

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

Received: 2016.3.17. Revised: 2016.5.11. Accepted: 2016.5.13.

Corresponding author: Ki Heon Lee

Department of Obstetrics and Gynecology, Cheil General Hospital & Women's Healthcare Center, Dankook University College of Medicine, 17 Seoae-ro 1-gil, Jung-gu, Seoul 04619, Korea

Tel: +82-2-2000-7577 Fax: +82-2-2000-7477

E-mail: 1103khl@hanmail.net

http://orcid.org/0000-0002-4079-9035

Articles published in *Obstet Gynecol Sci* are open-access, distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

Copyright © 2016 Korean Society of Obstetrics and Gynecology

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 para-aortic 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 laparoscopic 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

Table 1. Patient characteristics

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 (%).

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)	1.87 (focal–4.6)
≤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.

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.

Table 3. Obstetrical outcomes

Characteristics	Value
Attempted to conceive	4/12 (33.3%)
Pregnancy	2
Pregnancy type	
Natural	0
<i>In vitro</i> fertilization	2
Preterm labor and treatment	2
Delivery type	
Vaginal delivery	0
Cesarean section	2

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-

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 trachelectomy 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 trachelectomy in terms of oncological and fertility outcomes [15]. Universal indications for radical trachelectomy 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 trachelectomy 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 trachelectomy, such as laparoscopic, abdominal, or vaginal trachelectomy, have been reported. Radical vaginal trachelectomy 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 trachelectomy has some disadvantages, including difficulty learning radical vaginal surgery and a possible incomplete parametrial resection [17]. Abdominal trachelectomy is comparable to radical hysterectomy. In addition, abdominal trachelectomy has similar pregnancy rates to those reported after vaginal trachelectomy (16% vs. 24%) and a lower intraoperative complications rate (0.7% compared with vaginal trachelectomy (5.6%) [18,19].

Among these methods, laparoscopic radical trachelectomy is the more challenging surgical approach and seems to be the growing trend in radical trachelectomy [20,21]. Laparoscopic radical trachelectomy compensates for the deficits of vaginal trachelectomy and also improves upon the strengths

of abdominal trachelectomy. Several studies have shown that the outcomes of laparoscopic trachelectomy were acceptable and the morbidity rate was very low [20]. Park et al. [16] demonstrated that laparoscopic radical trachelectomy is a feasible and safe fertility-sparing surgery for young women with early-stage cervical cancer. Laparoscopic trachelectomy 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 trachelectomy, laparoscopic trachelectomy 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 trachelectomy in recent years [18,23,24]. We are well aware that IVF/ET is not necessary for all patients who undergo laparoscopic radical trachelectomy and pelvic lymphadenectomy; 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 trachelectomy. The preterm birth rate after laparoscopic radical trachelectomy was about 24% in several published studies [25]. Regardless of the type of radical trachelectomy, the preterm birth rate is higher than that of the general population (10%) [26]. The cervical shortening that occurs as the result of radical trachelectomy 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 trachelectomy plays an important role in the prevention of dilatation of the residual uterine cervical canal and the subsequent occurrence of premature prelabor 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-

cal 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.

References

1. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin* 2014;64:9-29.
2. Jung KW, Won YJ, Kong HJ, Oh CM, Seo HG, Lee JS. Cancer statistics in Korea: incidence, mortality, survival and prevalence in 2010. *Cancer Res Treat* 2013;45:1-14.
3. Lee YH, Choi KS, Lee HY, Jun JK. Current status of the National Cancer Screening Program for cervical cancer in Korea, 2009. *J Gynecol Oncol* 2012;23:16-21.
4. Jung KW, Won YJ, Kong HJ, Oh CM, Cho H, Lee DH, et al. Cancer statistics in Korea: incidence, mortality, survival, and prevalence in 2012. *Cancer Res Treat* 2015;47:127-41.
5. Quinn MA, Benedet JL, Odicino F, Maisonneuve P, Beller U, Creasman WT, et al. Carcinoma of the cervix uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. *Int J Gynaecol Obstet* 2006;95 Suppl 1:543-103.
6. Dargent D, Brun JL, Roy M, Remy I. Pregnancies following radical trachelectomy for invasive cervical cancer. *Gynecol Oncol* 1994;54:105.
7. Rob L, Skapa P, Robova H. Fertility-sparing surgery in patients with cervical cancer. *Lancet Oncol* 2011;12:192-200.
8. Plante M, Renaud MC, Hoskins IA, Roy M. Vaginal radical trachelectomy: a valuable fertility-preserving option in the management of early-stage cervical cancer. A series of 50 pregnancies and review of the literature. *Gynecol Oncol* 2005;98:3-10.
9. Diaz JP, Sonoda Y, Leitao MM, Zivanovic O, Brown CL, Chi DS, et al. Oncologic outcome of fertility-sparing radical trachelectomy versus radical hysterectomy for stage IB1 cervical carcinoma. *Gynecol Oncol* 2008;111:255-60.
10. Einstein MH, Park KJ, Sonoda Y, Carter J, Chi DS, Barakat RR, et al. Radical vaginal versus abdominal trachelectomy for stage IB1 cervical cancer: a comparison of surgical and pathologic outcomes. *Gynecol Oncol* 2009;112:73-7.
11. Kasamatsu T, Onda T, Sasajima Y, Kato T, Ikeda S, Ishikawa M, et al. Prognostic significance of positive peritoneal cytology in adenocarcinoma of the uterine cervix. *Gynecol Oncol* 2009;115:488-92.
12. Kuji S, Hirashima Y, Komeda S, Tanaka A, Abe M, Takahashi N, et al. The relationship between positive peritoneal cytology and the prognosis of patients with FIGO stage III uterine cervical cancer. *J Gynecol Oncol* 2014;25:90-6.
13. Sonoda Y, Abu-Rustum NR, Gemignani ML, Chi DS, Brown CL, Poyner EA, et al. A fertility-sparing alternative to radical hysterectomy: how many patients may be eligible? *Gynecol Oncol* 2004;95:534-8.
14. Watson M, Saraiya M, Benard V, Coughlin SS, Flowers L, Cokkinides V, et al. Burden of cervical cancer in the United States, 1998-2003. *Cancer* 2008;113(10 Suppl):2855-64.
15. Faber-Swensson AP, Perrin LC, Nicklin JL. Radical trachelectomy for early stage cervical cancer: the Queensland experience. *Aust N Z J Obstet Gynaecol* 2014;54:450-2.
16. Park JY, Joo WD, Chang SJ, Kim DY, Kim JH, Kim YM, et al. Long-term outcomes after fertility-sparing laparoscopic radical trachelectomy in young women with early-stage cervical cancer: an Asan Gynecologic Cancer Group (AGCG) study. *J Surg Oncol* 2014;110:252-7.
17. Plante M, Roy M. Fertility-preserving options for cervical cancer. *Oncology (Williston Park)* 2006;20:479-88.
18. Pareja R, Rendon GJ, Sanz-Lomana CM, Monzon O, Ramirez PT. Surgical, oncological, and obstetrical outcomes after abdominal radical trachelectomy: a systematic literature review. *Gynecol Oncol* 2013;131:77-82.
19. Plante M, Gregoire J, Renaud MC, Roy M. The vaginal radical trachelectomy: an update of a series of 125 cases and 106 pregnancies. *Gynecol Oncol* 2011;121:290-7.

20. Kim JH, Park JY, Kim DY, Kim YM, Kim YT, Nam JH. Fertility-sparing laparoscopic radical trachelectomy for young women with early stage cervical cancer. *BJOG* 2010;117:340-7.
21. Chang SJ, Ryu HS, Nam JH. Uterine artery-preserving laparoscopic radical trachelectomy for early cervical cancer: technical aspects. *Gynecol Oncol* 2012;126:277-8.
22. Nam JH, Kim JH, Kim DY, Kim MK, Yoo HJ, Kim YM, et al. Comparative study of laparoscopico-vaginal radical hysterectomy and abdominal radical hysterectomy in patients with early cervical cancer. *Gynecol Oncol* 2004;92:277-83.
23. Kim CH, Abu-Rustum NR, Chi DS, Gardner GJ, Leitao MM Jr, Carter J, et al. Reproductive outcomes of patients undergoing radical trachelectomy for early-stage cervical cancer. *Gynecol Oncol* 2012;125:585-8.
24. Hauerberg L, Hogdall C, Loft A, Ottosen C, Bjoern SF, Mosgaard BJ, et al. Vaginal Radical Trachelectomy for early stage cervical cancer: results of the Danish National Single Center Strategy. *Gynecol Oncol* 2015;138:304-10.
25. Lu Q, Liu C, Zhang Z. Total laparoscopic radical trachelectomy in the treatment of early-stage cervical cancer: review of technique and outcomes. *Curr Opin Obstet Gynecol* 2014;26:302-7.
26. Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al. Preterm birth. In: Cunningham FG, Leveno KJ, Bloom SL, Spong CY, Dashe JS, Hoffman BL, et al., editors. *Williams obstetrics*. 24th ed. New York (NY): McGraw-Hill; 2014. p.829-61.
27. Bernardini M, Barrett J, Seaward G, Covens A. Pregnancy outcomes in patients after radical trachelectomy. *Am J Obstet Gynecol* 2003;189:1378-82.
28. Kim M, Ishioka S, Endo T, Baba T, Akashi Y, Morishita M, et al. Importance of uterine cervical cerclage to maintain a successful pregnancy for patients who undergo vaginal radical trachelectomy. *Int J Clin Oncol* 2014;19:906-11.