Surgical and obstetrical outcomes after laparoscopic radical trachelectomy and pelvic lymphadenectomy for early cervical cancer

So-Eun Yoo, Kyeong A So, Seon-Ah Kim, Mi Kyung Kim, Yoo Kyung Lee, In-Ho Lee, Tae-Jin Kim, Ki Heon Lee

Department of Obstetrics and Gynecology, Cheil General Hospital & Women’s Healthcare Center, Dankook University College of Medicine, Seoul, Korea

Objective
The aim of this study was to evaluate the surgical and obstetrical outcomes of patients with early cervical cancer who underwent laparoscopic radical trachelectomy and pelvic lymphadenectomy.

Methods
We analyzed data from women who underwent laparoscopic radical trachelectomy and pelvic lymphadenectomy between July 2000 and October 2014.

Results
Of a total of 12 patients, 91.7% were FIGO (International Federation of Gynecology and Obstetrics) stages IA2 and IB1. Seven patients (58.3%) had squamous cell carcinoma. The median tumor size was 1.87 cm (range, focal to 4.6 cm) and two patients (16.7%) had a tumor larger than 2 cm. Lymphovascular space invasion in the tumor lesion was reported in six patients (50%). The following surgical complications were observed: neurogenic bladder (one patient), hemoperitoneum (one patient), and infection (one patient). A total of 33.3% had attempted to conceive, resulting in two pregnancies and two healthy babies. All pregnancies were achieved by in vitro fertilization and embryo transfer. Each woman underwent cesarean delivery because of premature pre-labor rupture of membranes at gestational weeks 27.3 and 33.3. After a median follow-up time of 4.4 years (range, 1 to 8 years), there were no recurrences or deaths.

Conclusion
Laparoscopic radical trachelectomy and pelvic lymphadenectomy should be offered as an alternative treatment for women with early stage cervical cancer who want to preserve their fertility.

Keywords: Cervical cancer; Laparoscopy; Pregnancy; Trachelectomy

Introduction
Cervical cancer is the fourth most common cancer in women worldwide with an estimated 528,000 new cases in 2012 [1], and it is the seventh most common female cancer and the seventh leading cause of female cancer death in the Republic of Korea [2,3]. According to the five major sites of cancer by age group and sex in Korea 2012, cervical cancer is the third most common cancer in females aged 15 to 35 [4].

The traditional treatment for early cervical cancer was radical hysterectomy, which confers a five-year survival of 90% for women with stage Ib1 disease and 95% for stage Ia2 disease [5]. However, this method was not suitable for young

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women who desire to preserve their fertility. Radical trachelectomy, a fertility-sparing treatment for early cervical cancer, was introduced by Daniel Dargent, and was widely accepted as a reasonable alternative to radical hysterectomy for young women [6,7].

Previous reports indicate that radical trachelectomy results in oncologic outcomes similar to those for traditional radical hysterectomy for early-stage cervical cancer [8-10]. The aim of this study was to evaluate the surgical and obstetrical outcomes of patients with early cervical cancer who underwent laparoscopic radical trachelectomy and pelvic lymphadenectomy at our institution.

Materials and methods

Following approval by our institutional review board, we retrospectively reviewed the medical records of all women who underwent laparoscopic radical trachelectomy and pelvic lymphadenectomy in the Division of Gynecologic Oncology at Cheil Women’s Hospital from July 2000 to October 2014. All patient information and outcomes are archived in a central database at our institution. Inclusion criteria were: (1) confirmed early cervical cancer (stage IA2 to IB); (2) 45-years-old or younger with a desire for future pregnancies; (3) squamous cell carcinoma, adenocarcinoma or adenosquamous carcinoma; and (4) patients who underwent radical trachelectomy with pelvic and/or parametrial lymph node dissection. Patients with positive frozen section and/or permanent pathology were excluded.

Laparoscopic radical trachelectomy with pelvic lymphadenectomy begins with/without peritoneal washing cytology and then pelvic lymph node dissection. Intraoperative frozen biopsy of pelvic lymph nodes was performed. If metastatic pelvic lymph nodes were identified, trachelectomy was abandoned. If malignancy was not identified in the pelvic lymph nodes, radical trachelectomy was performed with preservation of the ascending branch of the uterine artery. After radical trachelectomy, the cervical specimen was sent for frozen biopsy to ensure the surgical margin was tumor-free. If the margin was negative, cerclage was performed.

Results

Twelve women who had undergone radical trachelectomy with laparoscopy procedures by five different gynecological oncologists were identified. The surgery was based on the individual surgeon’s experience and preference, and no patient received neoadjuvant chemotherapy prior to laparoscopic radical trachelectomy.

The general characteristics of these 12 patients are shown in Table 1. The median age was 33 years (range, 28 to 41 years). Eight (66.7%) patients underwent diagnostic cervical conization before undergoing laparoscopic radical trachelectomy and pelvic lymphadenectomy. Four (33.3%) patients underwent only colposcopic biopsy before undergoing laparoscopic radical trachelectomy and pelvic lymphadenectomy. Ten (83.3%) patients were found to be infected with high-risk human papillomavirus. Nearly all of the patients (91.7%) were stage IA2 and IB1.

The oncologic outcomes of the tumors are shown in Table 2. The median tumor size in the surgical specimens was 1.87 cm (range, focal to 4.6 cm). Two patients (16.7%) had a tumor larger than 2 cm, eight patients (66.7%) had squamous cell carcinoma, and six patients (50%) had lymphovascular space invasion in the tumor lesion. Five patients had undergone

| Characteristics | Value |
|-----------------|-------|
| Age (yr)        | 33.3 (28–41) |
| Marriage        | 6 (50) |
| Parity          |       |
| Nulliparous     | 8 (66.7) |
| Multiparous     | 4 (33.3) |
| Human papillomavirus infection | |
| Positive        | 10 (83.3) |
| Negative        | 2 (16.7) |
| Squamous cell carcinoma antigen (ng/mL) | |
| ≤1.0            | 9 (75) |
| >1.0            | 3 (25) |
| Diagnostic conization | |
| Done            | 8 (66.7) |
| Not done        | 4 (33.3) |
| Stage           |       |
| IA2             | 2 (16.7) |
| IB1             | 9 (75) |
| IB2             | 1 (8.3) |
| Follow-up (mo)  | 48.7 (12–94) |

Values are presented as median (range) or number (%).
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Peritoneal washing with cytology, none of which revealed malignant cells. We performed peritoneal washing cytology of five patients because four of them had adenocarcinoma and adenosquamous carcinoma of cervix. Previous studies reported that positive peritoneal cytology was associated with poor prognosis only in the patients with adenocarcinoma or adenosquamous carcinoma, but not in those with squamous cell carcinoma [11,12]. The one of five who had a tumor size larger than 4 cm had peritoneal cytology by the subjective opinion of physician.

One patient received adjuvant chemotherapy with three cycles of paclitaxel and carboplatin because she was at intermediate-risk of recurrence due to a tumor diameter larger than 4 cm and also lymphovascular space invasion was positive. Although she had intermediate risk factors for recurrence, she had a strong desire to preserve her fertility. For this reason, we decided chemotherapy instead of concurrent chemoradiation therapy for preserving her ovarian function. This patient had no evidence of cancer recurrence until recently and is attempting to conceive with the assistance of an infertility specialist at our hospital.

Surgical outcomes were shown in Table 2. The mean operating time was 3 hours 50 minutes (range, 2.2 to 5.5 hours). The mean estimated blood loss was 691.7 mL (range, 300 to 2,500 mL). Perioperative transfusion was required in two patients (16.7%). One patient had hemoperitoneum requiring a second laparoscopy for uterine artery ligation. One patient had postoperative infection managed conservatively with intravenous antibiotics. None of these patients have persistent problems. However, one patient had neurogenic bladder and was treated by a urologist for five years. Of the 12 patients, one patient underwent laparoscopic-assisted vaginal hysterectomy one year after trachelectomy. She was suspected of recurrence with increased 18F-fluorodeoxyglucose uptake of cervical lip at follow-up positron emission tomography-computed tomography and wanted a curative treatment rather than preserving fertility.

Obstetrical outcomes are shown in Table 3. Six out of twelve were married and four out of twelve patients (33.3%) had attempted to conceive. Three patients conceived by in vitro fertilization and embryo transfer (IVF/ET), resulting in two pregnancies and two healthy babies. None of the women who became pregnant received adjuvant treatment after surgery. Both women underwent cesarean delivery because of premature pre-labor rupture of membranes at 27.3 and 33.3 gestational weeks. The patient who underwent cesarean de-

### Table 2. Oncological and surgical outcomes

| Characteristics                    | Value |
|------------------------------------|-------|
| Histology of tumor                 |       |
| Squamous cell carcinoma            | 8 (66.7) |
| Adenocarcinoma                     | 3 (25) |
| Adenosquamous carcinoma            | 1 (8.3) |
| Size of tumor (median [range], cm) |       |
| ≤2                                 | 10 (83.3) |
| >2                                 | 2 (16.7) |
| Lymphovascular space invasion      | 6 (50) |
| Cytology                           |       |
| Positive                           | 0     |
| Negative                           | 5 (100.0) |
| Harvested lymph node (range, number) | 23.5 (9–39) |
| Lymph node metastasis              | 0     |
| Adjuvant treatment                 |       |
| Chemotherapy                       | 1 (8.3) |
| Radiation                          | 0     |
| Recurrence                         | 0     |
| Death                              | 0     |
| Operative time (mean [range], hr)  | 3.85 (2.2–5.5) |
| Estimated blood loss (mean [range], mL) | 691.7 (300–2,500) |
| Transfusion                        | 2 (16.7) |
| Perioperative complications         | 3 (25) |
| Neurogenic bladder                 | 1 (8.3) |
| Hemoperitoneum                     | 1 (8.3) |
| Infection                          | 1 (8.3) |
| Hysterectomy                       | 1 (8.3) |

Values are presented as number (%) unless otherwise indicated.

### Table 3. Obstetrical outcomes

| Characteristics                  | Value |
|----------------------------------|-------|
| Attempted to conceive            | 4/12 (33.3%) |
| Pregnancy                        | 2     |
| Pregnancy type                   |       |
| Natural                          | 0     |
| In vitro fertilization           | 2     |
| Preterm labor and treatment      | 2     |
| Delivery type                    |       |
| Vaginal delivery                 | 0     |
| Cesarean section                 | 2     |
livery at 27.3 gestational weeks was hospitalized from 20.4 to 22.5 gestation weeks and received blood transfusions due to vaginal bleeding that continued from the cerclage site.

Discussion

Radical hysterectomy is the standard treatment for early stage cervical cancer in young women who desire to preserve their fertility. Potential candidates for radical trachelectomy are young women, who comprise more than 25% of cervical cancer diagnoses [13,14]. This means that the desire for radical tracheectomy would increase as the majority of these women would likely want to have a child after surgery. Several case series have been published supporting the safety of radical tracheectomy in terms of oncological and fertility outcomes [15]. Universal indications for radical tracheectomy in these women are (1) 40-years-old or less, (2) strong desire to preserve fertility, (3) usual histologic type including squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma, and (4) a tumor size less than 2 cm [16]. Even one of universal indications is a tumor size less than 2 cm, two of patients who had a tumor larger than 2 cm received laparoscopic tracheectomy with pelvic lymph node dissection because these patients were no evidence for metastatic lesion from other workup studies and had a strong desire to preserve their fertility.

Several methods for radical tracheectomy, such as laparoscopic, abdominal, or vaginal tracheectomy, have been reported. Radical vaginal tracheectomy with laparoscopic lymph node dissection for early cervical cancer was introduced and described by Daniel Dargent [7] and has been widely accepted. However, trans-vaginal tracheectomy has some disadvantages, including difficulty learning radical vaginal surgery and a possible incomplete parametrial resection [17]. Abdominal tracheectomy is comparable to radical hysterectomy. In addition, abdominal tracheectomy has similar pregnancy rates to those reported after vaginal tracheectomy (16% vs. 24%) and a lower intraoperative complications rate (0.7%) compared with vaginal tracheectomy (5.6%) [18,19].

Among these methods, laparoscopic radical tracheectomy is the more challenging surgical approach and seems to be the growing trend in radical tracheectomy [20,21]. Laparoscopic radical tracheectomy compensates for the deficits of vaginal tracheectomy and also improves upon the strengths of abdominal tracheectomy. Several studies have shown that the outcomes of laparoscopic tracheectomy were acceptable and the morbidity rate was very low [20]. Park et al. [16] demonstrated that laparoscopic radical tracheectomy is a feasible and safe fertility-sparing surgery for young women with early-stage cervical cancer. Laparoscopic tracheectomy has many advantages associated with minimally invasive procedures, including enhanced visualization, more precise dissection, less blood loss, fewer complications, and shorter length of hospital stay [22]. In our series, the surgical outcomes were also favorable. Even though we cannot draw comparisons with other methods of tracheectomy, laparoscopic tracheectomy offers many advantages to young women with early-stage cervical cancer who want to preserve their fertility.

There have been several studies of pregnancy rates after radical tracheectomy in recent years [18,23,24]. We are well aware that IVF/ET is not necessary for all patients who undergo laparoscopic radical tracheectomy and pelvic lymphadectomy; nonetheless all patients were successful with IVF/ET in this study. The Danish National Single Center Strategy study showed that 58 (75.3%) pregnancies were spontaneous, but as many as 40 of 72 patients were referred to fertility treatment [24]. It is very important to provide precise information about reproductive techniques, such as intrauterine insemination or in vitro fertilization with or without intracytoplasmic sperm injection.

There are several crucial pregnancy complications that can occur following radical tracheectomy. The preterm birth rate after laparoscopic radical tracheectomy was about 24% in several published studies [25]. Regardless of the type of radical tracheectomy, the preterm birth rate is higher than that of the general population (10%) [26]. The cervical shortening that occurs as the result of radical tracheectomy increases the risk of infection and can lead to cervical incompetence and decreased uterine blood flow during pregnancy [27]. Whether cerclage influences perinatal outcomes is a subject of controversy; however, a previous study showed that cervical cerclage placed at the time of radical tracheectomy plays an important role in the prevention of dilatation of the residual uterine cervical canal and the subsequent occurrence of premature labor rupture of membranes [28].

Our study has some limitations in that it was a retrospective study with a small number of patients and a lack of consistency in data recording. Multicenter prospective studies are needed to confirm our data. Nonetheless, laparoscopic radi-
Laparoscopic radical trachelectomy by a well-trained gynecological oncologist should be offered as an alternative treatment for women with early-stage cervical cancer who wish to preserve their fertility. The infertility team can also actively participate in the care of women who underwent radical trachelectomy given the risk of infertility. Women who do successfully conceive should be regarded as high-risk and should be followed carefully by dedicated obstetricians.

**Conflict of interest**

No potential conflict of interest relevant to this article was reported.

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