Comparison of Single-site and Three-port Hysterectomy for Benign Uterine Diseases: A Randomised Trial (LESS-H)

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Abstract

Objective To evaluate the feasibility and safety of laparoendoscopic single-site (LESS) vaginal hysterectomy compared to conventional three-port laparoscopic-assisted vaginal hysterectomy (LAVH) for benign and pre-invasive uterine disease. Design Randomised controlled trial. Setting South Korea. Population Patients who were scheduled to undergo laparoscopic hysterectomy for the benign and pre-invasive uterine diseases Methods Patients were randomised to LESS LAVH group and conventional three-port LAVH group. Main outcome Measures To compare the average length of postoperative hospital stay and the proportion of patients discharged within two days after surgery between the LESS and three-port groups. Results A total of 428 patients were randomised to the LESS group (n=216) and the conventional group (n=212). The two groups did not show significant differences in the average length of postoperative hospital stay (LESS vs. three-port, 2.17 days vs. 2.15 days, \( P = 0.757 \)) and the proportion of patients discharged within two days after surgery (LESS vs. three-port, 93% vs. 90%, \( P = 0.277 \)). There were also no significant differences in operating time, hemoglobin change, and perioperative complications. While the visual analogue score (VAS) pain score during hospital stay was similar between the two groups, the pain score at the first outpatient visit was significantly lower in the LESS group (LESS vs. three-port, 3.29 vs. 3.93, \( P = 0.012 \)). Conclusions Although LESS LAVH was not superior to conventional multiport surgery, it is a feasible, safe procedure for managing benign and pre-invasive uterine diseases.
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Randomised controlled trial.

**Setting**
South Korea.

**Population**
Patients who were scheduled to undergo laparoscopic hysterectomy for the benign and pre-invasive uterine diseases.

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**Main outcome Measures**
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A total of 428 patients were randomised to the LESS group (n=216) and the conventional group (n=212). The two groups did not show significant differences in the average length of postoperative hospital stay (LESS vs. three-port, 2.17 days vs. 2.15 days, \( P = 0.757 \)) and the proportion of patients discharged within two days after surgery (LESS vs. three-port, 93% vs. 90%, \( P = 0.277 \)). There were also no significant differences in operating time, hemoglobin change, and perioperative complications. While the visual analogue score (VAS) pain score during hospital stay was similar between the two groups, the pain score at the first outpatient visit was significantly lower in the LESS group (LESS vs. three-port, 3.29 vs. 3.93, \( P = 0.012 \)).

**Conclusions**
Although LESS LAVH was not superior to conventional multi-port surgery, it is a feasible, safe procedure for managing benign and pre-invasive uterine diseases.

**Keywords**
Hysterectomy, uterine diseases, laparoscopy, single-port

**Funding**
None

**Trial registration:** Clinicaltrial.gov identifier number: NCT01679548, https://clinicaltrials.gov/

**Introduction**
Unless there is any other reason to undergo laparotomy, laparoscopic-assisted hysterectomy is the preferred treatment for benign tumors of the uterus and precursor lesions of uterine cancer.\(^1\) While conventional laparoscopic-assisted vaginal hysterectomy (LAVH) is performed using three or four ports, laparo-endoscopic single-site (LESS) LAVH using only one multichannel trocar has recently become popular due to its advantages of fewer surgical wounds and faster recovery.\(^2, 3\) Many studies, including our own, have shown that LESS LAVH is as feasible as multi-port LAVH, with no significant difference in surgical outcomes.\(^4\)\(^-\)\(^8\) Additionally, the additional analgesic requirement after surgery and the severity of pain measured by the visual analogue scale (VAS) score were significantly lower in the LESS LAVH group.\(^5, 8\)
While previous randomised studies have compared the results of LESS LAVH versus multi-port LAVH or TLH (total laparoscopic hysterectomy), these studies have limitations such as small sample size and inconsistent control groups. Therefore, a randomised controlled trial involving a larger population with three-port LAVH as the control group is needed to provide more robust evidence for the feasibility and safety of LESS LAVH. Additionally, previous studies mainly compared the intensity of pain or the use of analgesics. To determine whether LESS LAVH is indeed a minimally invasive surgery compared to three-port LAVH, it is important to demonstrate faster postoperative recovery rather than just pain intensity. One of the most representative factors reflecting postoperative recovery is the length of hospital stay, and a study comparing this between the two groups is needed. Therefore, we aimed to determine whether single-port LAVH has a faster postoperative recovery than three-port LAVH through a large-sized randomised controlled trial.

Methods

Patient selection and randomisation

This trial included patients aged 20 to 70 years with gynecological diseases, such as leiomyoma, adenomyosis, endometrial hyperplasia (including endometrial intraepithelial neoplasia), cervical intraepithelial neoplasia (including carcinoma in situ), and abnormal uterine bleeding. Patients with an ASA (American Society of Anesthesiology Physical Condition Classification) score of 1-2, as well as those with previous abdominal and pelvic surgeries, were eligible for inclusion. To maintain consistency in the quality of surgeries, a study limited the number of participating surgeons to two at Asan medical center. The two participating surgeons in the study were highly experienced in performing laparoscopic-assisted vaginal hysterectomy (LAVH) procedures for benign diseases, with each surgeon individually conducting over 100 LAVH procedures annually at a high-volume gynecological surgery institution. In addition to laparoscopic hysterectomy, procedures such as oophorectomy, ovarian tumor resection, and salpingectomy were also allowed. It should be noted that the study only included patients who underwent surgery by two participating surgeons.

A randomisation table was created by an independent statistician using SAS (SAS Institute, Cary, NC, USA) software, and study subjects were assigned using a simple randomisation method the day before surgery. The study was approved by the institutional review board of Asan Medical Center (approval ID: 2012-0596, approval date: August 03, 2012) and informed consent was obtained from all patients before participation (ClinicalTrial.gov identifier number: NCT01679548).

Surgical procedures

In brief, LESS LAVH was performed using a commercially available four-channel, single-port system. A rigid, 0-degree, 5 mm laparoscope was used. An incision was made 2 cm linearly through the base of umbilicus. Conventional LAVH was performed using three ports, with a 12, 10, and 5-mm port placed in the umbilicus, left lower quadrant, and suprapubic area, respectively. A rigid, 0-degree, 12 mm laparoscope was introduced through the 12-mm port of the umbilicus. The surgical procedures for LAVH did not differ between the groups except for port placement. In both groups, patients were positioned in the dorsal lithotomy, 15-degree Trendelenburg position, and pneumoperitoneum was achieved using CO$_2$ gas at 10–12 mmHg. A Cohen cannula was used as a uterine manipulator. In all cases, the surgeons stood on the left side of the patient and used rigid laparoscopic instruments. The infundibulo-pelvic ligaments, ovarian ligaments, round ligaments, and fallopian tubes were cut using Ligasure®. The bladder peritoneum was opened, and the bladder was dissected from the uterine cervix using a monopolar bovie laparoscopic technique. This was followed by the intravaginal procedure, which involved making a circular incision around the cervix, performing anterior and posterior colpotomy, and clamping, cutting, and ligating the paracervical tissues and uterine arteries. After removal of the uterus, the peritoneum was closed using continuous running 2-0 absorbable suture material, and the vaginal stump was closed using continuous interlocking 1-0 absorbable suture material. Laparoscopic irrigation and bleeding control were performed. The port sites were meticulously closed layer-by-layer without the use of a closed drain system. In the LESS-LAVH group, the fascia was sutured to close the umbilical incision, while in the conventional group, the fascia was closed for the 12 mm and 10 mm incisions. The skin was closed using skin adhesive in both groups.
Postoperative management

The patients received intravenous patient-controlled analgesia (PCA) for 48 hours after surgery. The PCA regimen consisted of fentanyl 1000 μg in normal saline (total volume: 50 mL) and was programmed to deliver 1 mL/h as a basal infusion rate and 0.5 mL on demand with a 15-minute lockout. Nonsteroidal anti-inflammatory drugs (NSAIDs) were given intravenously every eight hours for pain control until discharge. Postoperative pain was recorded every eight hours and whenever the patients notified the medical staff of pain by using the VAS, scored from 1 to 10 (0 indicating no pain and 10 indicating agonizing pain). Whenever patients requested additional analgesia, they were administered parenterally. The goal of postoperative pain control was to maintain a pain score of less than 3.

Patients were discharged on postoperative day 2 when all the following criteria were met: (1) pain with a VAS score of 3 or less, (2) resumption of normal diet and voiding, and (3) no symptoms or signs of postoperative complications that may require treatment or readmission (e.g., fever, chills, severe abdominal pain, abdominal tenderness, rebound tenderness, or signs of ileus). Patients are discharged with a prescription of 80 mg of NSAIDs, which are to be taken three times a day for a duration of three days. No other pain relievers are provided. The follow-up appointments at the outpatient clinic were scheduled at 2 weeks (± 1 week), 3 months (± 2 weeks), and 6 months (± 2 weeks) after surgery.

Outcomes

The primary endpoint of this study was to compare the average length of postoperative hospital stay and the proportion of patients discharged within two days after surgery between the LESS and three-port groups. Additionally, we aimed to assess the safety and feasibility of LESS LAVH by analyzing various secondary endpoints such as operation time, postoperative VAS pain score, number of additional analgesics needed, blood loss, changes in hemoglobin levels before and after surgery, frequency of blood transfusions, and incidence of operation-related complications. Postoperative complications were evaluated for up to 6 months after surgery and graded according to Dindo’s classification of surgical complications.

Statistical analysis

The sample size for the study was calculated based on a one-sided test with an alpha-value of 0.05 and a beta-value of 0.8. The null hypothesis was that the proportion of patients discharged within 2 days after surgery was the same between the LESS LAVH group and the three-port LAVH group. The alternative hypothesis was that the proportion of patients discharged within 2 days after surgery was higher in the LESS LAVH group than in the three-port LAVH group. The effect size was the proportion of patients discharged within 2 days after surgery, with the LESS LAVH group at 83% and the three-port LAVH group at 73%, based on the results of our previous retrospective study. A total of 424 patients, with 212 patients in each group, were required for the one-sided test.

Continuous data were compared using Student’s t -test, Mann-Whitney U test, and paired T-test, while categorical data were analyzed using the Chi-squared test or Fischer’s exact test. If P < 0.05 (two-sided test), the difference between the two groups was considered statistically significant. All statistical analyses were conducted using the IBM SPSS Software for Windows, version 26 (IBM Corp., Armonk, NY, USA).

Results

Baseline characteristics

From November 2012 to December 2018, A total of 434 patients were randomly assigned to each group (n=217). However, one patient in the LESS group and five patients in the three-port group decided to withdraw their consent. As a result, the final number of patients included in the study was 216 in the LESS group and 212 in the three-port group. (Figure 1.) The baseline characteristics of patients are presented in Table 1. There were no significant differences in the baseline characteristics between the two groups. The clinical factors of the two groups including age, body mass index, parity, menopausal status, previous
abdominal surgery, initial hemoglobin, medical co-morbidities, ASA physical status, and indications for hysterectomy are also shown in Table 1.

**Surgical outcomes**

The comparison of surgical outcomes by surgical approach is shown in Table 2. Surgical procedures were similar between the two surgery groups. There was no significant difference in total operation time (LESS vs. three-port, 90.9±33.4 min vs. 96.3±36.7 min, *P* = 0.109). The mean hysterectomy time was shorter in the LESS group (LESS vs. three-port, 54.1±24.5 min vs. 56.8±28.2 min, *P* = 0.303), albeit without statistical significance. One patient (0.5%) in each group required an additional port, and four patients (1.9%) in the LESS group and five patients (2.3%) in the three-port LAVH group had to convert to laparotomy due to severe pelvic adhesion. There were no significant differences in the weight of removed uterus, mean peri-operative hemoglobin level change, estimated blood loss, and intra-operative and postoperative transfusion rates between the two groups.

The mean length of hospital stay after surgery was similar between the two groups. (LESS vs. three-port, 2.17±0.82 vs. 2.15±0.50, *P* = 0.757). The proportion of patients who were discharged within two days after surgery was higher in the LESS group (LESS vs. three-port, 93% vs. 90%, *P* = 0.277), albeit without statistical significance.

Table 3 shows the comparison of perioperative complications according to surgical methods. There was no significant difference in the intraoperative complication rate between the two groups. Bladder injuries occurred in two patients (0.9%) in the LESS group and three (1.4%) patients in the three-port LAVH groups, and all cases were minor enough to require only laparoscopic serosa repair without additional port or conversion to laparotomy. Bowel injuries occurred in one patient (0.5%) in the LESS group during the process of lysis of severe pelvic adhesion, and the operation was converted to laparotomy. A total of four cases (1.9%) of bowel injuries that occurred in the three-port LAVH group were also due to severe adhesions, and one case required an additional port while two cases were converted to laparotomy. In terms of postoperative complications, fever occurred in 23 patients (10.6%) in the LESS group and 19 patients (9.0%) in the three-port LAVH group (*P* = 0.374); all fever cases were successfully managed with conservative treatment. There was no incisional hernia in both group. One case of stump dehiscence occurred in the LESS group one month after surgery, and re-operation for suture was performed under general anesthesia.

**Postoperative pain and analgesics use**

Tables 4 and 5 show the postoperative pain score and analgesic requirements. In both groups, VAS pain scores gradually decreased over time. On the day of surgery, 85.6% (185/216) and 84.4% (179/212) of patients in the LESS and three-port LAVH groups, respectively, required additional analgesics (*P* = 0.762); on postoperative day 1, this percentage dropped to 19.9% (43/216) and 21.2% (45/212), respectively (*P* = 0.928). The first outpatient clinic visit occurred on an average of 17 days after surgery. At this visit, the pain score of the LESS group was significantly lower than that of the three-port LAVH group (3.29±1.63 vs. 3.93±1.90, *P* = 0.012).

**Discussion**

**Main findings**

In this randomised controlled study, there was no significant difference between the LESS LAVH group and the conventional three-port LAVH group in the mean length of hospital stay after surgery and in the proportion of patients discharged within 2 days after surgery. Additionally, various other surgical parameters did not differ significantly between the two groups. Since the weight of the uterus being removed was similar in both groups, indicating similar surgical complexity, it can be concluded that LESS-LAVH is as feasible as three-port LAVH in terms of intra-, peri-, and postoperative outcomes. While the visual analogue score (VAS) pain score during the hospital stay was comparable between the two groups, the pain score at the first outpatient visit was significantly lower in the LESS group.
Interpretation (in light of other evidence)

This study is the first randomised controlled trial to compare LESS LAVH to only three-port LAVH, and its aim was to evaluate the feasibility and safety of LESS. From the patient’s perspective, it is essential to assess the benefits of surgery not only in terms of pain relief but also in terms of the speed of postoperative recovery. The primary endpoint of our study was the average length of postoperative hospital stay, which is a crucial factor for assessing recovery and indicates that a patient has sufficiently recovered to resume their daily life. We only discharged patients who fulfilled specific requirements, including being able to manage their pain without intravenous analgesics, having a regular diet, voiding, and displaying no indications of complications. Although slightly more patients were discharged at about two days in the LESS group, the mean length of hospital stay was similar between the two groups. However, the proportion of patients discharged on postoperative day 2 in our current study was notably higher than that reported in our previous retrospective study that included multiple surgeons.

The study results showed that the transfusion rates in both the LESS LAVH group and the conventional three-port group were higher than those reported in previous studies, approximately 8% and 11%, respectively. This higher transfusion rate can be attributed to a significant number of patients in the study having uterine myoma and adenomyosis, conditions that can potentially lead to vaginal bleeding or increased menstrual flow. It is noteworthy that around 20% of patients in both groups had anemia before surgery, with a hemoglobin level of 10 or less, and approximately 10% had a hemoglobin level lower than 9. Importantly, half of the patients who required blood transfusions fell into the category of having an initial hemoglobin level of 10 or less. These findings suggest that the higher transfusion rates observed in the study were likely due to the presence of preoperative anemia rather than intraoperative blood loss.

Laparo-endoscopic single-site surgery, which utilizes a single multichannel trocar, is becoming more popular with increasing interest in minimizing pain and scars. This technique is gradually replacing traditional multi-port surgery not only in gynecologic surgery but also in other surgical fields. Several previous studies have shown that LESS is comparable to traditional multi-port surgery in terms of feasibility. As LESS LAVH requires fewer surgical wounds than multi-port LAVH, it is expected that patients will experience less postoperative pain, faster recovery, and a shorter hospital stay.

Previous research has focused on comparing LESS hysterectomy with multi-port laparoscopic hysterectomy for the treatment of benign and pre-malignant uterine diseases, with several randomised controlled trials reported. Among these studies, some utilized total laparoscopic hysterectomy (TLH) alone or in combination with LAVH. Specifically, two studies compared LESS LAVH with traditional three- or four-port LAVH, one with 39 patients and the other with 100 patients. Our study specifically focuses on comparing LESS LAVH with three-port LAVH, which is more commonly used in clinical practice for benign diseases than four-port LAVH. By using a three-port LAVH control group, our study provides a more realistic and uniform comparison. Additionally, our study has a larger sample size, including a total of 428 patients, compared to previous studies with smaller cohorts.

Regarding postoperative pain, while a previous randomised controlled trial showed that LESS LAVH resulted in less pain than four-port LAVH, our study did not find a significant difference in pain scores or additional analgesic requirements between the two procedures. However, both groups experienced a significant reduction in pain scores on the day after surgery compared to the day of surgery. The statistically significant difference in pain scores at the outpatient clinic visit after discharge suggests that LESS may offer pain management benefits.

In recent years, there has been a growing interest in minimally invasive surgical approaches in gynecology, including techniques like vNOTES (vaginal natural orifice transluminal endoscopic surgery). A recent review article highlighted the non-inferiority of vNOTES hysterectomy compared to laparoscopic hysterectomy in terms of surgical outcomes. Both vNOTES and LESS aim to minimize surgical wounds and have garnered
significant attention from patients and healthcare providers. The focus on reducing incision size reflects the importance placed on improving surgical outcomes and promoting faster patient recovery. LESS LAVH, with its single surgical wound located in the umbilicus, is often referred to as "no scar surgery." It is worth noting that our study found no cases of incisional hernia in the LESS group, which can occur due to a larger incision in the umbilicus compared to multi-port surgery.

**Strengths and limitations**

The study has several strengths, such as being the largest randomised controlled trial comparing LESS and three-port LAVH and considering peri- and postoperative outcomes of both groups. However, there are some limitations to the study. First, as we only included patients who received surgery from two surgeons at a single center, our findings may not be generalizable to other centers. It also took a long time to recruit enough participants for our study. Second, we did not use a standardized scoring system to evaluate the cosmetic effects of the wounds, which could be considered in future research for more detailed comparisons between the two surgical approaches.

**Conclusion**

Although LESS was not superior to conventional surgery in terms of postoperative hospital stay, we have demonstrated that LESS LAVH is a feasible, safe procedure for managing benign and pre-invasive uterine diseases.

**Conflict of Interest Disclosures:** The authors declare no conflicts of interest.

**Author Contributions:** K.-O.J. and P.-J.Y had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: P.-J.Y, N.-J.H.

Acquisition, analysis, or interpretation of data: K.-O.J., P.-J.Y, N.-J.H.

Drafting of the manuscript: K.-O.J., P.-J.Y.

Critical revision of the manuscript for important intellectual content: K.-O.J., P.-J.Y, N.-J.H.

Statistical analysis: K.-O.J., P.-J.Y.

Administrative, technical, or material support: P.-J.Y, N.-J.H.

Supervision: P.-J.Y, N.-J.H.

**REFERENCES**


**Figure 1. CONSORT flow diagram**

LAVH, laparoscopic assisted vaginal hysterectomy; LESS, laparo-endoscopic single site surgery

**Figure 2. Port placement for surgery**

Laparo-endoscopic single site (A), (B) and conventional laparoscopic assisted vaginal hysterectomy (C), (D)
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