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Original article

Effective thermal destruction of residual tubal epithelium using an advanced sealing device in opportunistic salpingectomy: A randomized trial



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ABSTRACT

Objective: To examine the effectiveness of proximal tube destruction at the uterine cornu by additional application of a sealing device.

Methods: A single-center randomized trial was conducted on 40 patients receiving a laparo-endoscopic single-site hysterectomy with opportunistic salpingectomy. We randomized patients into two groups at the time of admission to determine the laterality of additional thermal cauterization. Additional thermal cauterization for 10 seconds was applied on the right cornu in one group and on the left cornu in the other group. Three pieces of cornual tissue from each cornu were biopsied. One gynecological pathologist examined the cornual tissue to determine the residual tubal epithelium (TE) and thermal destruction of the specimens.

Results: Of the 40 patients enrolled in this study between September 2012 and July 2014, samples of 26 patients were subjected to tissue analysis. Residual TE was found in the cornu in 73.1% (19/26) and 65.4% (17/26) of tissues from the side of no additional cauterization (NO) and the side of additional cauterization (AD), respectively ($p < 0.001$). Residual TE was detected in 5.3% (1/19) and 94.1% (16/17) of the specimens from the NO and AD groups, respectively.

Conclusion: We observed that a high incidence of residual TE and efficacious cauterization-induced thermal destruction was achieved following 10 seconds of additional cauterization. These results suggest that additional cauterization of the uterine cornu using the sealing device effectively destroys residual TE after salpingectomy.

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Introduction

Ovarian cancer is the most lethal gynecologic cancer. Since there are no reliable screening methods to detect ovarian neoplasms, most patients are diagnosed in advanced stages of the disease, with no curative therapeutic options available.

Conflicts of interest: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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Salpingectomy has been suggested as a good strategy to reduce ovarian cancer risk in premenopausal women at either low or high risk for ovarian cancer. The fimbriae of the fallopian tubes have been proposed as one of the potential locations of tumor initiation in ovarian cancer.^{1–4} Although fimbriae are postulated to be the main initiation site of ovarian cancer, the proximal tube and ampulla can also be sites of initiation in high-grade serous ovarian cancer.⁴ Recently, opportunistic salpingectomy has become a reasonable option instead of tubal ligation in low-risk patients.⁵

Salpingectomy involves removing the whole fallopian tube, which arises within the uterine cornu and comprises layers of uterine muscle. The proximal portion of the fallopian tube is buried

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about 1 cm in the muscular layer of the uterine cornu, which makes it difficult to determine whether the entire fallopian tube is removed during salpingectomy.

The advanced bipolar vessel sealing system has become widely used due to its versatility, as laparo-endoscopic single-site surgery (LESS) is now increasingly used in gynecologic practices. In this system, thermal energy is generated and pressure is applied simultaneously via the surgical device's jaw in order to denature collagen and elastin in the tissue and blood vessels, allowing sealing and cutting of the tissue at the same time without the need to change devices. This system was developed to decrease the thermal spread by a feedback-programmed amount of bipolar diathermy,⁶ which minimizes lateral thermal spread and efficiently delivers thermal energy into the tissues between the jaws.

We hypothesized that additional cauterization using this device at the cornual portion of the uterus would induce complete destruction of the fallopian tubal tissue within the uterine muscle. To test this hypothesis, we histologically evaluated the incidence of residual fallopian tube epithelium (TE) cornua following additional cauterization using a sealing device.

Methods

Study design and patient population

A randomized study was conducted after gaining approval from the Institutional Review Board of Samsung Medical Center Seoul, Republic of Korea (Approval number: 2012-08-063, ClinicalTrials.gov identifier: NCT 01894971). We received informed consent from each patient for undergoing opportunistic salpingectomy in addition to planned hysterectomy. The patients were classified randomly into two groups, right cauterization (RC) and left cauterization (LC), by the surgeon using a table of random sampling numbers prior to the day of surgery (Figure 1). Additional cauterization was applied to the right cornu in the RC group and to the left cornu in the LC group. Inclusion criteria were age between 30 years and 60 years, presence of symptomatic uterine myomas and/or adenomyosis, such as dysmenorrhea, pelvic pain or discomfort, urinary symptoms, presence of a palpable mass, and increasing size of myomas or menorrhagia over the course of at least 2 months in patients for whom a hysterectomy was indicated for a benign disease or precancerous lesion, such as uterine prolapse, intra-epithelial disease, or atypical endometrial hyperplasia. Exclusion criteria included menopause, tubal pathology, uterine malignancy, previous tubal surgery, and previous history of pelvic radiation therapy.

Surgical procedures

Patients underwent LESS salpingectomy and hysterectomy using a single umbilical incision, as described previously.⁷ Briefly, the procedure was conducted as follows. A patient was placed in the lithotomy position. A single-port platform was positioned, followed by inflation with CO₂. Salpingectomy was performed at the most proximal part of the fallopian tube (Figure 2A). Additional thermal cauterization (AD) of one of the uterine cornua was performed using a vessel sealing device for 10 seconds after the removal of the fallopian tube, and no additional cauterization (NO) was applied to the other side. We grasped the cutting edge of the cornu with the jaw of a LigaSure (Covidien, Boulder, CO, US) (Figure 2B). Hysterectomy was performed, and the uterus was subsequently removed through the vagina, followed by closure of the vaginal stump and the abdominal skin incision. Three tissue samples were collected from each cornu. Tissue samples were numbered 1–6 (Figure 2C); lateral sections of the tissues were designated 1 and 6, intermediate

sections of the tissues were designated 2 and 5, and medial sections of the tissues were designated 3 and 4.

A LigaSure 5-mm blunt tip laparoscopic instrument (LigaSure; LF1537, Covidien, Mansfield, MA, USA) was used for salpingectomy and additional cauterization.

Histologic evaluation

A single gynecological pathologist blinded to information about the laterality of additional cauterization examined all the samples. The right- and left-sided cornua from the same uterus were examined to evaluate the existence of TE and the extent of thermal destruction of the tissue (Figure 3). When TE was found in at least one of the six samples from the same uterus, the uterus was regarded as positive for residual TE in the analysis. A set of tissue refers to three tissue samples from the same sided cornu, therefore, one patient provided two sets of cornual samples. If thermal effects were present in all three tissues from the same set, it was regarded as a completely destroyed set.

Statistical analyses

The sample size was calculated by assuming that the proportion of residual TE would be 60%. Additional cauterization was hypothesized to induce thermal destruction of over 90% of the residual TE. To prove this hypothesis with a 5% significance level and 90% power, 23 tube tissues were needed for both NO and AD. Since we collected both NO and AD tubes from single patients, we needed 23 patients. Based on the assumption of a 35% failure rate of tissue sampling and a 15% rate of withdrawal of consent, we planned to enroll 40 patients. The efficacy of thermal destruction for residual TE between tissues from NO and AD was compared using the Chi-square test.

Results

In total, 40 patients were enrolled in this study from September 2012 to July 2014. LESS total hysterectomy was successfully performed in all 40 patients. However, 14 patients were excluded from the data analysis; in 10 patients who received transvaginal morcellation, the cornual tissue could not be identified, and in the remaining 4 patients, histopathologic evaluation could not be performed due to insufficient tissue sampling. No patients withdrew consent. Thus, 26 patients were included in the data analysis. Additional thermal cauterization was applied to nine right-sided uterine cornua and 17 left-sided uterine cornua. Baseline characteristics are presented in Table 1. During surgery and in the 6-week follow-up period, no complications were recorded.

Histologic evaluations were available for 52 fallopian tubes (156 cornual tissue samples) from the 26 patients. The AD group comprised nine sets from the right cornu of the RC group and 17 sets from the left cornu of the LC group. The NO group comprised nine sets from the left cornu of the RC group and 17 sets from the right cornu of the LC group (Figure 1).

To evaluate the efficacy of thermal spread at the cornu, we compared thermal destruction between NO and AD tissues. The rates of thermal destruction of cornual tissues in the NO and AD groups were 3.8% (1/26) and 100% (26/26), respectively ($p < 0.001$). In the AD group, 80.8% (21/26) cornual tissues showed complete thermal destruction (Table 2, Supplement 1).

Next, we determined the positive rate of residual TE and the efficacy of thermal destruction of residual TE. Residual TE was found in 69.2% (36/52) of the uterine cornua. In NO and AD groups, 73.1% (19/26) and 65.4% (17/26) of cornua were positive for TE, respectively ($p = 0.764$). The rates of thermal destruction of

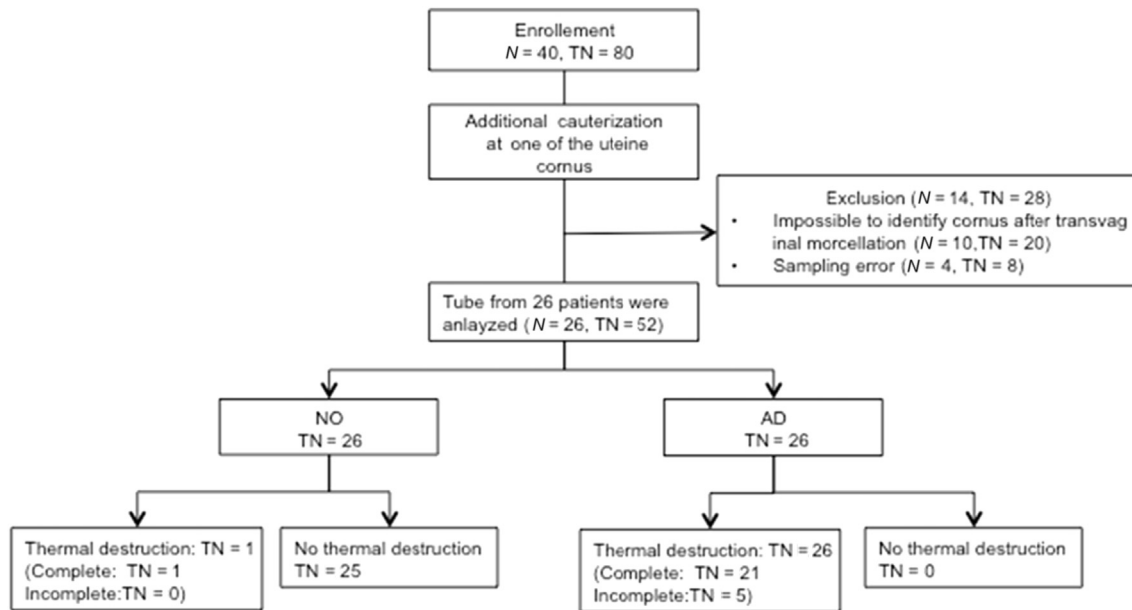


Figure 1. A total of 40 patients were enrolled in this study. The uterine cornu on one side was treated with additional cauterization. The laterality of additional cauterization was decided randomly. Fourteen patients were excluded from histopathologic examination. We collected a total of 52 cornual interstitial tubal tissues from 26 patients for histopathologic examination. AD = tissue group with additional cauterization performed with a sealing device at the uterine cornu; N = number of patients; NO = tissue group without additional cauterization performed with a sealing device at the uterine cornu; TN = number of interstitial cornual tubes.

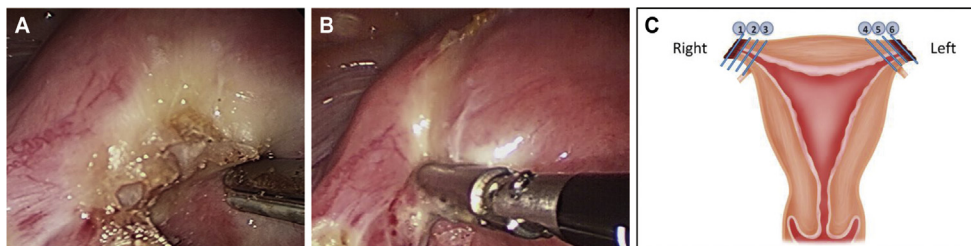


Figure 2. (A) First, the salpinx was resected using a sealing device. (B) After resection of the salpinx, additional cauterization was applied to the uterine cornu for 10 seconds. (C) After the uterus was extracted through the vagina, cornual tissues were obtained. Tissues were numbered from 1 to 6 sequentially from right lateral to left lateral.

residual TE were 5.3% (1/19) and 94.1% (16/17) in NO and AD groups, respectively ($p < 0.001$).

The number of patients with residual TE was determined. In total, 84.6% (22/26) patients displayed residual tube tissue in at least one of the tube samples in the microscopic examination. Furthermore, 95.5% (21/22) patient samples who received additional cauterization showed complete destruction of residual TE.

Discussion

To our knowledge, this is the first randomized clinical trial to evaluate the efficacy of thermal destruction of TE using a vessel sealing device at the uterine cornua to achieve complete removal of TE. Specifically, we describe the effect of 10 seconds of additional cauterization at the uterine cornu. The additional cauterization by the vessel sealing device induced thermal destruction of buried tubal tissue at the uterine cornu. The significance of our study is that we report the incidence of residual TE at the uterine cornu after salpingectomy and suggest a method to destroy residual TE at this location.

In an attempt to avoid complications of early menopause by reducing risk via bilateral salpingo-oophorectomy in patients with BRCA mutations,⁸ several studies are ongoing regarding

salpingectomy or salpingectomy and delayed oophorectomy (NCT01907789, NCT01929148, NCT01907789, NCT02321228, and NCT01608074). In our institute, we perform opportunistic salpingectomies in addition to other gynecologic surgeries, such as hysterectomies and oophorectomies, in low-risk patients if requested by the patient. However, it was unclear whether we are able to completely remove the TE with conventional procedures.

The advanced vessel sealing system relies on the application of a precise amount of bipolar electrocoagulation and pressure to the tissue. Hemostasis induced by this system results from the denaturation of collagen and elastin in vessel walls.⁹ Compared with conventional bipolar instruments, this vessel sealing system has a reduced thermal spread profile as it employs programmed feedback control.¹⁰ We had to reactivate cauterization to complete 10 seconds of activation time because of this feedback program. This repeated reactivation caused thermal spread to adjacent cornual segments.

We hypothesized that additional application of this device could completely destroy residual TE inside the uterine cornu. Thermal destruction of residual TE was effective, but complete destruction was not achieved (94.1% in AD tissues, 5.3% in NO tissues). This result indicates that additional cauterization facilitates destruction of residual TE.

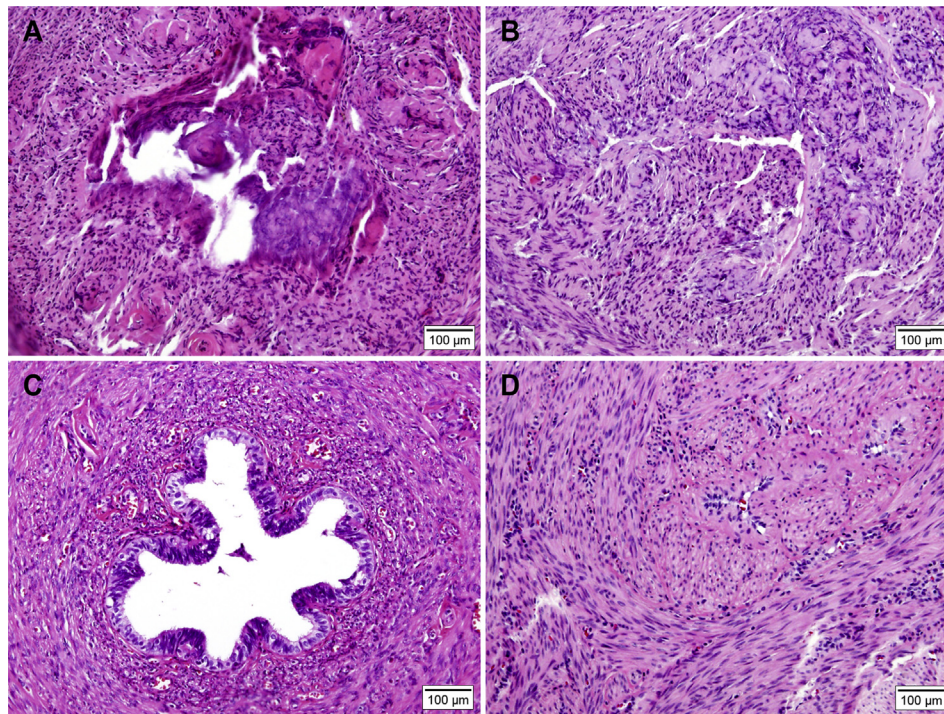


Figure 3. (A) Tubal epithelium presenting with thermal destruction. (B) Tubal epithelium without thermal destruction. (C) Tubal epithelium presenting without thermal destruction. (D) Tubal epithelium without thermal destruction. (Original magnification, $\times 200$).

Table 1
Baseline characteristics and surgical procedures.

| | Enrolled patients ($n = 26$) |
|--|--------------------------------|
| Age (y), median (range) | 43.5 (37–57) |
| Previous abdominal surgeries | |
| 1 | 1 (3.8) |
| 2 | 5 (19.2) |
| ≥ 3 | 1 (3.8) |
| Indication for surgery | |
| Symptomatic uterine myoma and/or adenomyosis | 22 (84.6) |
| Cervical dysplasia | 1 (3.8) |
| Endometrial pathology | 1 (3.8) |
| Uterine prolapse | 2 (7.6) |
| Surgical procedure | |
| TLH + BS | 21 (80.8) |
| TLH + BSO or USO + US | 4 (15.4) |
| TLH + BSO + uterosacral ligament suspension | 1 (3.8) |

Data are presented as n (%).

BS = bilateral salpingectomy; BSO = bilateral salpingo-oophorectomy; TLH = total laparoscopic hysterectomy; US = unilateral salpingectomy; USO = unilateral salpingo-oophorectomy.

Our study has several limitations. First, the sample size was too small for the results to be generalizable to a larger population. Second, we randomly selected one of the tubes based on the assumption that both tubes were in the same condition in a single patient's uterus, but in fact asymmetry existed around the cornua and tubes of the same uterus. Third, the rate of residual TE may be underestimated due to sampling difficulties. A uterine cornu must have TE, but we found only 69.2% TE. The location of sampling was a portion of the tube that transitioned to the uterine body. In addition, the shape of the uterus was often more globular than normal, or irregular, due to the presence of benign disease, such as adenomyosis or myoma. Therefore, it was nearly impossible to make an even perpendicular cut for tissue sampling. Characteristics of the uteri in our study led to difficulty in grabbing and sampling the

Table 2
Thermal destruction of tubal epithelium at the uterine cornu.

| | Residual TE | TD | Complete TD |
|-----------------|------------------|---------|-------------|
| NO (26) | 19 (TD: 1) | 1 | 1 |
| AD (26) | 17 (TD: 16) | 26 | 21 |
| <i>p</i> -value | 0.764* (0.001**) | < 0.001 | < 0.001 |
| Total (52) | 36 | 27 | 22 |

NO = no additional cauterization, AD = additional cauterization, TE = tubal epithelium, TD = thermal destruction. NO and AD were compared, and *p*-values were calculated. * *p*-value comparing proportion of Residual TE between NO and AD. ** *p*-value comparing of proportion of Thermal destruction between NO and AD.

uterine cornua. Underestimation of residual TE and incomplete thermal destruction may be attributed to these difficulties. Fourth, since this is the first study to remove residual cornual TE, we do not know how much this method has an additional effect in ovarian cancer prevention as compared to conventional salpingectomy without removal of cornual TE. A long-term follow-up study in a large population should be conducted to answer this question.

In conclusion, to achieve full prophylactic efficacy of salpingectomy, complete removal of TE is imperative. This study suggests a high incidence of residual TE after salpingectomy and that additional cauterization at the uterine cornu is a feasible method of destroying residual TE.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.gmit.2016.12.005>.

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