Treatment of Early Stage Endometrial Cancer by Transumbilical Laparoendoscopic Single-Site Surgery Versus Traditional Laparoscopic Surgery

A Comparison Study

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Abstract: To compare the outcomes of transumbilical laparoendoscopic single-site surgery (TU-LESS) versus traditional laparoscopic surgery (TLS) for early stage endometrial cancer (EC).

We retrospectively reviewed the medical records of patients with early stage EC who were surgically treated by TU-LESS or TLS between 2011 and 2014 in a tertiary care teaching hospital. We identified 18 EC patients who underwent TU-LESS. Propensity score matching was used to match this group with 18 EC patients who underwent TLS.

All patients underwent laparoscopic-assisted vaginal hysterectomy, bilateral salpingo-oophorectomy, and systematic pelvic lymphadenectomy by TU-LESS or TLS without conversion to laparoscopy or laparotomy. Number of pelvic lymph nodes retrieved, operative time and estimated blood loss were comparable between 2 groups. Satisfaction values of the cosmetic outcome evaluated by the patient at day 30 after surgery were significantly higher in TU-LESS group than that in TLS group (9.6 ± 0.8 vs 7.5 ± 0.7, P < 0.001), while there was no statistical difference in postoperative complications within 30 days after surgery, postoperative hospital stay, and hospital cost.

For the surgical management of early stage EC, TU-LESS may be a feasible alternative approach to TLS, with comparable short-term surgical outcomes and superior cosmetic outcome. Future large-scale prospective studies are needed to identify these benefits.

Abbreviations: BMI = body mass index, BSO = bilateral salpingo-oophorectomy, EC = endometrial cancer, LESS = laparoendoscopic single-site surgery, TLS = traditional laparoscopic surgery, TU-LESS = transumbilical laparoendoscopic single-site surgery.

INTRODUCTION

Endometrial cancer (EC) is one of the most common gynecologic malignancies with 280,000 cases per year globally. It is predicted that there will be 52,630 newly diagnosed cases of EC and 8590 deaths resulting from this disease in the United States in 2014.2 Most EC cases are diagnosed at an early stage and often could be cured with surgery alone, and the reported survival rate is up to 75%.3

Currently, the standard surgical treatment for EC includes hysterectomy and bilateral salpingo-oophorectomy (BSO). However, the benefit of complete surgical staging with lymphadenectomy, especially paraaortic lymphadenectomy, in patients with apparent early stage disease remains a topic of controversy. A retrospective trial of 734 cases showed a 1% to 1.6% rate of isolated paraaortic lymph node involvement in the setting of negative pelvic lymph nodes for both low- and high-grade EC.4 Pelvic lymph node involvement may play a crucial role in lymphatic metastasis of EC, and pelvic lymphadenectomy can improve surgical staging.5 Recently, SGO Clinical Practice Endometrial Cancer Working Group made the following recommendations: patients with grade 1 to 2 endometrioid tumors, less than 50% myometrial invasion, and tumor of 2 cm or less seem to be at low risk for recurrence and may not require surgical lymphadenectomy.5 Thus, in our practice we perform surgical staging with hysterectomy and BSO, as well as pelvic lymphadenectomy for early stage EC.

In recent years, laparoscopy is becoming a standard surgical approach for early stage EC, since it achieves similar survival rate and superior minimal invasion compared to laparotomy. Laparoendoscopic single-site surgery (LESS) emerges as an evolution of laparoscopy for further minimizing the invasive nature of surgery. Apparently, a fundamental advantage of LESS over traditional laparoscopic surgery (TLS) is that LESS requires fewer skin incisions, with subsequent improved cosmesis. TLS is conducted using multiple small incisions with ports for access within the abdomen. Conversely, LESS uses only 1 skin incision, typically within the umbilicus, through which multiple instruments can be passed and no visible scar is left after surgery. Besides, there has been some discussion on other advantages of LESS over TLS, such as less operative time, quicker convalescence, lower postoperative pain, lower cost, etc.6,7 But these discrepancies are associated with the type and scope of surgeries, the skill of surgeons, and various surgical equipments.

Admittedly, most surgeons believe that success and complications are the prime focus for any surgery, and patient’s concerns for cosmetic outcome should also be considered when several minimally invasive surgical approaches are possible.8,9 The desire of cosmesis is not the exclusive privilege enjoyed by young women. A recent study found that there was no
difference in the desire for cosmesis and perception of LESS according to the age. Thus, middle-aged women should also be counseled on LESS when indicated. Actually, the mean age in women diagnosed with EC in the United States is 60 years, and several studies have investigated the feasibility of transumbilical laparoendoscopic single-site surgery (TU-LESS) approach for EC treatment. Our group reported the 1st TU-LESS procedure for EC treatment in 2011, and so far we completed 18 consecutive cases. To our knowledge, few studies compared TU-LESS and TLS for EC treatment.

This study aimed to compare short-term outcomes in patients with early stage EC who underwent laparoscopic-assisted vaginal hysterectomy, BSO, and systematic pelvic lymphadenectomy via TU-LESS versus TLS approach.

**PATIENTS AND METHODS**

**Patients**

This study was approved by Ethics Committee of our hospital, and patients were informed and signed written informed consent. A retrospective study was conducted at our hospital from July 2011 to June 2014. Inclusion criteria were: FIGO (2009 version) stage IA; endometrioid adenocarcinoma with well (G1) or moderate (G2) differentiation; pre-operative assessment with magnetic resonance imaging showed no involvement of lymph node, cervical, or adnexal; adequate vaginal access; uterine size <12 weeks of gestation; and body mass index (BMI) <30 kg/m². Exclusion criteria included contraindications for general anesthesia or laparoscopy. Patient demographics and perioperative data were collected from the medical records. Patients were matched by the age (within ± 5 years), BMI (±3 kg/m²), tumor histology, and grade.

**Surgical Preparation**

All patients received a mechanical bowel preparation the day before the operation. All procedures were performed under general anesthesia with patients placed in the dorsal lithotomic position. Urinary catheter was placed after the anesthesia. Prophylaxis antibiotics were administered within 1 hour prior to surgical incision.

**TLS Procedure**

A standard 10-mm trocar placed at the umbilicus was utilized for laparoscope installment, and two 5-mm trocars were placed bilaterally. Another ancillary 5- or 10-mm trocar was dependent on patient’s body shape, which was often placed in the left upper quadrant of supra-pubic region or on the left side of the umbilical level. Peritoneal washing was routinely performed. Following the coagulation of the bilateral tubes, an intrauterine manipulator was positioned. Coagulation and section of ligaments and vessels above the uterine vessel, and pelvic lymphadenectomy were completed in laparoscopic phase. The anatomical margins for lymph node dissection were: the ureter medially, the body of the psoas muscle laterally, the obturator nerve inferiorly, the deep circumflex iliac vein caudally, and the cephalad bifurcation of the common iliac artery. Ligation of uterine vessel, cardinal and uterosacral ligaments, excision of uterus, remove of specimen, and vaginal stump closure were undertaken in vaginal phase. Each layer of the access port was separately sutured after pelvic hemostasis.

**TU-LESS Procedure**

A 2.5-cm cutaneous incision was made near or through the base of the umbilicus using the Hassen technique. A commercially available single port (TriPort, Olympus Winter & Ibe GmbH, Hamburg, Germany, Figure 1B, C) was introduced in the first 2 cases, while a homemade single-port device was applied in the remaining 16 cases (Figure 1D, E). The construction and application of homemade device were described previously and were shown in supplemental video produced by M-B L., http://links.lww.com/MD/A861 The multiple fingers of the glove functioned as a multiport for laparoscopic instruments. A 5-mm trocar was inserted through cutting edges of distal finger tips for carbon dioxide access and tied with silk suture to prevent the leakage of carbon dioxide. Once pneumoperitoneum (12–14 mm Hg) was achieved, another 5-mm...
trocar was inserted through cutting edges of middle finger tips for intraabdominal visualization with a 5-mm 30° laparoscope. The other 3 fingers were served as instrument channels (Figure 1E). Combination of a straight 5-mm instrument with a precurved one (Figure 1A) was used to prevent clashing between the instruments and the surgeon’s hands, and increase working force. Transformation in the position of the instruments and optics were performed according to the needs of the surgeon. The surgical procedures to perform laparoscopic-assisted vaginal hysterectomy, BSO, and systematic pelvic lymphadenectomy were identical to those of TLS described above.

Follow-Ups
Follow-up was via direct contact or telephone every 3 months for at least 12 months. Information about postoperative complications, cosmetic outcome, or any recurrence was recorded.

Outcomes
The primary outcomes included number of pelvic lymph nodes retrieved, operative time (the interval from surgical incision start to closure), and estimated blood loss.

The secondary outcomes included: postoperative complications within 30 days after surgery; satisfaction values of cosmetic outcome at day 30 after surgery. According to the literature, cosmetic outcome of the abdominal scar was estimated by the patient at day 30 after surgery, with a subjective satisfaction value from 0 to 10 (0 = bad and 10 = excellent); postoperative hospital stay; and hospital cost.

Statistical Analysis
All data were analyzed with SPSS 13.0 software (SPSS Inc., Chicago, IL). Data were verified for distributional assumptions with a Kolmogorov–Smirnov test. Continuous variables were expressed as means ± SD, while categorical variables were reported as absolute values and percentage. Continuous variables were compared with a 2 independent-sample t-tests, discrete variables were analyzed by a Chi-square test. Fisher exact test was used in the case of small sample comparison. All P values were 2-sided, and P values < 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

Eighteen pairs of eligible patients were included in this study. Demographic characteristics and perioperative data of all participants were summarized in Table 1. Overall, both 2 groups had comparable demographic characteristics after matching. In TLS group, 4 patients (22.2%) had preoperative comorbidities including 2 with diabetes mellitus and 2 with hypertension. And in TU-LESS group, 2 patients (11.1%) had preoperative comorbidities including one with diabetes mellitus and another one with hypertension. In TLS group, 1 patient (5.6%) had previous caesarean section; while in TU-LESS group, 3 patients had previous tubal ligation by laparotomy and 1 patient underwent previous laparoscopic myomectomy. No recurrence was identified in patients during follow-up.

As shown in Figure 2, pathological findings in all patients suggested that endometrioid adenocarcinoma confined to less than 50% myometrium invasion, with well (G1) or moderate (G2) differentiation. In G1 differentiation, the endometrial glands appeared regular (Figure 2A). Round or oval cell nucleuses were mainly localized at the base of columnar epithelium, with homogeneous chromatin and inconspicuous nucleoli (Figure 2C). In G2 differentiation, the endometrial glands appeared irregular, and glandular epithelium hyperplasia within the glandular lumen fused to cribriform architecture (Figure 2B). The cell nucleuses also have irregular shape, with chromat condensation and occasional prominent nucleoli (Figure 2D).

Primary Outcomes

All patients underwent laparoscopic-assisted vaginal hysterectomy, BSO, and systematic pelvic lymphadenectomy by TU-LESS or TLS without conversion to laparotomy or laparotomy. The mean number of total pelvic lymph nodes was comparable between TU-LESS group and TLS group (22 ± 6 vs 20 ± 8, P > 0.05). Compared with TLS approach, slightly more operative time was spent on TU-LESS approach, with no statistical differences (246.9 ± 36.4 vs 254.9 ± 32.8, P > 0.05). Two cases in TLS group had moderate hemorrhage...
during the separation of pelvic adhesions. Hence, the mean estimated blood loss in TLS group was higher compared to TU-LESS group, but with no statistical differences.

Secondary Outcomes
Postoperative complications were found in 4 cases of TLS group, including 3 with nausea and vomiting and 1 with mild fever, while in 3 cases of TU-LESS group, including 2 with diarrhea and 1 with mild fever. No severe complications occurred in early postoperative period (30 days).

On the right postoperative day, 4 abdominal skin incisions were detected in TLS group, with each 5 to 10 mm in length (Figure 3A), while single umbilical incision about 25 mm long was observed in TU-LESS group (Figure 3B). At day 30 after surgery, the incision in the umbilicus was healed and no visible scar was left in situ in both TU-LESS (Figure 1F) and TLS groups, but other 3 abdominal skin incisions in TLS group may result in scars, especially for women with scar constitution. At this point, satisfaction values of cosmetic outcome evaluated by patient were significantly higher in TU-LESS group than that in TLS group (9.6 ± 0.8 vs 7.5 ± 0.7, P < 0.001).

Compared to TLS group, postoperative hospital stay and hospital cost were lower in TU-LESS group (5.8 ± 0.8 vs 6.1 ± 0.8; 30624.6 ± 3861.5 vs 33941.1 ± 5668.6), but these differences had no statistical significance (P > 0.05).

DISCUSSION
Since the 1st application of TU-LESS in the field of gynecologic oncology,12–17 limited data have been published on the clinical benefits of TU-LESS for EC treatment.11–17 In this study, our results are consistent with previous studies that for experienced laparoscopic surgeons, TU-LESS approach is feasible and may be an appropriate surgical modality for the treatment of early stage EC.13

Lymphadenectomy is one of the cornerstone procedures in surgical staging of gynecologic malignancies. The procedure and setup via TU-LESS are essentially the same as for TLS, although there are some variations in port placement depending on the devices. In 2010, Escobar et al16 investigated the technique and feasibility of single-port laparoscopic pelvic and para-aortic lymph node sampling or lymphadenectomy in gynecologic malignancies such as endometrial, cervical, and ovarian cancer. In the present study, we compared short-term outcomes in the patients with early stage EC who underwent laparoscopic-assisted vaginal hysterectomy, BSO, and pelvic lymphadenectomy via TU-LESS or TLS approach. The 2 surgical approaches were associated with similar number of pelvic lymph nodes retrieved, which is not consistent with the results reported by Escobar et al.11 It was reported that the number of pelvic lymph nodes obtained were significantly higher in TU-LESS group than those in TLS group. The possible explanation for this discrepancy could be due to individual variation of the patients and laparoscopic skill of the surgeons. Our findings included comparable operative time, estimated blood loss, postoperative complications, and postoperative hospital stay between 2 groups, which are consent with the results reported by Escobar et al.11 Consequently, TU-LESS may be a feasible alternative to TLS for complex gynecologic oncology procedures, with comparable short-term surgical outcomes.
Furthermore, in our study, the abdominal incisions appearance and the subjective satisfaction values of cosmetic outcome in TU-LESS group were superior to TLS group. These findings are in accordance with several comparative studies reported.\textsuperscript{8,21,22} Cosmetic benefit would be achieved as a result of reduced incisions and a relatively hidden umbilical scar. Based on its indication and feasibility, TU-LESS approach may be suitable for women concerning for cosmesis, especially with scar constitution. For malignant cancers, theoretically, a single-access site could provide not only scarless appearance but also potential reduction of port-site trauma and metastasis.

Notably, with the advancement of new techniques, the ability to detect disease at early stages will change not only the approach to surgery but also the indications for each approach. Although TU-LESS is innovative in laparoscopic surgery, it still presents some unique challenges such as instrument crowding, lack of triangulation, and loss of depth perception. And these critical points have not yet been settled by the presence of various optics and ergonomic tools. In our study, for the surgical treatment of early stage EC, TU-LESS is not only a feasible alternative approach to TLS with comparable short-term surgical outcomes, but also has improved cosmetic outcome compared to TLS. The conclusions drawn were based on the eligible patients.

First, EC is often associated with obesity (defined as having a \textbf{BMI > 30 kg/m}^2),\textsuperscript{23,24} which may result in increased perioperative complications such as pelvic organ damage and poor wound healing. So, patients included in our study had a lower BMI (<30 kg/m\textsuperscript{2}) to avoid potential complications. Second, initial attempt of an innovative surgical approach should be confined to early stage of disease. Our pathological findings confirmed endometrioid adenocarcinoma as early stage, in agreement with other studies that all or most patients with early stage EC were surgically treated via TU-LESS approach.\textsuperscript{13,14} Preoperative imaging and frozen section analysis during operation contribute to assess the graded severity of this disease. Hence, selection of suitable cases would be the key to ensure the accomplishment of EC treatment via TU-LESS performed by laparoscopic surgeons.

In terms of research methodology, we used propensity score matching to reduce confounding factors and achieve well balanced demographic characteristics. Nevertheless, our study still has some limitations. First, although we proved that TU-LESS may be a feasible alternative approach to TLS for the treatment of early stage EC, the retrospective nature made further research necessary. Second, as for postoperative hospital stay and hospital cost, although TU-LESS tended to be superior than TLS, the differences between the 2 groups did not achieve statistical significance. This might be caused by the limited sample size and follow-up time, which should be further verified in further investigation. Despite these limitations, it seems that based on our results, TU-LESS approach was promising in the surgical treatment of early stage EC.

In summary, our findings suggest that TU-LESS is a feasible alternative approach to TLS for the management of early stage EC, with comparable short-term surgical outcomes and better cosmetic outcome. Future randomized prospective studies are needed for further confirmation.

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