

Original Article

Radical trachelectomy for early stage cervical cancer: A case series and literature review



Chin-Jui Wu ^{a, b}, Wen-Chun Chang ^{a, b}, Chi-Hau Chen ^{a, b}, Chi-An Chen ^{a, b},
Su-Cheng Huang ^c, Bor-Ching Sheu ^{a, b, d, *}

^a Department of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan

^b College of Medicine, National Taiwan University, Taipei, Taiwan

^c Department of Obstetrics and Gynecology, Buddhist Tzu-Chi General Hospital, Taipei Branch, Taipei, Taiwan

^d Centre for Optoelectronic Biomedicine, National Taiwan University College of Medicine, Taipei, Taiwan

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ABSTRACT

Objective: Radical trachelectomy (RT) is an alternative treatment for preserving fertility in patients with cervical cancer. Because women with operable cervical cancer opting for fertility preservation are scarce, few cases have been reported in Taiwan. Here we report our cases series.

Materials and Methods: We retrospectively evaluated seven patients who underwent vaginal RT and three patients who underwent abdominal RT in a single medical institute for a median follow-up period of 5 years.

Results: The oncological outcome was highly satisfactory. All patients survived and are currently disease-free, except for two who had recurrence and received additional concurrent chemoradiation therapy. Other complications included urinary tract infection, cervical stenosis, and unilateral hydronephrosis. All complications were manageable with little long-term effects. However, no pregnancy was observed during the 5-year follow-up period.

Conclusion: RT is considered a complicated surgical procedure among gynecological operations. Here we review the literature and describe several factors associated with higher pregnancy rates.

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Introduction

The incidence of cervical cancer has declined since the implementation of the National Health Insurance program in Taiwan in 1995, and it has dropped from 20.1/100,000 cases in 1995 to 13.4/100,000 cases in 2012 [1,2]. In all new-onset cervical cancer cases, approximately 23% occur during fertility [2]. Radical trachelectomy (RT) is a traditional treatment option with satisfactory oncological and obstetrical outcomes. RT can be performed through a vaginal, abdominal, laparoscopic, or robotic approach and is coupled with an open or laparoscopic pelvic lymph node dissection. According to the 2014 National Comprehensive Cancer Network cervix cancer guidelines, RT can be performed in patients with early stage cervical cancer (Stage IA1 with lymph-vascular space invasion, Stage IA2, and Stage IB1) who desire fertility preservation; however, the

guidelines state, “fertility-sparing surgery for stage IB1 has been validated for tumors < 2 cm.” Vaginal RT (VRT) should not be performed in patients with tumors ≥ 2 cm because of a high relapse rate (22%) [3–5].

Dr. Daniel Dargent introduced RT in 1987 [6,7] and removed the uterine cervix and adjacent tissues. RT for patients with early stage cervical cancer is associated with a satisfactory live birth rate [7,8]. The pregnancy and live birth rates after vaginal, abdominal, or laparoscopic trachelectomy vary from 10% to 30%. However, the operative method appears to have improved given the recent increase in the pregnancy rate. Papers published after 2006 have reported higher conception rates [9]. The first published RT in Taiwan was in 2003 [10]. After that, we found little data on RT in Asian women. The large-series reviews are mainly in Western countries.

The aim of this article was to compare the oncologic and pregnancy outcomes of RT in the past decade in Taiwan. Based on our data and review of the literature, we propose some improvements for the surgery.

* Corresponding author. Department of Obstetrics and Gynecology, National Taiwan University Hospital, Number 7, Chung-Shan South Road, Taipei 100, Taiwan.
E-mail address: bcsheu@ntu.edu.tw (B.-C. Sheu).

Materials and methods

Study population

Between 2002 and 2015, 11 young women diagnosed with early stage cervical cancer underwent fertility-preserving RT at National Taiwan University Hospital, Taipei, Taiwan. All patients underwent preoperative magnetic resonance imaging for precise cancer staging. The inclusion criteria for candidate selection were as follows: (1) histologically proven with clinical and image Stage IA2–IB1 cervical cancer; (2) age < 40 years; (3) desiring fertility preservation; (4) no evidence of endocervical involvement; (5) no evidence of pelvic or paraaortic lymphadenopathy; (6) exclusion of unfavorable histology (small cell or neuroendocrine); and (7) tumor size < 2 cm. One patient was excluded because of an inadequate indication. All other patients received detailed consultations regarding the operation, and informed consent was obtained. We have the Institutional Review Board (National Taiwan University Hospital) approval for release of medical records for research purposes (201603010RIN).

Seven of the patients underwent VRT. However, three patients underwent abdominal RT (ART). We included these three patients for comparing the outcomes of both procedures. We retrospectively reviewed patients' medical charts and conducted telephone interviews for assessing menstrual and pregnancy conditions. Follow-up data were collected and analyzed.

Surgical techniques for VRT

The VRT procedure applied was a modification of the Schauta-Stoeckel technique. First, the lymph nodes were laparoscopically dissected. The dissected nodes were then sent for frozen section examination to ensure their true-negative status. The vaginal region was resected at least 2 cm starting from the vaginal cuff. Subsequently, the paravesical and pararectal spaces were vaginally opened and developed for identifying the ureter in the uterovesical ligament. We resected half of the cardinal and uterosacral ligaments to free them from the surrounding tissue. The cervix was transected at the lower uterine segment with at least 5 mm of the free endocervical margin. We sutured the lower uterine segment with Mersilene (Mersilene tape, Ethicon, San Angelo, Texas, USA). The vaginal mucosa was sutured to the lower uterine segment. An 8-French rubber catheter was placed in the endocervical canal for 3 weeks. Figure 1 shows the resected specimen.

Surgical techniques for ART

The ART procedure was similar in part to a radical hysterectomy procedure. We exposed the uterus and dissected the bilateral pelvic

lymph nodes first. After the development of the pararectal and paravesical spaces, the bilateral parametria were exposed. The rectovaginal space was exposed, and the uterosacral ligaments were resected. We cut the cervix at the level of the isthmus including at least 2 cm of the upper vagina. Finally, we sutured the vaginal cuff with the lower uterine segment with 1-0 synthetic absorbable surgical suture (Coated Vicryl, Ethicon). Cerclage was performed vaginally as in VRT. We performed a suprapubic cystostomy before closing the abdominal wound to prevent urine retention and removed it 2–3 weeks postoperatively.

Results

Among the remaining 10 patients, seven underwent VRT while three underwent ART. The operation time was approximately 300 minutes with little variation. Postoperative pathology revealed that seven patients had squamous cell carcinoma, and three had adenocarcinoma. Two patients had lymphovascular space invasion, and only one patient had positive lymph nodes. The average number of lymph nodes dissected was 25.7 (range, 17–48). The tumor size ranged from microscopic to as large as 3.5 cm in diameter (Table 1). Blood loss during the operation ranged from 300 mL to 800 mL. The postoperative hospital stays of patients who underwent VRT and ART were 15.8 days (10–21 days) and 17 days (13–22 days), respectively. One patient had a longer postoperative hospital stay because she was subjected to adjuvant therapy due to a positive vaginal margin. The mean follow-up period was 5.3 years.

In our case series, hydronephrosis was the main complication (Table 1). Two patients who underwent VRT developed unilateral hydronephrosis after returning home (Table 1). One case was transient and the other required regular ureter catheter replacement. One patient developed a urinary tract infection that was resolved with antibiotic treatment (Table 1, No. 4). Moreover, she developed cervical stenosis and required cervical dilatation twice. We did not encounter vaginal bleeding, pelvic lymphocele, or abscess as reported in other case series. All patients had resumed menstruation approximately 8 weeks after the operation. Three patients who underwent VRT reported spontaneous abortion, and none of the 10 patients reported live birth.

Only one patient who underwent VRT and laparoscopic pelvic lymph node dissection in 2007 exhibited recurrence (Table 1, No. 5). Her postoperative pathology revealed vaginal involvement, and she was diagnosed with Stage IIa1 cervical cancer. Her section margin was free, and a follow-up smear showed no abnormality. She did not require adjuvant therapy; she was regularly monitored as an outpatient after surgery. However, computed tomography performed 6 months later revealed a heterogeneous 3.8-cm diameter tumor extending from the lower part of the uterus to the vagina. Local recurrence was diagnosed. She was treated with

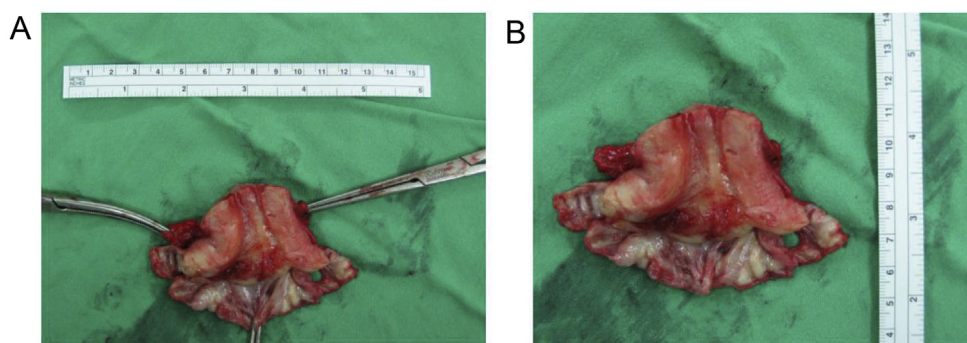


Figure 1. Vaginal radical trachelectomy specimens. (A) Cervical specimen with the bilateral parametria and vagina. (B) Cervix dissected to expose the cervical canal that is 4.3 cm in length.

Table 1
Patient characteristics and outcomes.

No.	Operation method	Age (y)	Parity	Marital status	Clinical stage	Pathologic stage	Histology	Tumor size (cm)	LVSI	Positive LN	Margin status	Complication	Follow-up (y)
1	VRT + LSC PLND	31	0	No	Ib1	Ib1	Adenocarcinoma	1.2	Negative	0	Negative	Nil	13
2	VRT + LSC PLND	39	0	No	Ib1	Ib1	SCC	1.5	Positive	0	Negative	Nil	3
3	VRT + LSC PLND	38	0	No	Ib1	Ib1	SCC	HSIL only	Negative	0	Negative	Hydronephrosis	7
4	VRT + LSC PLND	37	2	Yes	Ib1	Ib1	Adenocarcinoma	3	Negative	0	Negative	UTI, cervical stenosis	6
5	VRT + LSC PLND	29	0	No	Ib1	Ila1 ^a	SCC	3.5	Negative	0	Negative	Hydronephrosis	8
6	VRT + LSC PLND	33	0	Yes	Ib1	Ib1	SCC	0.3	Negative	0	Negative	Nil	3
7	VRT + LSC PLND	31	0	No	Ib1	HSIL	SCC	HSIL only	Negative	0	Negative	Nil	5
8	ART + PLND	31	0	No	Ib1	Ib1	SCC	2.3	Negative	0	Negative	Nil	4
9	ART + PLND	37	0	Remarried	Ib1	Ib1	SCC	1.6	Negative	0	Negative	Nil	3
10	ART + PLND	29	0	No	Ib1	Ila1	Adenocarcinoma	1.5	Positive	2	Vagina margin	Nil	1

ART = abdominal radical trachelectomy; HSIL = high-grade squamous intraepithelial carcinoma; LN = lymph node; LSC = laparoscopic; LVSI = lympho-vascular space invasion; PLND = pelvic lymph nodes dissection; SCC = squamous cell carcinoma; UTI = urinary tract infection; VRT = vaginal radical trachelectomy.

^a (5th patient, pathologic stage). The pathology report showed free surgical margin, but a perforation was found in the vaginal part of the specimen. Therefore, whether or not the lesion invaded the vagina could not be evaluated grossly. Based on our institutional conference, Stage Ila1 was suggested.

concurrent chemoradiation therapy. Radiation-induced bilateral obstructive uropathy occurred 1 year after adjuvant therapy. The patient required long-term, regular ureter catheter replacement; she had no evidence of recurrence.

Another patient had cervical cancer recurrence with a preoperatively estimated 1.5-cm diameter tumor (Table 1, No. 10). In 2014, she underwent ART, bilateral pelvic lymph node dissection, and prophylactic cerclage. The pathology revealed two lymph node metastases and vaginal margin involvement. She was informed about the local recurrence and fertility risks of adjuvant therapy with concurrent chemoradiation therapy or chemotherapy. She decided to undergo chemotherapy.

In addition to the two patients, who had a higher stage post-operatively than preoperatively, the other two patients (Table 1, No. 3 and No. 7) had pathologically high-grade squamous intraepithelial carcinoma. Compared with clinical Stage Ib1 preoperatively, the reason for the later occurrence of high-grade squamous intraepithelial carcinoma could have been the resection of invasive lesion during the previous diagnostic conization.

Discussion

Dr. Dargent published his first series on RT in 1994 [6]. The technique described included laparoscopic pelvic lymph node dissection and VRT through the preperitoneal approach. VRT is associated with a high preterm birth rate, which may be attributed to increased infection risk or cervical incompetence [9]. Several studies have reported the pregnancy outcomes of VRT (Table 2) [3–5,7,11–14]. We retrospectively reviewed a large case series (>30 patients) and observed that the term birth rates varied from 23.5% to 54.7%. The preterm birth rates were also high, ranging from 22.6% to 47%. Plante et al [5] reported the highest term birth rate and the lowest preterm delivery rate compared with those in other studies. This difference may be attributed to the various methods of operation used in different studies. Plante et al [3] performed cervical amputation 8–10 mm below the isthmus and an additional endocervical curettage. The retention of an additional 3–5 mm of endocervical tissue was supposed to produce a more favorable pregnancy outcome. Our procedure retained less endocervical

Table 2
Literature review of pregnancy outcomes.

1 st author (year)	Bernardini [15] (2003)	Hertel [14] (2006)	Marchiole [16] (2007)	Shepherd [13] (2006)	Einstein [17] (2009)	Plante [5] (2011)
Patient nos.	91	106	118	138	36	125
Operation type	VRT	VRT	VRT	VRT	VRT	VRT
Age (y)	30 (NA)	32 (21–41)	NA	30.6 (21–45)	31 (20–40)	31 (20–42)
Histology						
SCC	40	74	90	103	24	69
AC	50	33	25	51	16	48
Others	3	1	3	4	3	8
Tumor size (cm)						
<2	83	105	91	NA	36	111
>2	8	1	27	NA	0	14
LN positive	2	4	9	7	2	5
Lvsi	31	38	43	49	NA	32
Recurrence (cm)						
<2	5	3	1	NA	1	3
>2	1	1	6	NA	0	3
Death	4	2	5	4	1	2
Conception	22	17	56	88	11	106
1 st Trimester loss	3	3	14	22	3	21
2 nd Trimester loss	3	0	8	12	0	5
3 rd Trimester preterm	6	8	5	10	0	19
Term birth	12	4	29	35	4	58

AC = adenocarcinoma; LN = lymph node; LVSI = lympho-vascular space invasion; NA = not applicable; SCC = squamous cell carcinoma; VRT = vaginal radical trachelectomy.

tissue (<5 mm). The oncological outcome did not show a considerable difference in the recurrence rate among those with the additional 3–5 mm of the endocervix. This small variation needs further research to weigh the balance between pregnancy and recurrence adequately.

We evaluated the pregnancy outcomes in patients with early stage cervical cancer after they underwent fertility-preserving RT. Among our patients, none conceived successfully during the long-term follow-up period. This could have been because most of our patients were unmarried. We preserved their fertility, but we could not predict their marriage status. Median patient age in other case studies was around 30 years (30–32.6 years) [5,13–17], whereas that in our study was 35.5 years. The patient age in other studies ranged from 20 years to 45 years, and our youngest patient was 28 years old. Moreover, in the studies involving fewer than 30 patients [18], the average conception rate was approximately 22%, which is lower than studies with over 30 cases (Table 2, the number of conception divided by patients). The conception rates seem to be lower in patients who underwent ART, but only small series were reported [18]. Endometriosis also affects fertility. However, none of our patients had endometriosis.

Regarding complications, our major complication is hydronephrosis and minor complication is urinary tract infection. Compared with other literature, bladder hypotonia is the main complication reported [4]. Among our patients, bladder function usually recovered within 2–3 weeks. Although the number of patients in our study was small, the complication rates were similar to those in other studies [12,13,19].

In the literature, there are patients who did not fulfill the criterion of less than 2-cm tumor size for the indication of VRT [20,21]. In our case series, we also found that one patient (Table 1, No. 5) who underwent VRT had a recurrence. The reason could have been due to her 3.5-cm tumor size. For patients with a tumor > 2 cm desiring fertility preservation, neoadjuvant chemotherapy with subsequent VRT was proposed by other study. Kobayashi et al. [22] reported the case of a patient with cervical cancer having a 3-cm squamous cell carcinoma who underwent four chemotherapy courses followed by conization. Several case series have reported different chemotherapy regimens followed by conization or VRT [21,23,24]. Due to the small case numbers, additional studies evaluating the long-term oncological outcomes are warranted.

In conclusion, we report the first RT series involving a median follow-up period of 5 years in Taiwan. Although no live birth was achieved, we believe that laparoscopic pelvic lymphadenectomy and VRT are safe and feasible treatment options for patients with early stage cervical cancer. These treatment procedures are associated with satisfactory oncological outcomes.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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