperative recovery and obtain complete clinical data, resulting in a relatively comprehensive study design. Moreover, our hospital has implemented vNOTES since 2018, and there are nearly 2,000 vNOTES cases per year in the last 2 years; thus, all operations were performed according to a standardized surgical procedure.

The pilot study enhances our understanding of LESS and vNOTES for ovarian cystectomy. However, our study had several limitations. First, the sample size of this study was relatively small compared to similar studies of multiport and LESS. Second, this study is retrospective, and vNOTES has been widely used in gynecology for only 5 years. Prospective follow-up of patients after ovarian cystectomy can provide further insight into short- and long-term complications and the potential impact of vNOTES on sexual function, pregnancy, and vaginal delivery. Therefore, a large-scale multicenter study involving more patients and different types of gynecological diseases is needed to further promote the widespread use of vNOTES.

Conclusion

Vaginal natural orifice transluminal endoscopic surgery was equally safe and effective for ovarian cystectomy compared to that of LESS. vNOTES aligned with the concept of the day-care procedure due to its reduced postoperative pain, shorter exhaust time, and absence of scarring. However, surgeons should conduct a comprehensive preoperative evaluation and exclude patients who are suspected to have severe pelvic adhesions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author contributions

YLin, YJ, and XG conducted the study and provided funding resources. XL and AX analyzed the data and drafted the manuscript. HW, YLiu, LW, JL, JY, ZY, JZ, LH, TL, and YLi critically revised the manuscript. All authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Clinical efficacy analysis of laparoscopic uterine artery pre-ligation combined with hysteroscopic curettage in the treatment of type II cesarean scar pregnancy

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Objective: To explore and evaluate the clinical therapeutic effect of laparoscopic uterine artery pre-ligation combined with hysteroscopic curettage in the treatment of type II cesarean scar pregnancy.

Methods: This study analyzed the clinical data of patients with cesarean scar pregnancy (CSP) in the Maternal and Child Health Hospital of Hubei Province from 2018 to 2022. A total of 134 patients with type II cesarean section were enrolled, out of which 78 patients were included in the final analysis. Treatment included either uterine artery embolization (UAE) combined with hysteroscopic curettage ($n = 37$ patients) or laparoscopic uterine artery pre-ligation (LUAP) combined with hysteroscopic curettage ($n = 41$ patients). The demographic and clinical characteristics of these two groups were recorded, and their short- and long-term complications on follow-up were compared. For patients with subsequent fertility requirements, we followed up these patients for 2 years after surgery, then collected and analyzed the compared subsequent pregnancy outcome.

Results: We found no significant discrepancies in the success rate of operation, length of hospital stay, and intraoperative blood loss between the two different operation modes. The cost of LUAP was significantly lower than that of UAE. Furthermore, the incidence of short-term postoperative complications such as fever and pelvic pain was lower in patients treated with LUAP than in those treated with UAE. In terms of long-term postoperative complications, the recovery time for menstruation in the LUAP group (49.81 ± 11.47) was earlier than that in the UAE group (34.90 ± 7.41) ($p < 0.05$). Additionally, 4.9% of patients in the LUAP group had decreased menstrual flow, while 59% of patients in the UAE group had a marked decrease in menstrual flow, and the incidence and severity of intrauterine adhesions were significantly lower in the LUAP group than in the UAE group($p < 0.05$). Consistent with the aforementioned observations, patients treated with LUAP had better postoperative re-pregnancy outcomes than those treated with UAE.

Conclusions: Based on the findings, LUAP combined with hysteroscopic curettage is a safe and effective surgical scheme for the treatment of type II CSPs. In addition, compared with UAE, LUAP is associated with a lower surgical cost,

fewer short and long-term complications, and better postoperative pregnancy outcomes. Thus, it should be widely applied in patients with type II CSPs.

KEYWORDS

cesarean scar pregnancy, uterine artery pre-ligation, uterine artery embolism, intrauterine adhesions, pregnancy outcome

1. Introduction

Cesarean scar pregnancy (CSP) is defined as a gestational embed either on the scar created by a previous cesarean delivery or within the anterior wall myometrial defect or niche (1). In recent years, the incidence of CSP has continued to increase, representing approximately 1.15% of all pregnancies (2). It is associated with serious complications including placenta accreta, pensive placenta previa, uterine rupture, and even maternal death (3). Transvaginal ultrasound has been found to be the most practical and effective method for diagnosing CSP (4). In the "Chinese expert consensus on cesarean scar pregnancy," according to the direction of growth of the gestational sac (GS) and the thickness of the myometer between the GS and the bladder, CSPs have been split into three types. Nonetheless, the pathogenesis of CSP remains unclear, and the optimal management remains uncertain. According to the guidelines of the Society for Maternal-Fetal Medicine, early detection, early treatment, and prompt individualized treatment are recommended, while avoiding expectant therapy and simple curettage. There are various treatment methods for CSP in clinics. These methods can be divided into medically conservative treatments and surgical treatments. Conservative treatment has several disadvantages, including long duration, persistent risk of uterine rupture and bleeding, and the need for additional treatments. Patients undergoing transvaginal lesion resection are mostly treated with methotrexate before the operation, which has the risk of gastrointestinal reactions, liver function damage, bone marrow suppression, and other adverse reactions. Furthermore, the surgical procedure is difficult, requires a highly skilled surgeon, and has few clinical applications. In addition, high-intensity focused ultrasound and double-balloon compression of the uterine cavity have been mentioned in the literature, but these procedures are rarely used, and their surgical effect and safety are difficult to evaluate. Laparoscopic lesionectomy is the preferred surgical method; its safety and efficacy have been confirmed, with a success rate of up to 85%, especially for patients with pregnancy needs. With this method, cesarean section scar repair can be performed (5). All of the above-mentioned surgical procedures have potential risks such as bleeding, uterine rupture, uterine arteriovenous fistula, and even hysterectomy (6). However, regardless of the method applied, multiple treatment measures for CSP may cause massive intraoperative blood loss because of the highly vascular nature of the site of pregnancy (7). Consequently, uterine artery embolization (UAE) is an option used in clinical practice to prevent intraoperative blood loss. However, UAE carries a risk of post-embolization syndrome, including complications such as fever, ovarian function damage, irregular vaginal bleeding, lower abdominal pain, and intrauterine adhesions (8). To reduce the incidence of post-embolization syndrome, we adopted the laparoscopic uterine artery pre-ligation (LUAP) procedure to temporarily block the blood supply to the uterus. This procedure is less invasive than UAE. It uses only sutures and does not require the use of special equipment. In addition, LUAP blocks the blood flow for only a few minutes, thereby potentially reducing the incidence of postoperative complications due to interrupted blood supply. It also ensures the reduction of massive intraoperative bleeding. Hence, we used the LUAP approach for the first time in the treatment of type II cesarean scar pregnancy and evaluated its safety and efficacy.

2. Materials and methods

2.1. Patient selection and data collection

The ethics committee of Hubei Maternal and Child Health Hospital sanctioned the retrospective study. All patients ruled out contraindications before the operation; they were fully informed of the condition and the possible risks of the operation and signed the operation notification form. Data from 134 patients with type II CSP treated in the hospital during 2018–2022 were obtained and collected from the hospital's record room. The collected information comprised demographic data, medical history, prior experience of cesarean section, abortion history, and intraoperative indicators. The patients were followed up via regular telephone contact for 24 months; short- and long-term complications and postoperative pregnancy outcomes were documented following their discharge. The flow diagram of the study is shown in Figure 1.

2.2. Surgery method

In the LUAP group, the retroperitoneum was opened, and bilateral ureters were identified. Approximately 1.5 cm of the initial end of the uterine artery was free, and bilateral uterine arteries were relegated with a slipknot with 1-0 absorbable thread (Figure 2). Then, the uterine arteries on both sides were blocked temporarily. The peritoneum was separated at the lower part of the uterus where the bladder is inverted, and a slight bulge was observed in the scar of the lower uterine segment. Subsequently, curettage was performed transvaginally under laparoscopic monitoring. The uterine cavity and uterine incision diverticulum were examined by hysteroscopy. The 1-0 silk thread was taken out under a laparoscope, and the color of the uterus was observed. The time from uterine artery ligation to

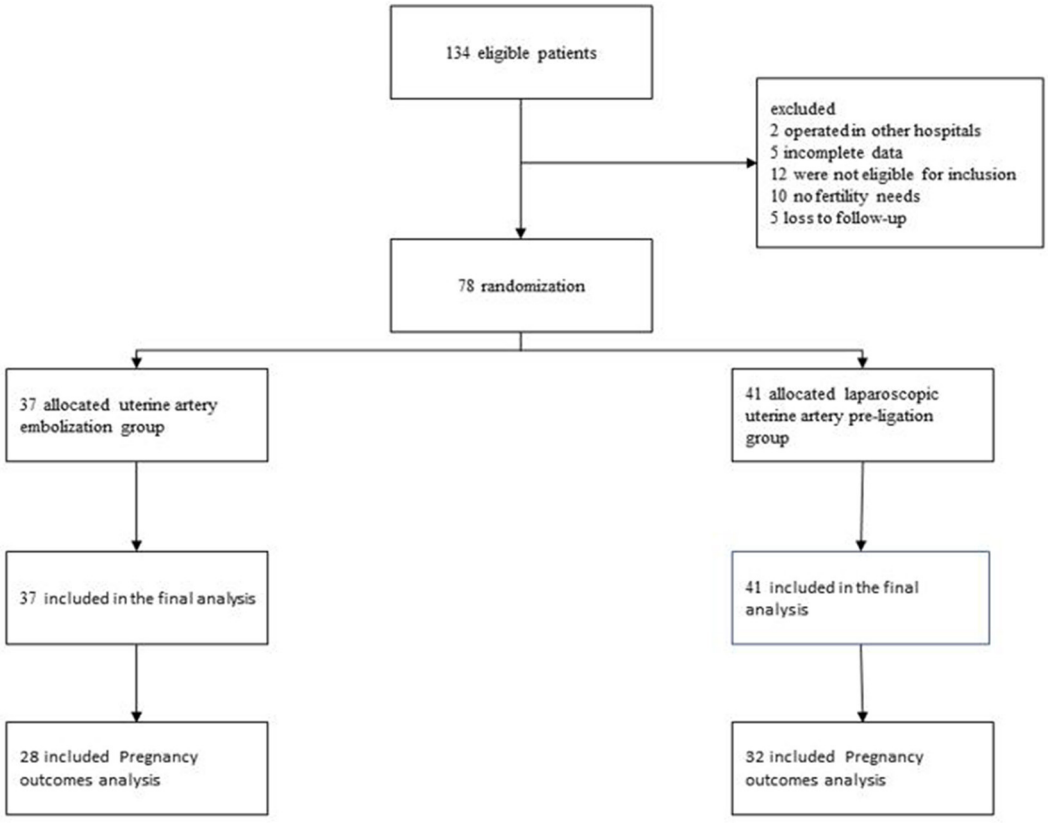

FIGURE 1
Flow diagram of study.

blood flow recovery was approximately 10 min. All the tissues were scraped out of the uterine cavity after the operation and sent to the pathology department to exclude hydatidiform moles.

In the LUAP group, the right transfemoral approach was selected for artery access. The uterine artery was selectively catheterized with a 5F-Y ashier catheter and embolized with gelatin sponge particles of sizes 560–700 um. Angiograms were conducted to confirm whether the occlusion of blood flow was complete. Hysteroscopic curettage was performed 24 h after UAE to remove pregnant tissues. All the tissues were scraped out of the uterine cavity after the operation and sent to the pathology department to exclude hydatidiform moles.

2.3. Patient follow-up

We collected the basic information of patients after surgery (including age, clinical symptoms, the number of induced abortions, days of menorrhea, the number of cesarean sections, the diameter of the gestational sac, and surgical cost). We then followed up on the short-term postoperative complications, including the evaluation of procedural success rate, monitoring intraoperative bleeding, and measuring hospital stay duration. We documented the short-term complications after surgery, such as fever and pain. We conducted outpatient follow-up to calculate the recovery time of the first menstruation, menstrual volume alteration, and the duration of pain in the pelvic area. Two months later, the patients were reexamined by hysteroscopy, and the status of intrauterine adhesion was evaluated [the score of intrauterine adhesion was based on the American Reproductive Society (AFS) score in 1988]. Finally, patients who had pregnancy needs were followed up for 24 months to observe their pregnancy outcomes (including delivery conditions, preterm birth, abortion, re-scarred pregnancy, and placental abnormalities).

2.4. Statistical analysis

The mean standard deviation ($\pm$s) is used to express the measurement data. Basic information and clinical characteristics of patients were tested by performing a two-sample t-test with normal distribution. Non-parametric tests were performed when the data were skewed and non-normally distributed. The X^2 test was performed to compare the count data, and Fisher's exact test was performed when $n < 5$. Statistical analysis was performed using SPSS 26.0. Statistical tests performed were two-sided, and $p < 0.05$ was considered significantly different.

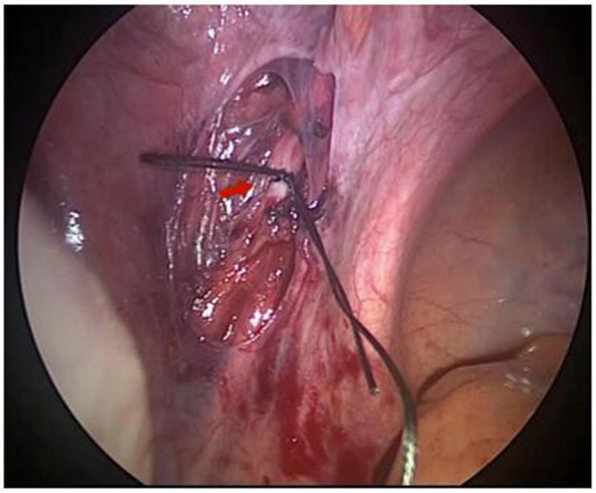

FIGURE 2
The uterine artery was preligated laparoscopically and the red arrow indicates the uterine artery.

TABLE 1 Comparison of the baseline characteristics of CSP patients.

Groups	UAV ($n = 37$)	LUAP ($n = 41$)	X^2	p-value
Age (y)	32.73 ± 3.78	32.46 ± 4.84	0.278	0.781
Clinical symptoms	45.9% (17/37)	39% (16/41)	0.382	0.647
Number of induced abortions	1.68 ± 1.13	1.49 ± 1.26	/	0.317
Number of cesarean sections	1.41 ± 0.55	1.35 ± 0.54	/	0.443
Days of menopause (d)	51.90 ± 15.78	45.54 ± 9.92	1.355	0.179
Diameter of gestational sac (cm)	2.85 ± 1.13	3.27 ± 1.33	1.498	0.138
surgical cost ($)	16,213.49 ± 2,502.94	19,388.49 ± 8,706.60	2.140	0.038

3. Results

3.1. Basic information and characteristics of patients

The study included 134 patients with type II CSP, out of which 78 patients were included in the final analysis. Among them, 31 patients experienced minimal vaginal bleeding before the operation, two patients had vaginal bleeding and abdominal pain before the operation, and the remaining had no clinical symptoms and were diagnosed by transvaginal ultrasound. Table 1 displays the baseline clinical characteristics of CSP. Age, clinical symptoms, number of induced abortions, days of menorrhea, number of cesarean sections, or the diameter of the gestational sac did not significantly differ between the two groups. However, the operational expenses of LUAP were considerably lower than those of UAE, and this difference was statistically significant.

3.2. Clinical features and short-term complications

No patients were missed during the follow-up evaluation. The operation of patients in both groups was smooth without serious complications such as a massive hemorrhage or ureteral injury. The surgical success rate of patients in both groups was 100%. The two groups did not show any notable distinction in terms of the length of hospital stay, the amount of blood loss during surgery, and the uterine perforation rate. Out of the 37 patients who underwent UAE, three patients experienced mild fever following the procedure. Furthermore, 25 patients experienced moderate to severe pain after their surgery. In the long-term follow-up, 17 patients had pelvic pain for more than 2 weeks, and 6 patients had pelvic pain for 6 months without obvious relief. In the LUAP group, only one patient experienced low fever, and none experienced long-term pelvic pain (Table 2). In addition, in the LUAP group, postoperative pain disappeared within 1 day without the requirement of any intervention. However, the duration of pain was longer in the UAE group, with most patients requiring nonsteroidal anti-inflammatory drugs and even opioids for pain relief, than in the LUAP group. In conclusion, the incidence and severity of short-term complications were lower in the LUAP group than in the UAE group.

3.3. Long-term postoperative complications

The comparison of long-term postoperative complications between the two groups is presented in Table 3. The first appearance of menstruation after the operation occurred earlier for patients in the LUAP group than for patients in the UAE group. Furthermore, the two groups differed significantly in terms of changes in menstrual volume, duration of pelvic pain, and intrauterine adhesion score. In the LUAP group, the menstrual volume of two patients decreased by 1/3 compared with the preoperative volume, and one patient experienced postoperative pelvic pain that receded within 1 day. Throughout the 6-month monitoring period, mild intrauterine adhesions were observed only in two patients. Contrarily, the menstrual volume of 22 patients in the UAE group decreased by 1/3 compared with the preoperative volume. More importantly, 23 patients experienced chronic pelvic pain, six of whom had persistent chronic pelvic pain without relief. Furthermore, 21 patients had moderate to severe intrauterine adhesions, of whom five patients had to undergo surgical treatment for severe intrauterine adhesions. Thus, compared with UAE, LUAP demonstrated significant advantages in restoring menstruation and reducing the incidence of postoperative pelvic pain and intrauterine adhesions.

TABLE 2 Clinical features and short-term complications.

Variables		UAV ($n = 37$)	LUAP ($n = 41$)	X^2	p-value
Success rate (%)		100% (37/37)	100% (41/41)	0.278	1.000
Duration of hospital stay (d)		7.29 ± 0.93	7.22 ± 0.89	0.371	0.712
Intraoperative blood loss (ml)		22.29 ± 5.72	21.95 ± 9.21	1.97	0.854
Perforation of the uterus (n)		8.1% (3/37)	2.4%(1/41)	/	0.353
Complication rate (%)		75.6% (28/37)	4.8%(2/41)	41.187	0.000
Fever (n)		3	1	/	0.034
Postoperative pain (n)		25	1	37.123	0.000
Postoperative pain score	<4	2	41	37.123	0.000
	5–6	13	0		
	>7	10	0		

Postoperative pain: using a numerical rating scale (NRS), 4 or less was defined as mild pain (pain did not affect sleep), 4–6 was defined as moderate pain, and 7 or more was defined as severe pain (could not sleep due to pain or woke up in pain).

TABLE 3 Long-term postoperative complications.

Variables		UAV ($n = 37$)	LUAP ($n = 41$)	X^2	p-value
Time of first menstrual resumption		34.90 ± 7.41	49.81 ± 11.47	6.737	<0.001
Changes in menstrual volume	Decrease 1/3 Decrease 1/2	22 (22/37) 10 (10/37)	2 (2/41) 0 (0/41)	52.677	0.000
Duration of pelvic pain	<1 Day	2 (2/37)	1 (1/41)	31.123	0.000
	>2 week	17 (17/37)	0 (0/41)		
	>6 months	6 (6/37)	0 (0/41)		
Intrauterine adhesions score	1~4	2 (2/32)	2 (2/41)	29.304	0.000
	5~8	12 (12/32)	0 (0/41)		
	9~12	9 (9/32)	0 (0/41)		

Uterine adhesions were scored with reference to the 1988 American Fertility Society (AFS) score: 1–4 for mild adhesions, 5–8 for moderate adhesions, and 9–12 for severe adhesions.

3.4. Postoperative pregnancy outcome

We followed up two groups of patients with pregnancy intentions for up to 24 months, as presented in Table 4. We found that the pregnancy rate was comparable in both groups, without any notable differences in the outcomes. In the UAE group, 37 patients had pregnancy intentions, 28 of whom had successful pregnancies. In the LUAP group, 37 patients had pregnancy intentions, 32 of whom had successful pregnancies. The rate of CSP patients who became pregnant again after undergoing UAE treatment was 75.6%, and that of CSP patients who underwent LUAE treatment was 78%. However, the rate of CSP in the UAE group was 4.571 times that in the LUAP group. In the LUAP group, there were 32 cases of successful pregnancies, including 23 full-term birth cases (cesarean section), two preterm birth cases, two pregnancy state cases, and two spontaneous abortion cases. All 28 cases in the UAV group were CSPs (6 cases were placental abnormalities), 11 cases were full-term deliveries, four cases were premature deliveries, and five cases were spontaneous abortions.

The results revealed that the two groups had no significant differences in the rate of preterm birth, mid-pregnancy, and spontaneous abortion. In addition, six cases of placental abnormalities occurred in the UAE group, and the difference was statistically significant when compared with the LUAP group. Of the six cases, there were two cases of placenta accrete, and four cases of placenta previa. All the cases had different degrees of postpartum hemorrhage, and two patients underwent blood transfusion. Furthermore, two out of four preterm pregnancies were terminated early at approximately 35 and 31 weeks of gestation, respectively, due to placental abnormalities. There was no uterine rupture in the two groups. Based on the above results, the pregnancy outcome of patients in the LUAP group was better than that in the UAE group.

4. Discussion

First reported in 1978 by Larsen and Solomon (9), CSP is a specific type of ectopic pregnancy. In the last decade, the detection rate of CSP has gradually increased with the increase in the number of cesarean sections and improvement in the level of ultrasound diagnosis (10). However, a full understanding of the

TABLE 4 Surgical pregnancy outcomes.

Postoperative pregnancy outcome	UAV (n = 37)	LUAP (n = 41)	X^2	p-value
Number of pregnancies	28 (28/37)	32 (32/41)	0.062	0.804
Full-term delivery	11 (11/28)	23 (23/32)	6.459	0.018
Premature birth	4 (4/28)	2 (2/32)	/	0.396[a]
Mid-pregnancy	0 (0/28)	2 (0/32)	/	0.494[a]
Spontaneous abortion	5 (5/28)	3 (3/32)	/	0.454[a]
Re-scarred pregnancy	8 (8/28)	2 (2/32)	/	0.036[a]
Placental abnormalities	6 (6/28)	0 (0/32)	/	0.008[a]

[a]Fisher's precision probability test.

pathogenesis of CSP is lacking. Some studies believe defects in the scar tissue following a cesarean section to be the direct cause. Owing to poor healing of the muscular layer and endometrium at the uterine incision, a sinus or fissure is formed, and in severe cases, even a diverticulum of the uterine incision is formed (11). Some studies reported that the occurrence of CSP is also related to the decrease of local blood supply in the uterine incision, trophoblast invasion of the hypoxic environment, and the chemotactic effect of inflammatory factors. All of these factors work together to induce the implantation of fertilized eggs and implantation in the cesarean section scar (12).

The symptoms and indications of CSP lack specificity. Darwish et al. reported that 47.6% of the patients in their study exhibited no symptoms, 33.3% of the patients experienced vaginal bleeding, and 19.1% experienced abdominal pain along with vaginal bleeding (13). In our study, of the 78 type II CSP patients, 39.7% reported experiencing minor vaginal bleeding, and 10.2% reported experiencing lower abdominal pain along with vaginal bleeding. The remaining patients exhibited no symptoms and were diagnosed by ultrasound examination. If the first pregnancy ultrasound is performed later, the diagnosis may be delayed due to asymptomatic CSP (14). Once the diagnosis is delayed, a CSP can easily cause placenta implantation, which may result in massive hemorrhage and even hemorrhagic shock. Therefore, optimal prognosis can only be achieved through early diagnosis and treatment (15).

To the best of our knowledge, no standardized treatment for CSP has been established. Available therapies include medical interventions, surgery, or a combination of the two. In recent years, experience with the management of CSP has increased, and more patients with CSP are treated by minimally invasive surgery (16). Nonetheless, the optimal surgical options, their efficacy, and the correlated risk factors have yet to be conclusively determined. According to some previous studies, the treatment of CSP with UAE before curettage could help reduce the incidence of massive intraoperative bleeding (17). However, UAE may potentially lead to ovarian function and urinary system damage, causing intrauterine adhesions and even resulting in sepsis and embolic syndrome (18). Considering the above risks, obstetricians and gynecologists have been attempting to find new treatments for CSP. In recent years, laparoscopic resection of lesions has been applied to the treatment of CSP, and its safety and effectiveness have been confirmed by several studies (19, 20). However, direct resection of the lesion under laparoscopy increases the risk of massive intraoperative bleeding. On this basis, in our operation, we added the method of uterine artery pre-ligation to avoid massive intraoperative and postoperative bleeding.

In this study, the efficacy, safety, postoperative complications, and pregnancy outcomes of LUAP in the treatment of type II CSP were evaluated. We compared it with UAE because UAE has been routinely used in the treatment of CSP to prevent massive intraoperative bleeding. We found that both approaches exhibited similar surgical success rates, lengths of hospital stays, rates of postoperative pregnancy, and intraoperative blood losses. The rate of short-term complications in the UAE group was higher than that in the LUAP group (75.6 % vs. 4.8%). Moreover, the total cost of treatment in the UAE group was remarkably higher than that in the LUAP group. After 24 months of follow-up, the recovery time for menstruation in the LUAP group was earlier than that in the LUAP group, and there was no visible reduction in menstrual volume after surgery. In addition, compared with patients in the UAE group, patients in the LUAP group experienced no long-term chronic pelvic pain, and the incidences of intrauterine adhesions were fewer and less severe. Furthermore, pregnancy outcome after surgery was superior in the LUAP group compared with the UAE group.

In the treatment of LUAP, we performed pre-ligation of the uterine artery before hysteroscopic curettage, which can result in a marked decrease in blood loss during surgery in patients. The removal of scar tissues under direct laparoscopic vision can ensure the complete excision of CSP lesions, significantly reducing the risk of scar pregnancy and placental abnormalities in subsequent pregnancies. Pre-ligation of the uterine artery for only a few minutes of blood flow occlusion can minimize the negative impact on the direction of the uterine and ovarian vessels and drastically reduce the patient's postoperative complications. Compared with UAE, LUAP treatment is a minimally invasive and comfortable treatment modality without the risk of lower limb immobilization.

In this study, there was no significant difference in intraoperative blood loss between the two groups. In the UAE group, three patients experienced mild fever following the procedure. We hypothesized that this fever could be attributed to an inflammatory reaction *in vivo* triggered by the embolization material, specifically the gelatin sponge used during the procedure. Although intraoperative blood flow occlusion with uterine artery pre-litigation was limited to a few minutes, minimizing the impact on surrounding tissues and reducing the incidence of postoperative complications in patients are necessary. Compared with UAE, LUAP was advantageous in diminishing postoperative complications.

Ovarian insufficiency, intrauterine adhesions, and amenorrhea are potential late complications of UAE (21). In our study, the UAE group had a longer recovery time for menstruation than the

LUAP group and a marked reduction in menstrual volume. In the UAE group, 23 patients experienced intrauterine adhesions of varying degrees, and five patients underwent hysteroscopic surgery due to severe intrauterine adhesions. In contrast, only two patients in the LUAP group experienced mild intrauterine adhesion, and most patients had no intrauterine adhesions. Although patients had a history of curettage, which could also cause intrauterine adhesions, no intrauterine adhesions were found in either group preoperatively, and there was no difference in the number of induced abortions between the two groups. Thus, the potential long-term negative impacts of LUAP were considerably low compared with UAE.

We paid attention to not only the occurrence of severe complications but also the preservation of patients' fertility. A study involving 398 pregnancies following UAE reported the following risks: malpresentation (17%), cesarean delivery (58%), preterm delivery (28%), small for gestational age (7%), and postpartum hemorrhage (13%) (21). A retrospective analysis of pregnancy outcomes after uterine fibroid embolization suggested a higher risk of miscarriage and a significant increase in postpartum hemorrhage in post-UAE pregnancies (22). In our study, we removed the scar tissue under direct laparoscopic vision after pre-ligation of the uterine artery, which could ensure complete resection of the CSP lesion. Uterine scar repair is performed when necessary, which is important for patients with fertility requirements. We found that both LUAP and UAE can achieve a satisfactory natural pregnancy rate, but the rate of cesarean scar is higher in re-pregnancy after UAE, which increases the risk of scar pregnancy and placental abnormalities such as placenta previa and accreta. Placental abnormalities increase the incidence of preterm birth, and preterm infants often have a worse prognosis than full-term infants. Abnormal placentas are prone to complications with postpartum hemorrhage, which increases the risk of hysterectomy and severely affects women's physical and mental health.

The strength of this study is that it is a comprehensive retrospective cohort study in which we statistically analyzed the clinical efficacy, safety, and pregnancy outcomes of LUAP in patients with type II CSP. We have extensive experience in the treatment of CSP with LUAP combined with hysteroscopic curettage. However, our study also has some limitations. In the follow-up of postoperative complications, we used telephone follow-up, and the conclusions drawn were subjective to some extent. The sample size was small, and some patients are still in long-term follow-up. In addition, patients' ovarian function was not evaluated, and we will conduct prospective studies in the future.

Thus, LUAP was associated with lower surgical costs and lesser equipment requirements than UAE. Above all, it was associated with faster postoperative patient recovery, fewer postoperative complications, and better pregnancy outcomes than UAE for the treatment of type II CSP. Based on this, LUAP should be popularized and used in type II CSP. This surgical approach can, perhaps, be used as an alternative to UAE.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

DT performed data management, project management, and writing of the original draft. HG explored the surgical protocol for the study. YL participated in the literature design and validated the analytical methods. TM and XS contributed to the clinical data collection. JS provided the documentation design of the study and revised the manuscript. All authors discussed the results and contributed to the final manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Minimizing blood loss in laparoscopic myomectomy with temporary occlusion of the hypogastric artery

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Introduction: Uterine leiomyomas are common benign pelvic tumors. Currently, laparoscopic myomectomy (LM) is the preferred treatment option for women in the fertile age group with symptomatic myomas. The authors hypothesize that combining LM with a bilateral temporary occlusion of the hypogastric artery (TOHA) using vascular clips minimizes uterine blood flow during surgery and can significantly reduce surgery-associated blood loss.

Materials and methods: This single-center, prospective randomized study was conducted at the Department of Obstetrics and Gynecology, Municipal Emergency Clinical Hospital Timisoara, Romania. Patients aged between 18 and 49 who preferred laparoscopic myomectomy and wished to preserve fertility were included, provided they had intramural uterine leiomyomas larger than 4 cm in diameter that deformed the uterine cavity. The study analyzed data from 60 laparoscopic myomectomies performed by a single surgeon between January 2018 and December 2020. Patients were randomly assigned to either: "LM + TOHA" group (29 patients), and "LM" group (31 patients). The study's main objective was to evaluate the impact of TOHA on perioperative blood loss, expressed as mean differences in Hb (delta Hb).

Results: Delta Hb was statistically lower in the "LM + TOHA" group compared to "LM" group, with mean ± standard (min–max): 1.68 ± 0.67 (0.39–3.99) vs. 2.63 ± 1.06 (0.83–4.92) g/dL, respectively ($p < 0.001$). There was a statistically significant higher need for postoperative iron perfusion in the "LM" group, specifically 0 vs. 12 patients ($p < 0.001$), and lower postoperative anemia in "LM + TOHA" group ($p < 0.001$). Necessary artery clipping time was 10.62 ± 2.47 (7–15) minutes, with no significant impact on overall operative time: 110.2 ± 13.65 vs. 106.3 ± 16.48 ($p = 0.21$). There was no difference in the length of hospitalization or 12-month post-intervention fertility.

Discussion: Performing bilateral TOHA prior to laparoscopic myomectomy has proven to be a valuable technique in reducing surgery-associated blood loss, while minimizing complications during surgery, with no significant increase in the overall operative time.

Clinical trial registration: ISRCTN registry, (www.isrctn.com), identifier ISRCTN66897343.

KEYWORDS

blood loss, temporary occlusion of the hypogastric artery (TOHA), clipping, operative time, laparoscopic myomectomy, uterine leiomyoma, uterine myomectomy

1. Introduction

Uterine leiomyomas, also referred to as fibroids or myomas in the literature, are the most frequently occurring solid benign pelvic tumors in women (1–3). It has been estimated that among Caucasian women in the United States, lifetime incidence of uterine leiomyomas is as high as 40% by the age of 35, and exceeds 70% among women aged 50 and above (4). Reported prevalence of diagnosed uterine fibroids among five European countries ranged between 11.7% in France to 23.6% in Italy (4).

Leiomyomas, frequently asymptomatic and often diagnosed incidentally, can result in complications given by the compression or displacement of adjacent pelvic organs such as pelvic pressure, pain, increased urinary frequency, constipation, as well as local implications, such as irregular or excessive menstrual bleeding, recurrent pregnancy loss, and even infertility (5).

Laparoscopic myomectomy (LM) is a minimally invasive and fertility-preserving procedure which has several advantages over laparotomy, such as reduced postoperative pain, a shortened hospital stay and recovery time, and a decreased risk of adhesion formation (6, 7). Therefore, it is the current preferred method for performing a myomectomy (8–10).

Surgery that involves the uterus and myomas can lead to substantial blood loss because of their rich vascularity, irrespective of surgical approach (11). To address this concern and minimize intraoperative bleeding, several techniques have been developed over time. These can be either: (a) non-surgical, such as intramyometrial injections with vasopressin, or the use of misoprostol or tranexamic acid; or (b) surgical, including the use of a pericervical tourniquet, permanent uterine artery occlusion via bipolar coagulation, uterine artery embolization, and a recent combination approach that involves LM and a temporary uterine artery occlusion (TUAO) with sutures or clips (12–14). This article introduces a new technique of LM combined with temporary occlusion of the hypogastric artery (TOHA). This technique involves the bilateral clipping of the anterior trunk of the hypogastric artery (also known as the internal iliac artery) cranially to uterine artery emergence. Authors underline the paucity in the literature of this specific approach for temporary clipping during LM.

This study aims to investigate the effectiveness of TOHA in reducing surgery-associated blood loss during laparoscopic myomectomy.

2. Materials and methods

2.1. Study design and data collection

This research article was designed as a single-center, prospective randomized study, following the Consolidated Standards of Reporting Trials (CONSORT) guidelines (15, 16).

To evaluate the impact of performing a concomitant temporary occlusion of the hypogastric artery during LM, 62 patients were randomly allocated to one of two groups: 31 patients who underwent LM and TOHA with clipping ("LM + TOHA" group), and 31 patients who benefited from standard LM without clipping ("LM" group). After randomization, two patients from the LM + TOHA group did not undergo surgery and were eliminated from the study: one patient had decompensated heart failure diagnosed before surgery, and another had deep infiltrating endometriosis with limited access to the left side wall. Follow-ups were scheduled at two weeks, six weeks, six months, and one year after surgery.

This study was reviewed and approved by the Human Ethical Committee of the University of Medicine and Pharmacy "Victor Babes," Timişoara, Romania (Nr 44/10.12.2018). It was conducted between the 1st of January 2018 and the 31st of December 2020 at the Municipal Emergency Clinical Hospital, Timisoara, Romania.

2.2. Patient selection and characteristics

The main indication for myomectomy was abnormal uterine bleeding. Inclusion criteria were: (a) patients aged between 18 and 49; (b) patient preference for laparoscopic myomectomy and their desire to preserve fertility; and (c) patients who had intramural uterine leiomyomas greater than 4 cm in diameter, which also deformed the uterine cavity.

Exclusion criteria were as follows: (a) patients who did not agree to the enrollment or did not pass inclusion criteria (such as: age over 50, no preference for fertility preservation, personal option for hysterectomy); (b) cases with other types of myomas (such as submucosal or subserosal location), or intramural myomas under 4 cm which did not have an impact on the uterine cavity; and (c) cases suspected of malignancy. Aforementioned criteria were represented in the CONSORT flowchart (Figure 1).

Necessary sample size was determined based on the primary objective of comparing blood loss and surgery duration (namely a *t*-test for independent samples). The analysis used a power of 0.9, alpha level of 0.05, two-sided alternative, and Cohen's d, effect size of 0.9. The calculation indicated a minimum of 27 patients in each group. To account for potential dropouts, a 15% coefficient was applied, resulting in a final required sample size of 31 patients in each group. Randomization was single-blind and performed with the R package "blockrand" v. 1.5. Two TOHA patients were lost after randomization to the treatment groups. As this was a surgical investigation, on-treatment analysis of data was conducted, so the final groups were of unequal sizes, but required statistical power was maintained.

Preoperatively, a diagnostic ultrasound examination was performed in order to assess the most suitable surgical approach.

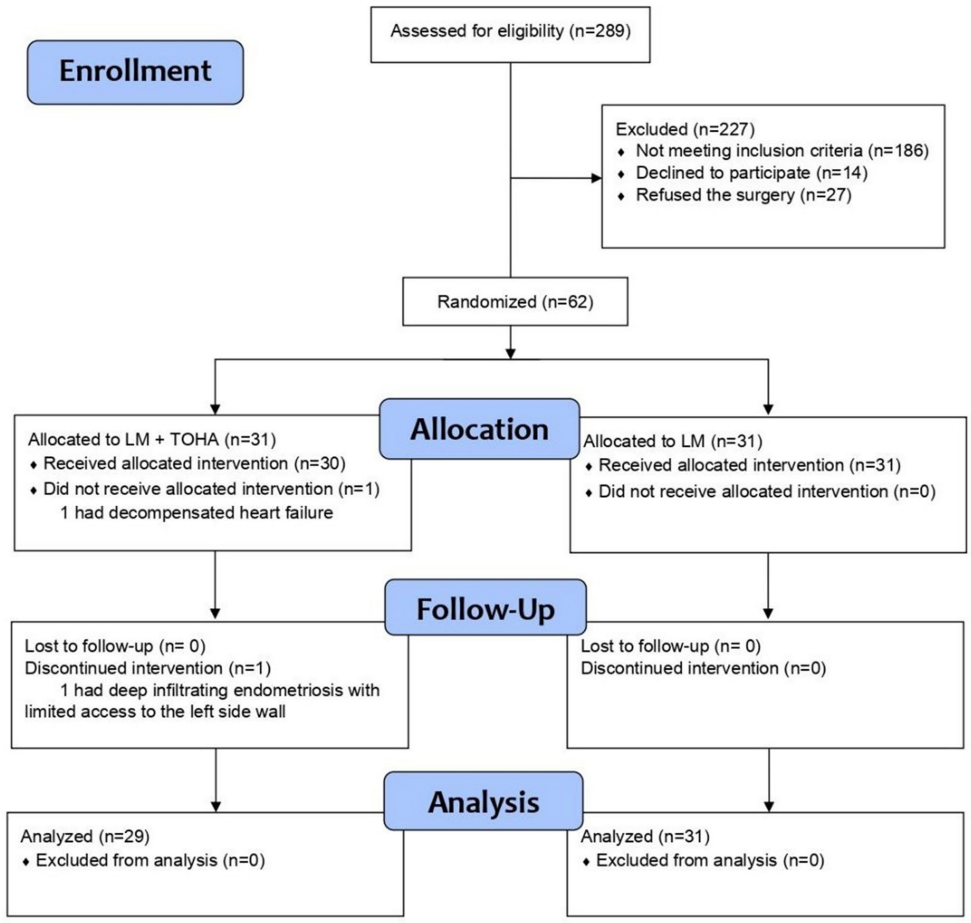

FIGURE 1
Diagram of patients who underwent laparoscopic myomectomy, according to CONSORT 2010.

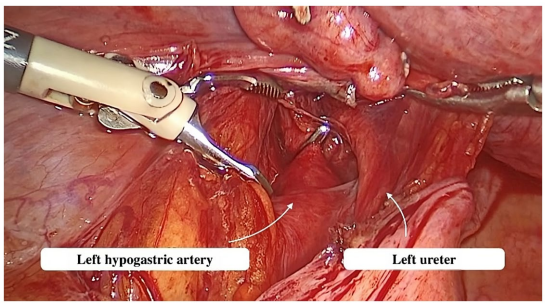

FIGURE 2
Dissection of the hypogastric artery.

2.3. TOHA and LM procedures

All surgical procedures were performed by a single and highly proficient surgeon with over a decade of experience in laparoscopic surgery. Prior to the surgery, neither Gonadotropin-Releasing Hormone (GnRH) agonists nor any intra-operative hemostatic drugs, such as vasopressin injection, were employed. Before initiating surgical procedures, general anesthesia was induced concomitantly with orotracheal intubation.

Abdominal access was obtained via a direct trocar entry technique. CO2 insufflation was utilized to create a pneumoperitoneum with a low intra-abdominal pressure of up to 12 mmHg. A single 10 mm trocar was positioned on the median line, 8 cm away from the umbilicus, while two 5 mm trocars were situated on each side of the lower abdomen. The patient was then reclined in a Trendelenburg position. The parietal peritoneum was incised below the lumbo-ovarian ligament. The ureter and anterior trunk of the hypogastric artery were identified in the area where these two structures run parallel (Figure 2). The ureter and hypogastric artery were identified using blunt dissection. A metallic clip was then placed on the anterior trunk of the hypogastric artery, cranially to the uterine artery emergence.

The uterine wall was incised, and the myoma/s were located and then removed using traction and countertraction maneuvers. Next, in-bag morcellation was used to remove the leiomyoma/s. The uterine wall was sutured with a double-layer stitch, utilizing a 29 mm, 3/8 circle needle, and Vicryl 2.0 thread. Once the uterine wall had been closed, hemostatic clips were gently removed by traction using atraumatic Johan fenestrated forceps.

TABLE 1 Clinical data in the two study groups of laparoscopic myomectomy (LM): with and without transient occlusion of hypogastric artery (TOHA).

Variable	LM + TOHA $N = 29$	LM $N = 31$	p-value
Age (years) [a]	34.5 ± 5.2 (26–44)	36.5 ± 5.2 (28–46)	0.136
BMI (kg/m^2) [a]	26.5 ± 4.2 (17.1–33.2)	27.0 ± 3.7 (18.9–33.2)	0.681
Symptoms			
Infertility [b]	18 (62.1%)	8 (25.8%)	0.005**
Menstrual disorder / Meno-metrorrhagia [b]	13 (44.8%)	22 (71.0%)	0.04*
Pain [b]	9 (31.0%)	21 (67.7%)	0.04*
Nulliparous [b]	18 (62.1%)	9 (29%)	0.01*
Number of leiomyomas [c]	1.31 ± 0.66 (1–3)	1.32 ± 1.14 (1–7)	0.445
Number of leiomyomas/patient [d]			0.483
1	23 (79.3%)	27 (87.1%)	
2	3 (10.3%)	2 (6.5%)	
3	3 (10.3%)	1 (3.2%)	
4	0	0	
5	0	0	
6	0	0	
7	0	1 (3.2%)	
Size of the largest leiomyoma (cm) [c]	7.21 ± 1.66 (5–12)	7.42 ± 2.1 (4–12)	0.77
Location of dominant leiomyoma [d]	38 (100%)	41 (100%)	0.972
Anterior wall	13 (34.2%)	11 (26.8%)	
Posterior wall	15 (39.5%)	18 (43.9%)	
Fundical	10 (26.3%)	11 (26.8%)	
Lateral (intraligamentary)	0	1 (2.4%)	

Data presented as mean ± standard deviation (min-max) for numerical variables, or n (%) for categorical variables. [a] t-test for independent samples; [b] asymptotic Chi-square test; [c] non-parametric Mann–Whitney U-test; [d] Chi-square, Monte Carlo simulation (10,000 samples). Statistical significance: *$p < 0.05$; **$p < 0.01$. LM, laparoscopic myomectomy; TOHA, transient occlusion of the hypogastric artery; BMI, body mass index.

TABLE 2 General surgical data in the two study groups of laparoscopic myomectomy (LM): with and without transient occlusion of hypogastric artery (TOHA).

Variable	LM + TOHA $N = 29$	LM $N = 31$	p-value
History of abdominal surgery [d]	3 (10.3%)	2 (6.5%)	0.256
Conversion to laparotomy [e]	1 (3.4%)	1 (3.2%)	0.962
Pre-operative Hb level (g/dL) [a]	13.23 ± 1.1 (9.5–14.8)	12.23 ± 1.72 (8.78–15.02)	0.01*
Pre-operative anemia [d]	1 (3.4%)	0	0.3
Pre-operative transfusion for severe anemia [d]	1 (3.4%)	0	0.3
Post-operative Hb level (g/dL) [a]	11.56 ± 0.94 (9.11–13.2)	9.60 ± 1.79 (6.01–12.5)	<0.001**
Operative time (min) [c]	110.2 ± 13.65 (90–135)	106.3 ± 16.48 (90–140)	0.21
Clipping length (min)	10.62 ± 2.47 (7–15)	NA	NA
Hospital stay after surgery (days) [c]	2.1 ± 0.6 (1–3)	2.4 ± 0.8 (1–4)	0.076
Myoma removal technique			
Morcellation [d]	28 (96.6%)	25 (80.6%)	0.104
Minilaparotomy [d]	1 (3.4%)	6 (19.4%)	0.104

Data presented as mean ± standard deviation (min-max) for numerical variables, or n (%) for categorical variables. [a] t-test for independent samples; [b] asymptotic Chi-square test; [c] non-parametric Mann–Whitney U-test; [d] Chi-square, Monte Carlo simulation (10,000 samples); [e] Fisher's exact test. Statistical significance: *$p < 0.05$; **$p < 0.01$. LM, laparoscopic myomectomy; TOHA, transient occlusion of the hypogastric artery; Hb, hemoglobin; NA, not applicable.

2.4. Statistical data analysis

Categorical variables were described by the observed frequencies (i.e., counts) and their corresponding percentages; The Chi-square test was applied for statistical significance (either asymptotic, or Monte-Carlo simulation based on 10,000 samples).

Normality of numerical variables was tested with Kolmogorov–Smirnov statistical test; their descriptive statistics comprised the mean ± standard deviation and (minimum–maximum) interval, irrespective of their distribution. To compare normally distributed series of values, the t-test for independent groups was applied for the means, and Levene's test for the variances. To compare non-normal numerical data across two groups, a non-parametric Mann–Whitney U-test was applied.

The statistical analysis was conducted at a 95% level of confidence (i.e., 5% level of statistical significance). All reported probability values were two-tailed, and statistical significance was explicitly marked. Data were analyzed with the statistical software IBM SPSS v. 20.0 and R v. 4.2.2 (package "pwr").

3. Results

The only clinical differences between the two study groups that proved to be statistically significant were the higher nulliparity rate in the "LM + TOHA" group [18 (62.1%) vs. 9 (29%), $p = 0.01$], and reported symptoms such as infertility, meno-metrorrhagia, and pain (Table 1).

Statistically significant differences were observed for the levels of preoperative and postoperative hemoglobin (Hb) ($p = 0.01$ and $p < 0.001$, respectively) (Table 2). The significantly lower Delta Hb in the "LM + TOHA" group is apparent for all patients, irrespective of the location of dominant leiomyoma, namely anterior/posterior wall or fundical (Figure 3).

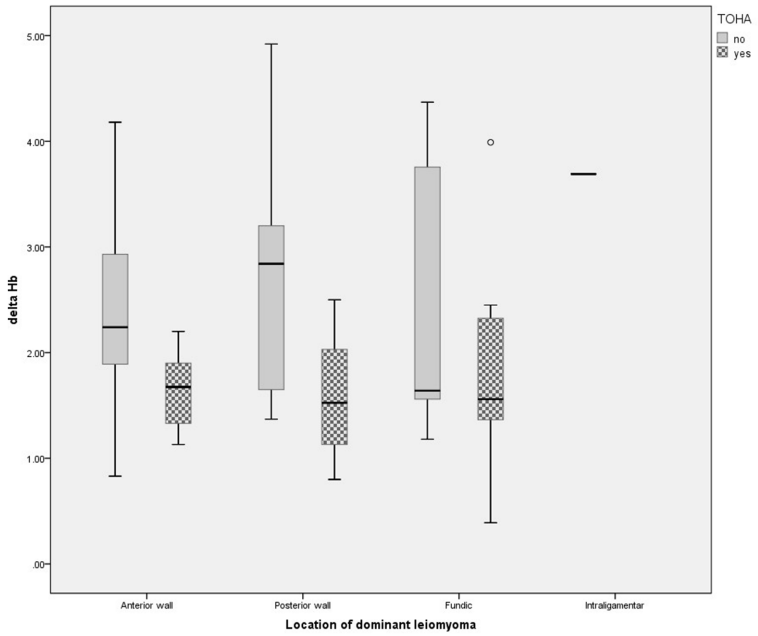

FIGURE 3
Change in hemoglobin level for different location of dominant leiomyomas in the two study groups of laparoscopic myomectomy (LM): with and without transient occlusion of hypogastric artery (TOHA). The boxes are proportional to the inter-quartile range (IQR) with medians marked between them, and whiskers are proportional to 1.5*IQR (or trimmed to the minimum/maximum values, except for the outlier marked as a bullet).

TABLE 3 Study outcomes in the two groups of laparoscopic myomectomy (LM): with and without transient occlusion of hypogastric artery (TOHA).

	LM + TOHA	LM	*p*-value
Variable	*N* = 29	*N* = 31	
Change in hemoglobin level (g/dL) [a]	1.68 ± 0.67 (0.39–3.99)	2.63 ± 1.06 (0.83–4.92)	<0.001**
Need for post-operative iron perfusion [b]	0	12 (38.7%)	<0.001**
Need for post-operative blood transfusion [d]	0	5 (16.1%)	0.053
Moderate to severe post-operative anemia [d]	4 (13.8%)	17 (68.7%)	0.001**
12-month post intervention fertility [d]	4 (13.8%)	2 (6.5%)	0.682

Data presented as mean ± standard deviation (min-max) for numerical variables, or *n* (%) for categorical variable. [a] *t*-test for independent samples; [b] asymptotic Chi-square test; [d] Chi-square, Monte Carlo simulation (10,000 samples). Statistical significance: *$p < 0.05$; **$p < 0.01$. LM, laparoscopic myomectomy; TOHA, transient occlusion of the hypogastric artery.

The mean ± standard deviation clipping length of the anterior trunk of the hypogastric artery was 10.62 ± 2.47 min (between 7 and 15 min), with no statistically significant difference in the overall operative time between the two groups: 110.2 ± 13.65 vs. 106.3 ± 16.48 ($p = 0.21$). Moreover, the number of hospitalization days after the procedure was not impacted: 2.1 ± 0.6 vs. 2.4 ± 0.8 ($p = 0.076$) (Table 2).

Histopathological abnormal findings were leiomyoma with cellular atypia (one case in the LM + TOHA group, two cases in the LM group) and one leiomyosarcoma in the LM group.

The change in Hb was statistically significantly reduced in the "LM + TOHA" group compared to the "LM" group: 1.68 ± 0.67 (0.39–3.99) vs. 2.63 ± 1.06 (0.83–4.92), respectively ($p < 0.001$). Postoperative iron perfusion was significantly higher in "LM" group ($p < 0.001$), postoperative blood transfusion was marginally higher in "LM" group ($p = 0.053$), moderate to severe postoperative anemia was significantly higher in "LM" group ($p = 0.001$), and for the 12-month post-intervention fertility there were no differences between the two groups ($p = 0.682$) (Table 3). Figure 4 shows the balance between these latter two secondary aspects (namely, post-operative anemia and fertility) in terms of odds ratios. There is quantitative evidence favoring TOHA with regard to these categorical outcomes of LM surgery: there is more than 7 times less risk of post-operative anemia in the TOHA group (namely, 1/0.14 = 7.14); although lacking the statistical significance (95% CI includes 1 and is very large, therefore imprecise), there is a better chance of 12-month fertility in the TOHA group. One patient from the LM + TOHA group required conversion to laparotomy due to major bleeding which was difficult to manage, and from the LM group a patient who had seven leiomyomas. Subsequent follow-ups showed that there were no postsurgical complications. Additionally, none of the patients had to be readmitted, and there were no reports of any deaths.

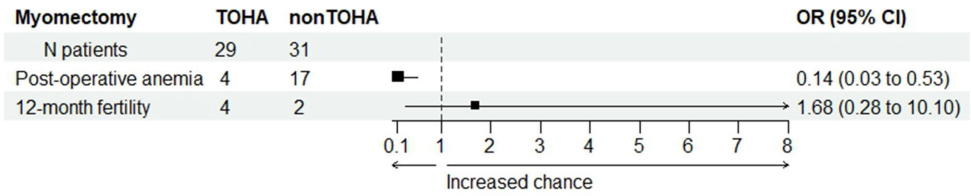

FIGURE 4
Comparison between the two study groups with regard to post-operative anemia and post-intervention fertility. Odds ratio (OR) values provide quantitative evidence towards favoring transient occlusion of hypogastric artery (TOHA) concerning both surgical outcomes.

4. Discussion

Over the past few decades, there have been significant changes in the treatment of fibroids. Minimally invasive surgery offers several advantages over laparotomy, including quicker recovery, less postoperative pain, decreased morbidity and a more satisfactory cosmetic outcome (6). Predictors for postoperative pain after laparoscopic procedures and adequate management methods are an important topic in continuous development (17). However, the choice of surgical approach depends on factors such as the size and number of fibroids, surgeon's skill and patient's desire for fertility preservation.

To date, making an accurate preoperative differential diagnosis between benign uterine tumors and uterine malignancy has proven to be challenging, yet critical for the appropriate surgical management. Proper patient selection is key in minimizing the incidence of misdiagnosed sarcomas. Studies have demonstrated that adenomyosis can coexist with, and may even be the cause of, endometrial cancer (18). Since the preoperative diagnosis of malignant tumors remains a challenge, focus has shifted towards investigations that can distinguish cancer from adenomyosis, such as ultrasound evaluations of subendometrial vascularity (19). In our study, all patients underwent preoperative evaluations using ultrasound and other imaging methods as available. As an additional precaution, leiomyomas were excised using in-bag morcellation, with a tissue retention system for the fragments. This approach was used to restrict intraperitoneal tissue spread, in case the postsurgical histopathological examination indicated malignancy.

Despite the benefits offered by laparoscopy, maintaining hemostasis throughout the procedure can occasionally be challenging. Fortunately, several treatments are available for managing hemostasis during myomectomy, including uterotonics, vasopressin, antifibrinolytic drugs, gelatin-thrombin as a hemostatic sealant, peri-cervical mechanical tourniquet, or laser dissection (12, 13, 20, 21).

Around the turn of the century, Liu et al. (22) introduced a new technique of uterine artery occlusion (UAO), namely laparoscopic bipolar coagulation of uterine vessels. It was initially investigated as a standalone treatment option for leiomyomas in response to the potential complications given by uterine artery embolization (23, 24). Over the following decades, various approaches to UAO have been researched, including combinations between myomectomy and UAO with either permanent or transitory uterine vessel occlusion. This was achieved through coagulation, ligation using suture, or vessel clips (24–26). Preventive UAO during LM has been shown to reduce significantly intraoperative bleeding, minimize the risk of complications, and shorten hospital stay compared to LM alone (27–30). These results have been thoroughly confirmed in multiple systematic reviews over the past decade (31, 32). A more recent systematic review and meta-analysis published by Sanders in 2019 found compelling evidence that combining myomectomy with UAO has the benefit of significantly reducing surgery-associated blood loss without added complications (24).

In 2022, Hiratsuka et al. published a case–control study demonstrating that a temporary uterine artery ligation using sutures has the advantage of reducing intraoperative blood loss, while being less invasive than clipping (25). However, compared to other surgical approaches where clips were used, suturing was found to prolong the surgery time by an additional 40 min (25). One crucial surgical outcome of our study is that TOHA did not prolong the overall operating time, a finding which is consistent with other studies (20, 33).

Regarding concerns raised by some authors (25, 34) that uterine artery clipping might pose potential risks of masked bleeding after the removal of vascular clamps and the chance of promoting postoperative cervical hematoma, our study did not report any clipping-related injuries.

Even though hypogastric/internal iliac artery ligation has been recognized as a method for managing hemorrhage in obstetrics and gynecology since 1893, it was Peter Siegel who underscored its significance due to its remarkable potential to save lives (35). A form of temporary hypogastric artery occlusion using an endovascular balloon has been widely explored in combination with myomectomy or hysterectomy (36–39). Nonetheless, there is a gap in the literature concerning the use of vascular clips for temporary hypogastric artery occlusion during laparoscopic myomectomy. As far as the authors are aware, no other articles have discussed the application of this specific technique as depicted in this manuscript. Similar articles on this topic focus on the transitory occlusion of the uterine artery. Our analysis suggests that the anterior trunk of the hypogastric artery is more accessible for dissection and provides a safer clip application. Compared to the uterine artery, the anterior trunk of the hypogastric artery has a larger diameter and a thicker wall, which minimizes the risk of avulsion during clip removal.

TOHA's effectiveness in reducing surgery-associated blood loss can be evaluated using parameters such as the postoperative drop in hemoglobin, intraoperative blood loss, and postoperative rate of transfusions. Measuring preoperative and postoperative hemoglobin levels provide an assessment of whether performing TOHA was

effective in reducing blood loss. While intraoperative blood loss may be challenging to measure accurately due to the variability in irrigation fluid usage, postoperative Hb drop may constitute a more reliable indicator of the effectiveness of TOHA in reducing bleeding during surgery (34).

In our study, the primary outcome was surgery-associated blood loss as measured by the change in Hb level. We found that the laparoscopic TOHA at the time of LM, compared with LM alone, resulted in a statistically significant reduction in blood loss expressed as the mean differences in Hb measured before and after the surgery. The difference in Hb level (delta Hb) was significantly lower in the TOHA group, compared to the non-clipping approach: 1.68 ± 0.67 vs. 2.63 ± 1.06 ($p < 0.001$). Controlling operative bleeding is critical during surgical procedures, particularly those involving multiple or large fibroids, to avoid complications such as massive intraoperative bleeding and the need for conversion to laparotomy.

The rate of required iron perfusion or transfusions, other indirect measures of blood loss, can also be used to evaluate the effectiveness of TOHA. In our study, there was a statistically significant higher rate of postoperative iron perfusion in the non-clipping group (0 vs. 12 patients), with no statistical differences in the number of patients who required a postoperative blood transfusion.

The aim of this study was to evaluate the feasibility and effectiveness of our new and particular approach, TOHA, during laparoscopic myomectomy, in reducing surgery-associated blood loss. The novelty of our approach is represented by the placement of titanium clips at the level of the anterior trunk of the hypogastric artery, cranially to the emergence of the uterine artery. Benefits of this approach include easier and faster dissection, no need to open the broad ligament, and the ability to identify vascular structures under the parietal peritoneum on the pelvic side wall. Although TOHA adds another layer to the surgical technique during LM, our study showed it does not prolong operative times when compared to a standard LM.

This article describes an efficient method to minimize blood loss during conservative uterine surgery. Other types of surgical uterine-sparing procedures such as caesarean scar ectopic pregnancy, uterine arterio-venous fistulas or interstitial cornual pregnancies can also benefit from TOHA for minimizing intraoperative bleeding (40). As previously stated, TOHA has virtually the same applications as the laparoscopic temporary clipping of the uterine arteries, with some supplementary potential benefits (34).

The limitations of our investigation can be attributed to the single-center design, the fact that all procedures were performed by a single team, and due to hospital's protocol, the estimation of blood loss was done by only measuring differences in hemoglobin. The strengths of our study come from the prospective design, being a proof of concept with the very advantage of consistency throughout all the surgical approach except for the technique used for the temporary artery occlusion, TOHA. The key strength is that we introduced this new technique for limiting blood loss with numerous potential applications for uterine-sparing procedures.

In conclusion, performing TOHA prior to LM provides numerous benefits, including reducing surgery-associated blood loss, minimizing the risk of complications, and lowering the occurrence of postoperative anemia. The technique does not significantly impact the operative time, making it a viable option for improving patient outcomes. Further studies are necessary to evaluate the impact of TOHA on fertility.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Human Ethical Committee of the University of Medicine and Pharmacy "Victor Babes," Timișoara, Romania. The patients/participants provided their written informed consent to participate in this study.

Author contributions

LB, MP, SB, CS, DG, RC, and LP: conceptualization. LB, AP, MP, and LP: methodology. LB, CS, and LP: validation. AP, SN, and DL: formal analysis and visualization. CS and LB: investigation and resources. SN, AP, and DL: data curation. LB, AP, SN, DL, and LP: writing—original draft preparation. LB, MP, SN, AP, and DL: writing—review and editing. DL and LP: supervision. LB: funding acquisition. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Comparison of laparoscopic sacrocolpopexy with vaginal reconstructive procedures and abdominal sacrocolpopexy for the surgical management of vaginal vault prolapse: a systematic review and meta-analysis

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Introduction: Vaginal vault prolapse, also known as apical prolapse, is a distressing condition that may affect women following hysterectomy, necessitating surgical intervention when conservative measures prove ineffective. The surgical management of apical compartment prolapse includes procedures such as laparoscopic sacrocolpopexy (LSCP), abdominal sacrocolpopexy (ASCP) or vaginal reconstructive procedures (VRP). This systematic review and meta-analysis aims to compare the outcomes of these interventions.

Methods: A comprehensive search of electronic databases was conducted to identify eligible studies. Fourteen studies comprising a total of 1,289 women were included. The selected studies were analyzed to evaluate outcomes such as duration of surgery, length of hospital stay, blood loss, complication rates, and patient satisfaction.

Results: LSCP did not demonstrate significant advantages over VRP in terms of perioperative or long-term outcomes. However, when compared to ASCP, LSCP showed shorter hospital stay, reduced blood loss, decreased postoperative pain, and lower rates of ileus.

Discussion: This systematic review contributes to evidence-based decision-making for the surgical treatment of vaginal vault prolapse. While LSCP did not exhibit substantial benefits over VRP, it emerged as a preferable option compared to ASCP due to shorter hospital stays and reduced postoperative complications. The findings from this study provide valuable insights for clinicians and patients in selecting the most appropriate surgical approach for vaginal vault prolapse. However, future research should focus on long-term follow-ups, standardizing outcomes, and outcome measures, and evaluating cost-effectiveness to further enhance clinical practice.

KEYWORDS

apical prolapse, vault prolapse, sacrocolpopexy, sacrospinous fixation, vaginal mesh, randomized trial, cohort study, meta-analysis

1. Introduction

Hysterectomy remains a common gynaecological procedure, although its prevalence has been decreasing in some countries in recent years due to advancements in conservative treatment options, increased utilization of minimally invasive techniques, and a shift towards more organ-preserving approaches (1).

Vaginal vault prolapse, a condition characterized by the descent of the vaginal apex following hysterectomy, has an overall prevalence ranging from 0.2 to 43% (2–5) and represents a significant concern for many women worldwide. This distressing condition can lead to a multitude of symptoms, including pelvic pressure, discomfort during sexual intercourse, low back pain, voiding dysfunction, and an overall diminished quality of life (6). When conservative measures such as pelvic floor physiotherapy, pessary use, or lifestyle changes fail, surgical intervention often becomes a necessity to restore pelvic support, alleviate symptoms, and enhance a patient's well-being. Currently, it is estimated that 23% of women with symptomatic apical prolapse eventually undergo surgical intervention (7, 8).

Surgical management options for apical prolapse include various procedures, such as sacrocolpopexy (laparoscopic, robotic, or abdominal), sacrospinous ligament fixation, uterosacral ligament suspension, iliococcygeus fixation, as well as transvaginal mesh procedures. Advancements in minimally invasive surgical techniques, such as laparoscopic approach, have become more and more accessible and expanded the options for surgical treatment, allowing for potentially faster recovery times and reduced postoperative morbidity. Laparoscopic sacrocolpopexy (LSCP) has emerged as the current gold standard for the surgical treatment of apical pelvic organ prolapse (9–12).

The specific surgical technique choice depends on factors such as the severity of prolapse, the patient's overall health, surgeon expertise, and individualized treatment goals. As the medical community strives to optimize patient outcomes, it becomes crucial to thoroughly explore and compare these surgical techniques to determine their respective benefits, limitations, and overall efficacy.

This article aims to provide a comprehensive, pooled analysis and comparison of three commonly used surgical techniques for the treatment of vaginal vault prolapse, namely LSCP, abdominal sacrocolpopexy (ASCP), and vaginal reconstructive procedures (VRP). By assessing their outcomes, complications, and patient satisfaction rates, we seek to offer clinicians and patients alike a detailed understanding of the advantages and potential drawbacks of each technique.

By comparing LSCP with both VRP and ASCP, this study aimed to evaluate the differences in surgical outcomes, including improvement in symptoms, complication rates, length of hospital stay, operative time, and patient satisfaction. These outcomes were selected to provide a comprehensive assessment of the comparative effectiveness and safety of different surgical approaches. The inclusion of multiple comparators allows the exploration of the advantages and disadvantages of each technique, providing valuable insights in making informed decisions regarding the most appropriate surgical management for vaginal vault prolapse.

2. Methods

2.1. Study design

This systematic review and meta-analysis included randomised controlled trials (RCT) and retrospective or prospective cohort studies reporting outcomes of surgical interventions performed for apical prolapse after hysterectomy. Systematic reviews, case reports, letters to editor, commentaries, educational articles, study protocols, non-comparative studies were excluded from our analysis. The identified studies were selected and reported in accordance with the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (13).

2.2. Participants

Comparative studies including women of any age or ethnicity suffering from apical prolapse who opted for surgical management of their condition were included.

2.3. Comparators

In this systematic review and meta-analysis, we aimed to compare the outcomes of LSCP with two alternative surgical procedures for the treatment of vaginal vault prolapse, namely VRP and ASCP. The selection of these comparators was based on their frequent utilization in clinical practice, the presence of pertinent studies for inclusion in our analysis, and the recent trend favouring minimally invasive surgical approaches.

It is worth emphasizing that the choice of comparators in this study was also guided by the current evidence, that highlighted a lack of comparisons of LSCP, VRP, and ASCP in women with a history of hysterectomy, suffering from prolapse of the apical compartment. Hence, through a meticulous and systematic search process, our objective was to identify studies that directly compared LSCP with either VRP or ASCP technique in this specific patient population. This approach aimed to ensure that the findings of our study would be relevant, applicable in clinical practice, and fill an important gap in the current clinical literature.

2.4. Systematic review protocol

This study has been registered in the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42023441528).

2.5. Search strategy and data sources

A comprehensive literature search was conducted using electronic databases (Medline, Embase, Cochrane Library, Scopus, Google Scholar) from inception to July 2023 to identify relevant studies. The search strategy included a combination of the following keywords and Medical Subject Headings (MeSH) terms: "apical prolapse," "vault prolapse," "middle compartment prolapse," "laparoscopic sacrocolpopexy," "randomised controlled trial," "RCT," "randomized trial." The terms were combined using logical operators such as 'AND' and 'OR' to retrieve relevant results. The records were deduplicated. Additional sources, such as reference lists of relevant articles were also searched to ensure comprehensive coverage of the literature through "snowballing technique." This technique allowed the expansion of the initial list of selected articles by following the chain of citations and references to uncover more potentially relevant studies. The search process was not restricted based on language, allowing for the inclusion of studies published in any language.

2.6. Data extraction

A standardized data extraction form was used to extract relevant information from the included studies. The following data were collected: study characteristics (first author, publication year, study design, sample size, hysterectomy status) and type of surgical procedures that have been compared. Data extraction was performed independently by two reviewers, and any discrepancies were resolved through discussion and consensus within the research team. Among the three surgical techniques compared, LSCP was considered the primary comparator. The other two techniques were VRP and ASCP. Studies that assessed the same surgical procedures were grouped together for the purpose of pooled analyses.

2.7. Data analysis

The statistical analyses for dichotomous and continuous data were conducted using Review Manager 5.4. The effect size of different surgical interventions for apical prolapse was presented as an odds ratio with a corresponding 95% confidence interval (CI) for dichotomous variables or as mean difference with a 95% CI for continuous data. The degree of heterogeneity among studies was assessed using the I^2 statistic. When substantial homogeneity was observed ($I^2 < 50\%$), pooled summary statistics were calculated using fixed-effects models. In instances of notable heterogeneity ($I^2 > 50\%$), random-effects models were utilized.

3. Results

3.1. Prisma diagram

Following comprehensive searches of multiple databases, a total of 114 studies reporting outcomes of three distinct surgical techniques for vaginal vault prolapse were initially identified and considered potentially eligible for inclusion in this systematic review and meta-analysis. After deduplication of records, 89 studies remained and were screened by title. Of those, 45 were excluded. The remaining 44 articles were sought for retrieval and screened by abstracts. Finally, after assessing eligibility based on the full-text articles, a total of 14 studies including 1,289 women were deemed eligible for the analysis. In one study, two arms were included, consisting of one RCT and one prospective cohort study (8). The inclusion process and the number of studies ultimately meeting the eligibility criteria are summarized in the Prisma Flow Diagram (Figure 1).

3.2. Study selection and characteristics

The characteristics of the included studies are presented in Table 1.

With the exception of one study (27), all the studies included in this review directly compared the outcomes of only two surgical techniques for vaginal vault prolapse. Okcu et al. conducted a study that compared the outcomes of three different procedures, namely LSCP, ASCP, and VRP (17). Among the included studies, five studies conducted comparisons between LSCP and VRP, while ten studies focused on comparing LSCP with ASCP.

Meta-analyses were conducted for those outcomes that were consistently reported across at least three primary studies in a comparable fashion.

3.3. Synthesized findings

For studies comparing LSCP with VRP, meta-analyses were carried out for the following outcomes: duration of surgery, length of hospital stay, blood loss, pelvic organ prolapse at follow-up, urinary symptoms at follow-up, dyspareunia, and Urogenital Distress Inventory (UDI) scores. Random effects forest plots (Figure 2) showed that only the duration of surgery significantly differ among those groups, LSCP lasting significantly longer than VRP ($p < 0.0001$).

The forest plots for the outcomes that did not yield significant differences between LSCP and VRP are shown in Figure 3.

Meta-analyses were conducted to assess the following outcomes when comparing LSCP with ASCP: duration of surgery, length of hospital stay, blood loss, haemorrhage, bladder/bowel injury, urinary symptoms at follow-up, pain, wound infection, ileus rates, pulmonary embolism (PE) /deep vein thrombosis (DVT), UDI and Incontinence Impact Questionnaire (IIQ) scores. The meta-analyses showed significant differences in terms of hospital stay ($p < 0.00001$), blood loss ($p < 0.00001$), pain ($p = 0.02$) and rates of postoperative ileus ($p = 0.03$). Women in the LSCP group had shorter hospital stay, less blood loss and pain, as well as lower rates of ileus (Figure 4).

For the remaining outcomes mentioned above, no statistically significant differences were found among the groups (Figure 5).

3.4. Assessment of risk of bias

This meta-analysis encompasses evidence derived from both RCT, which are designed to minimize systematic errors, and from non-randomized studies, which may be more susceptible to bias. To

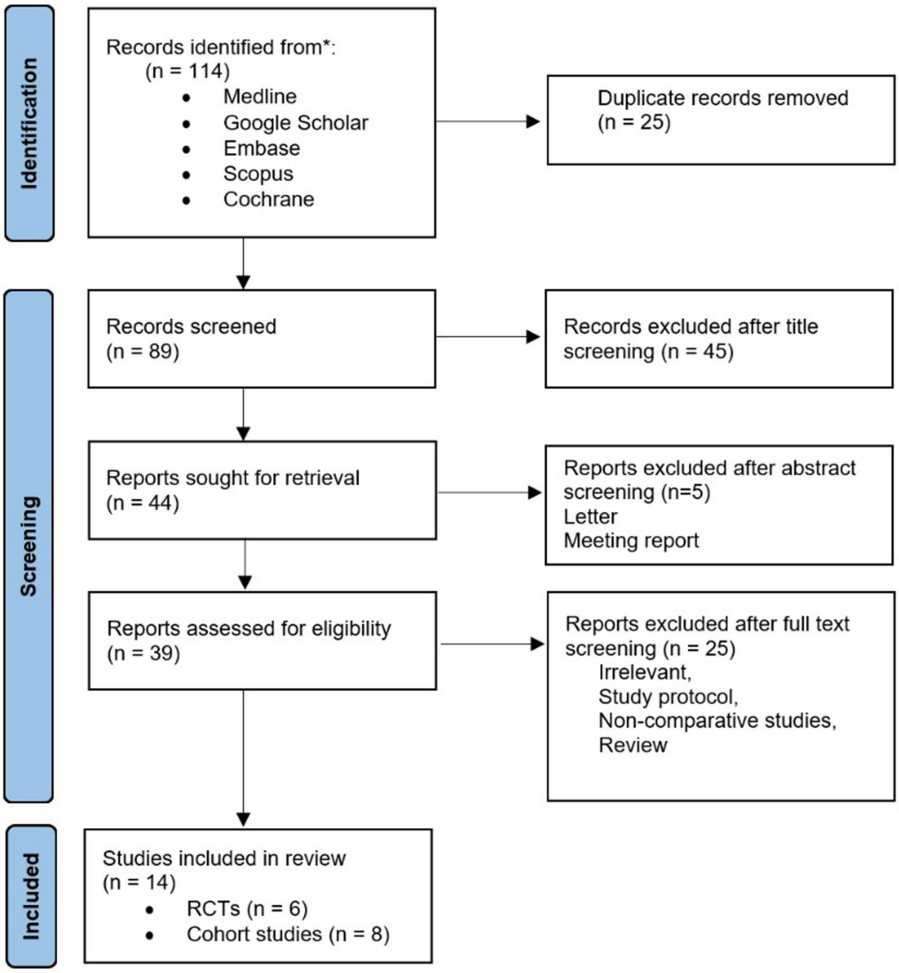

FIGURE 1
Prisma flow diagram.

evaluate the risk of bias as well as the quality of the included studies we used Critical Appraisals Skills Programme (CASP) tools for randomised and cohort studies (28, 29). Two researchers critically appraised the included studies. Any disagreements were resolved through discussion within the research team. Tables 2, 3 present CASP criteria for RCT and cohort studies.

As indicated in Table 2, blinding of both patients and medical professionals was unfeasible in the included RCTs due to the specific types of incisions required for each type of surgical procedure. Due to this valid rationale, none of the trials met the "blinding" criteria. Additionally, the presence of lost-to-follow-up patients contributed to another criterion that could not be met in terms of study quality by five out of six included RCTs. Another identified source of bias pertained to the precision of the reported estimate of the intervention or treatment effect.

Table 3 reveals that in the cohort studies, there were certain concerns raised regarding the accuracy of exposure measurement and the adequacy of follow-up length and completeness. Isolated concerns regarding potential confounding factors and the manner of cohort recruitment were also identified and highlighted in Table 3.

4. Discussion

4.1. Summary of main findings

A variety of surgical approaches have been developed, optimised, and implemented to surgically treat vaginal apical prolapse (30). These include LSCP, open ASCP, as well as VRP. Each of these approaches offers distinct benefits compared to one another. Given that the LSCP has achieved the status of the current gold standard, primarily due to its high cure rates (31, 32), it is reasonable to synthesize data on this procedure as well as comparisons between LSCP and alternative surgical techniques.

This systematic review and meta-analysis offer valuable insights into the differences of pooled outcomes of LSCP compared to ASCP or VRP. Our analyses showed that LSCP does not have significant perioperative or long-term advantages over VRP performed for vaginal vault prolapse. Moreover, when compared with LSCP, VRP were associated with a significantly shorter duration of surgery ($p < 0.0001$). These data could render VRP particularly advantageous for elderly women with underlying health conditions. Published data supports the benefits of shorter operative time that include reduced

TABLE 1 Characteristics of the included studies.

Study	Publication year	Sample size	Study design	Hysterectomy status	Laparoscopic sacrocolpopexy	Abdominal sacrocolpopexy	Vaginal reconstructive procedure
Marcickiewicz et al. (14)	2007	111	Retrospective cohort	History of hysterectomy	x		x
van Oudheusden et al. (8)*	2023	64	RCT	History of hysterectomy	x		x
van Oudheusden et al. (8)**		115	Prospective cohort		x		x
Maher et al. (15)	2012	108	RCT	History of hysterectomy	x		x
Withagen et al. (16)	2013	97	Prospective cohort	History of hysterectomy	x		x
Okcu et al. (17)	2021	65	Prospective cohort	Concurrent hysterectomy during apical prolapse surgery	x	x	x
Costantini et al. (18)	2016	120	RCT	Concurrent hysterectomy during apical prolapse surgery	x	x	
Freeman et al. (19)	2013	53	RCT	History of hysterectomy	x	x	
van Oudheusden et al. (20)	2022	41	RCT	History of hysterectomy	x	x	
Coolen et al. (21)	2017	74	RCT	History of hysterectomy	x	x	
Coolen et al. (22)	2013	85	Prospective cohort	History of hysterectomy	x	x	
Klauschie et al. (23)	2009	84	Retrospective cohort	History of hysterectomy or concurrent hysterectomy during apical prolapse surgery	x	x	
Paraiso et al. (24)	2005	117	Retrospective cohort	History of hysterectomy	x	x	
Poovathai et al. (25)	2023	50	Prospective cohort	History of hysterectomy	x	x	
Cho et al. (26)	2022	105	Retrospective cohort	Concurrent hysterectomy during apical prolapse surgery	x	x	

anaesthesia time and surgical risks, enhanced patient comfort, faster recovery, reduced resource requirements, and improved surgical throughput (33). Since the operating time was longer for LSCP, one would expect more blood loss in those cases. However, our study showed that was not the case, as blood loss showed lower values in the LSCP group, although this difference did not reach statistical significance. It is plausible that reduced blood loss in case of laparoscopic procedures can be attributed to better visualisation, easier tissue manipulation and access (34, 35). Furthermore, the choice of anaesthesia may potentially influence blood loss outcomes. Nonetheless, it is essential to highlight that our review did not include data pertaining to the specific anaesthesia types employed for each

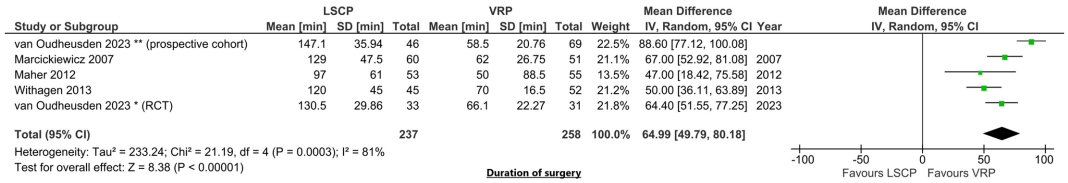

FIGURE 2
Forest plot of duration of surgery, the sole outcome that showed statistical significance when comparing LSCP and VRP.

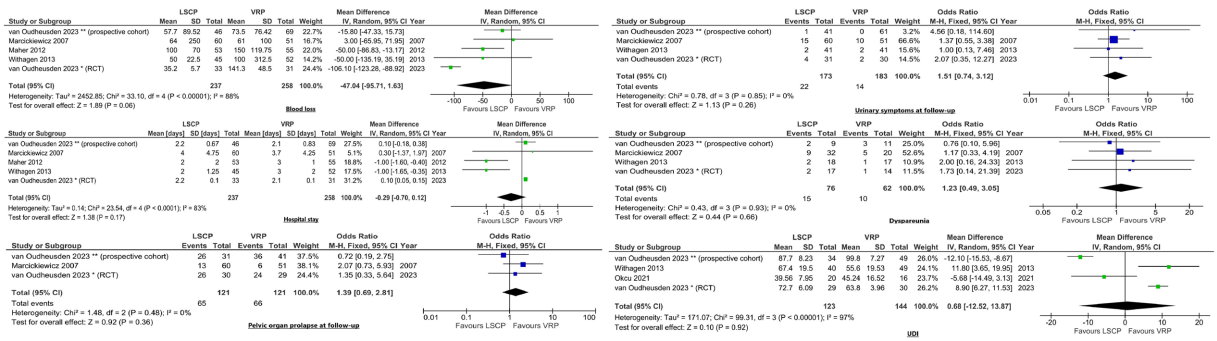

FIGURE 3
Forest plots displaying outcomes comparing LSCP with VRP, where statistical significance was not observed.

procedure as not all the primary studies included documented this information.

Outcomes such as hospital stay, pelvic organ prolapse or urinary symptoms at follow-up, dyspareunia and UDI scores did not significantly differ between LSCP and VRP groups. However, some of these outcomes such as hospital stay showed significant differences between groups in individual studies (15, 17). The discrepancy between individual study results and pooled analyses can be attributed to various factors, such as study sample sizes, variability in patient populations, and study design differences.

On the other hand, this meta-analysis showed that when compared to ASCP, patients undergoing LSCP had significantly shorter hospital stay, less blood loss and pain, as well as lower ileus rates ($p < 0.05$). Most of the primary studies included in this analysis reported similar results, with the exception of one study (23). Klauschie et al. reported similar levels of pain in both ASCP and LSCP groups (23). However, when pooling multiple studies in a meta-analysis, the increased sample size enhances the statistical power to detect significant differences between the two surgical techniques.

Furthermore, this study indicated that the LSCP groups exhibited lower IIQ total scores, wound infection and bladder injury rates compared to the ASCP groups, but statistical significance was not achieved for those outcomes. Although individual studies might have shown significant differences between those outcomes, pooled analyses allowed the combination of data from multiple studies, mitigating the impact of individual study variations and providing a more comprehensive assessment of the overall effect.

Comparing these findings with those of other meta-analyses is challenging due to the variations in the inclusion criteria. Most reviews or meta-analyses evaluating surgical approaches for apical pelvic organ prolapse have included a broader population, encompassing both women post hysterectomy and those with a uterus (30, 36, 37) while our study included only women without a uterus. As a result, direct comparisons between our findings and those of previous meta-analyses were not straightforward.

The inclusion of only women with a history of hysterectomy is the most notable strength of our study, as it enhances the homogeneity of the target population. By focusing specifically on this subgroup, we were able to minimize potential confounding factors related to the presence or absence of a uterus. This targeted approach allows for a more precise analysis and interpretation of outcomes related to apical pelvic organ prolapse in women who have undergone hysterectomy. Consequently, our study provides valuable insights specific to this homogeneous population, which can contribute to a more accurate understanding of the effectiveness and safety of the studied interventions.

4.2. Future directions

As the field of surgical approaches for vaginal vault prolapse continues to evolve, a few topics for future research and improvement can be identified. This meta-analysis provides valuable insights into the comparative effectiveness and safety of different surgical techniques. However, there are still areas that warrant further investigation to advance clinical practice and patient outcomes.

Firstly, given the increasing prevalence of robotic surgery, future studies should focus on comparing robotic procedures with the currently established laparoscopic techniques performed for vaginal vault prolapse. Robotic surgery offers potential advantages, and evaluating its outcomes and benefits in comparison to traditional laparoscopic approaches will help elucidate its role and potential

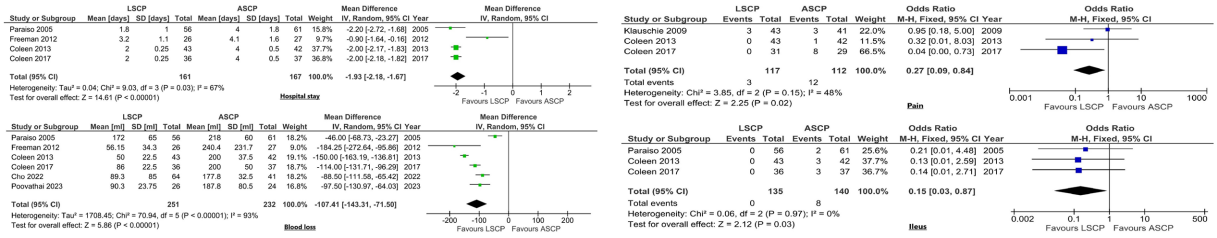

FIGURE 4
Forest plots illustrating outcomes that exhibited significant differences among LSCP and ASCP group.

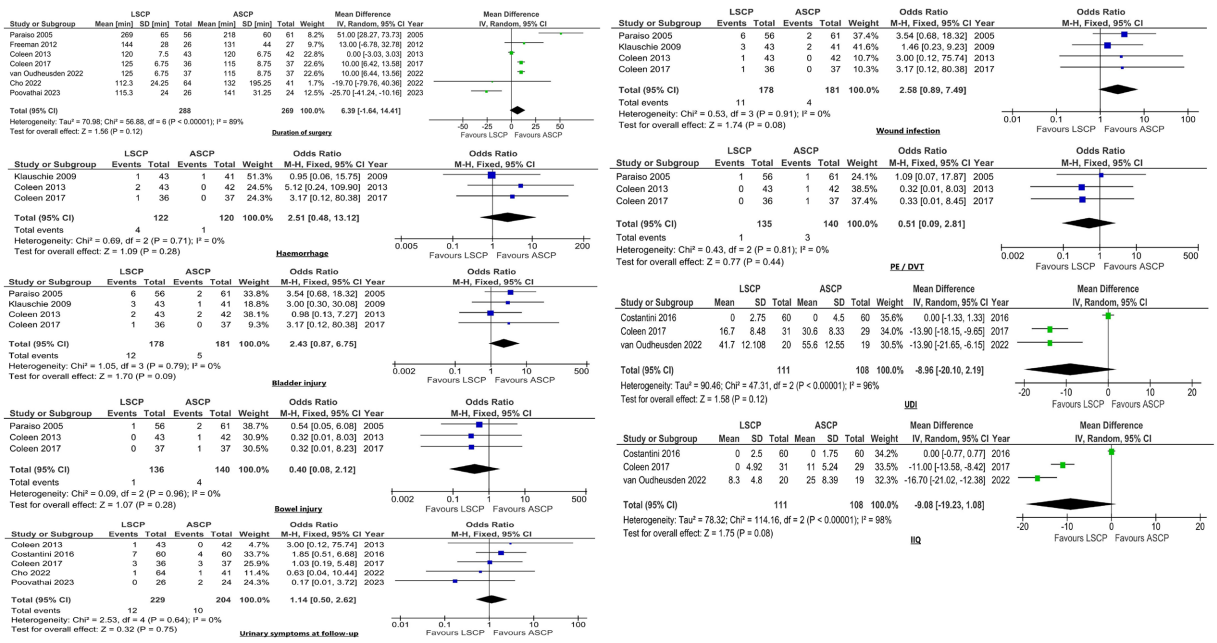

FIGURE 5
Forest plots depicting the outcomes that showed no significant differences among the groups (LSCP vs. ASCP).

benefits. Anticipated progress is not limited solely to the realm of robotics, as the laparoscopic field also shows promise. Techniques like vaginal natural orifice transluminal endoscopic surgery (vNOTES) offer a hopeful outlook as a surgical solution for vaginal apical prolapse. By utilizing the vaginal pathway, this approach minimizes incisions and reduces the likelihood of scarring. This approach aligns with patient preferences for less noticeable surgical outcomes and quicker postoperative recovery. However, it is important to acknowledge that the successful adoption and progression of robotic surgery as well as vNOTES requires thorough training and expertise among surgeons. The goal should always be to tailor the surgical approach to the individual patient's needs, rather than adhering strictly to a single method.

Secondly, long-term follow-up studies are needed to assess the durability of outcomes and the potential for recurrence or complications over time. While our meta-analysis included studies with various follow-up durations, extended, standardized, follow-up periods are crucial to determine the sustained effectiveness of different surgical interventions and provide more comprehensive information for both patients and healthcare providers.

Also, a standardized methodology to report outcomes and outcome measures is urgently needed to allow robust comparisons. Due to the high variety in outcome reporting by primary studies, our study only allowed comparisons of perioperative outcomes and of two, medium-and long-term outcome measures, namely UDI and IIQ. Although the primary papers included in this study evaluated various outcome measures such as The Australian Pelvic Floor Questionnaire (APFQ) (15), Defecation Distress Inventory (DDI) (15, 21), Pelvic Organ Prolapse/Urinary Incontinence Sexual Function Questionnaire (PISQ) (8, 15, 17), Female Sexual Function Index (FSFI) (18), Pelvic Floor Distress Inventory (PFDI) (17), Pelvic Organ Prolapse Distress Inventory (POPDI) (17), and Colorectal-Anal Distress Inventory (CRADI) (17), it was not feasible to conduct meta-analyses for those outcome measures because they were reported in isolated fashion, by only one or two studies. It is important to prioritize those outcomes in future studies to ensure that research is relevant to clinical practice.

Another interesting aspect arises from complications associated with mesh materials. In this study, we aimed to investigate the outcomes and complications associated with

TABLE 2 CASP criteria for RCT.

CASP criteria/ RCT	Coolen et al. (21)	Costantini et al. (18)	Freeman et al. (19)	Maher et al. (15)	van Oudheusden et al. (8)	van Oudheusden et al. (20)
Did the trial address a clearly focused issue?	y	y	y	y	y	y
Was the assignment of patients to treatments randomised?	y	y	y	y	y	y
Were all of the patients who entered the trial properly accounted for at its conclusion?	n	n	n	y	n	n
Were patients, health workers and study personnel 'blind' to treatment?	n	n	n	n	n	n
Were the groups similar at the start of the trial?	y	y	ct	y	y	y
Apart from the experimental intervention, did each study group receive the same level of care (that is, were they treated equally)?	y	y	y	y	y	y
Were the effects of intervention reported comprehensively?	y	y	y	y	y	y
Was the precision of the estimate of the intervention or treatment effect reported?	y	n	y	y	n	y
Do the benefits of the experimental intervention outweigh the harms and costs?	y	y	y	y	y	y
Can the results be applied to your local population/in your context?	y	y	y	y	y	y
Would the experimental intervention provide greater value to the people in your care than any of the existing interventions?	y	y	y	y	y	y

Y, yes; n, no; ct, cannot tell.

different suspension techniques in vaginal vault prolapse surgery. While we acknowledge the importance of examining graft-related complications and their comparative analysis between these techniques, it is crucial to note that our study's focus was primarily on the specific outcomes and complications we could assess with the available data.

Graft-related complications represent an important area of concern in pelvic organ prolapse surgery, and their analysis could potentially provide valuable insights into the overall efficacy and safety of the suspension techniques. Unfortunately, due to limitations in data availability, we were unable to perform a comparative analysis of graft-related complications in this study.

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TABLE 3 CASP criteria for cohort studies.

CASP criteria/ cohort study	Marcickiewicz et al. (14)	Klauschie et al. (23)	Coolen et al. (22)	Withagen et al. (16)	Okcu et al. (17)	Paraiso et al. (24)	Poovathai et al. (25)	Cho et al. (26)
Did the study address a clearly focused issue?	y	y	y	y	y	y	y	y
Was the cohort recruited in an acceptable way?	y	y	y	y	y	y	n	y
Was the exposure accurately measured to minimise bias?	n	n	y	y	y	y	n	n
Was the outcome accurately measured to minimise bias?	n	y	y	y	y	y	y	y
Have the authors identified all important confounding factors?	y	y	y	y	y	y	n	y
Have they taken account of the confounding factors in the design and/or analysis?	y	y	y	y	y	y	n	y
Was the follow up of subjects complete enough?	n	y	n	y	ct	n	n	n
Was the follow up of subjects long enough?	y	y	n	y	y	n	n	y
Do you believe the results?	y	y	y	y	y	y	y	y
Can the results be applied to the local population?	y	y	y	y	y	y	y	y
Do the results of this study fit with other available evidence?	y	y	y	y	y	y	y	y

We recognize this as a limitation of our work and believe that future research endeavours should prioritize the collection and analysis of data related to graft-related complications in the context of different suspension techniques.

Lastly, cost-effectiveness analyses are essential to evaluate the economic implications of various surgical approaches. Assessing the costs associated with different procedures, including initial costs, perioperative costs, and long-term follow-up costs, will aid in healthcare resource allocation and decision-making.

4.3. Limitations

Several limitations of this meta-analysis should be acknowledged. Firstly, the analysis was limited to the available studies identified through the multiple database searches and snowballing process, and potential publication bias cannot be completely ruled out. Secondly, the included studies exhibited heterogeneity in terms of study design, which may have influenced the overall results and comparability. Additionally, the quality and reporting of the included studies varied, which could impact the reliability and generalizability of the findings. Finally, the limited number of studies available for some specific outcomes may have affected the power and precision of the pooled analyses.

5. Conclusion

In summary, this meta-analysis highlights that LSCP does not present substantial advantages over VRP for apical prolapse after hysterectomy, while demonstrating certain advantages over ASCP in terms short term outcomes such as hospital stay, blood loss, pain, and ileus rates. These findings contribute to the understanding of the comparative effectiveness of different surgical techniques, assisting clinicians in making informed decisions regarding the most suitable approach for the surgical management of apical prolapse.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Author contributions

RC: Conceptualization, Supervision, Writing – review & editing. M-PR: Conceptualization, Formal analysis, Methodology, Writing – original draf. AM: Writing – review & editing. CB: Data curation, Formal analysis, Writing – review & editing. CO: Data curation, Writing – review & editing. IN: Data curation, Writing – review & editing. DM: Supervision, Writing – review & editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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