

Pregnancy outcome and obstetric management after vaginal radical trachelectomy

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Abstract. – OBJECTIVE: Radical vaginal trachelectomy (VRT) is widely prescribed as a surgical procedure to treat early-stage cervical cancer while preserving fertility. However, the ideal obstetric standard of care for patients who have undergone VRT has not yet been established. Aim of this report is to analyze pregnancy outcomes and optimal obstetric management during pregnancy and delivery after vaginal radical trachelectomy (VRT).

PATIENTS AND METHODS: Forty-six cases of VRT from December 2003 to April 2013 in Peking Union Medical College Hospital were analyzed.

RESULTS: The mean age of the patients at the time of VRT was 30.6 years and the mean follow-up time was 39.5 months. Of the 32 patients who attempted to conceive, 12 had 16 successful conceptions. There were two miscarriages and two elective abortions. One case of ectopic pregnancy and one case of second trimester loss occurred in this cohort. Ten cases reached the third trimester. Two patients delivered before 32 weeks, and four before 37 weeks. The total preterm delivery rate was 60%. All ten patients delivered by Cesarean section through a high transverse uterine incision. No uterine rupture or postpartum hemorrhage occurred.

CONCLUSIONS: There is an increased occurrence of preterm delivery after VRT. Cesarean section after full term pregnancy through a high transverse incision should be considered as a suitable and safe procedure.

Key Words:

Radical vaginal trachelectomy, Pregnancy, Complication, Perinatal management, Obstetric management, Conception.

Introduction

Radical vaginal trachelectomy (VRT) was first reported as an effective fertility-preserving treatment for early-stage cervical cancer in 1994 by Dargent¹. VRT has since been established worldwide as a safe and feasible treatment procedure

for young patients with early-stage cervical cancer because of low recurrence and mortality rates. To date, approximately 700 cases of VRT have been reported². However, the optimal prenatal management of pregnancy and related complications in women who have undergone VRT remains controversial. In this study, we have summarized the clinical profile of pregnancy after VRT in Chinese women, and we review the obstetric management of pregnancy and delivery as well as pregnancy outcomes.

Patients and Methods

Patient Information

From December 2003 to April 2013, a total of 46 patients were diagnosed with early-stage cervical cancer and treated by VRT in Peking Union Medical College Hospital (PUMCH). The operative procedure used was almost identical to that previously described by Dargent et al¹. The procedure involves removal of the majority of the cervix and parametrium after laparoscopic pelvic lymphadenectomy to ensure that the cancer has not metastasized³. Initially, nylon was used to place a McDonald cerclage at the lower end of the uterus or the remaining cervix. Since 2006, insertion of a cervical cerclage during VRT is no longer being done.

The patients were fully informed of possible complications and fertility outcome including the desired fertility preservation, and a signed consent form was obtained from each patient. Of the 46 patients, 12 women conceived 16 pregnancies after VRT. Information on these patients was recorded in a computerized database, and included the patient's age, any complaints, clinical features, process of pregnancy trimesters, complications of pregnancy, obstetric treatment modality, and outcome of the pregnancies. These results

were analyzed in this study. The study was approved as an exempt study by the Hospital Institutional Review Board.

Evaluation of the Patients

Regular follow-up including Pap smear, pelvic examination and PET-CT scan was carried out for all patients after VRT by a gynecological oncologist. After 6 months of follow-up without any evidence of residual or recurrent disease, patients were advised to try to conceive. When pregnancy was confirmed by HCG assay and ultrasonography, patients were referred to the obstetric clinic for perinatal assessment. Pregnant women were followed by the obstetrician and gynecological oncologist jointly during the pregnancy. Cervical cytology was regularly done before, during and after pregnancy every three months. A detailed gynecologic and colposcopic evaluation was carried out if there was any abnormal cytological finding. Infertility work-up and artificial reproductive treatment were performed if patients failed to conceive 2 years after the VRT procedure.

Strategies of Obstetrics Management

HCG assay and ultrasound was performed to confirm viability of pregnancy, and to estimate gestational age in the first trimester. A close evaluation and measurements of the lower uterine segment and cervical length was carried out by ultrasound and/or physical examination at 12 weeks of gestation and repeated at every following prenatal examination. At 24 weeks, cervical cytology was examined to monitor for recurrence of cervical cancer, and cervical length was re-checked by physical examination. Fetal fibronectin (fFN) was detected to predict the risk of preterm birth. If the patient had vaginal bleeding, regular contractions, shortened cervical length and/or a positive fFN test, bed rest as well as mechanical stockings, ritodrine and corticosteroids were prescribed temporarily. At 32 and 36 weeks, a vaginal swab was taken to screen for group B streptococcus (GBS) infection. Antibiotics were administered if there was evidence of GBS infection. If there was a threat of preterm birth or preterm premature rupture of the membrane (PPROM) occurred, tocolytic therapy was given to prolong gestational age and antenatal corticosteroids were administered to accelerate fetal lung maturity. Emergency cesarean section (CS) was done if there was intrauterine infection or onset of labor. Otherwise,

elective CS through a high transverse uterine incision was performed shortly after 37 weeks of gestation.

Postnatal Follow-up

All of the patients were followed-up six weeks after delivery to evaluate for recovery of the uterus, postpartum depression and to perform a complete physical examination including cervical cytology. Colposcopic evaluation was advised if there was any abnormal cytological finding. The patients were subsequently followed up as per the routine for cervical cancer.

Results

Clinical Profiles of the Patients, post-VRT

Forty-six patients with early-stage cervical cancer were treated by VRT in our department since 2003. The mean age of the patients was 30.6 ± 3.7 years old with a range of 24-37 years. The International Federation of Gynecology and Obstetrics (FIGO) stages were as follows: 4 (8.7%) cases were Ia1 with capillary lymphatic space invasion, 4 (8.7%) cases were Ia2 and 38 (82.6%) cases were Ib1 diseases. Histological findings of squamous cell carcinoma were found in 42 (91.3%) patients and 4 (8.7%) patients had adenocarcinoma or adenosquamous carcinoma. The mean follow-up time was 39.5 months, ranging from 1 to 77 months. Four cases (8.7%) developed recurrence of cancer and received post-operative radiotherapy. One case (2.2%) died of recurrent disease. The recurrent disease in three other cases was successfully controlled by radiotherapy.

Clinical Characteristics of the Pregnant Patients after VRT

1. Pregnancy rate. Of the 46 patients, 33 (71.7%) attempted to conceive after VRT. The other 13 patients either did not desire to conceive because of personal reasons or had been recently operated on. Twelve (36.4%) of the 33 patients had sixteen successful pregnancies. The total conception rate in our series (16 conceptions amongst the 33 patients who attempted to conceive) was 48.5%. The mean time from the end of treatment to conception was 17.0 ± 18.4 months, ranging from 3 to 60 months. Cervical cerclage were performed only in 4 patients during the VRT and all of the four cerclages were removed before pregnan-

cy. The clinical characteristics of the twelve pregnant patients who underwent VRT are presented in Table I.

- 2. Fertility outcome.** Four patients had a first trimester loss. Two patients underwent an elective abortion for personal reasons and two patients had a first trimester miscarriage. One patient had an ectopic pregnancy treated by laparoscopic salpingectomy. There was one case of second trimester loss. Ten patients reached the third trimester. Of these 10 patients, 4 delivered babies before 37 weeks of gestation. Of these, one delivered at 30 weeks and the others delivered at 32, 35 and 36 weeks. However, 6 cases delivered at term (≥ 37 weeks of gestational age). The pregnancy outcome of the twelve patients after VRT is presented in Table II.
- 3. Obstetric outcome.** All patients were delivered by CS. The mean delivery week was 35.9 ± 2.8 weeks, ranging from 30 to 39 weeks. All 10 patients delivered live-born infants. The mean neonatal birth weight was 2664 ± 686 g, ranging from 1460 g to 3290 g (Table II). Two preterm infants were transferred to NICU because of significant prematurity.

Four CS were performed at 30, 32, 35 and 36 weeks respectively because of either preterm labor or PPRM. The remaining six patients delivered by CS between 37 and 38 weeks. We have performed this operation safely through a transverse section on the upper part of the uterus for all ten patients. No cases of uterine rupture or hemorrhage occurred.

Case Reports

Case 1

A 31 year-old nulliparous woman was diagnosed with stage Ib1 squamous cell carcinoma by diagnostic laser conization at a local hospital. She was admitted to our hospital for fertility-sparing treatment. VRT was performed in October 2008 and cervical cerclage was not done. The excised uterine cervix (1.2 cm) and lymph nodes were negative for cancer as determined by pathological examination. Twelve months after the operation, the patient became pregnant naturally. At 12 weeks of gestation, ultrasound revealed cervical length of 1.5 cm. The patient was subsequently followed by serial speculum examination. Her cervix demonstrated no changes as the pregnancy progressed. Fetal growth was good. At 37 weeks of gestation, an emergency CS was performed because of premature rupture of membranes. Intra-abdominal examination revealed a largely absent lower uterine segment and uterine-vesical peritoneum, with many prominent veins. The uterus was incised through a transverse incision in the upper part of the uterus, which was smaller than usual. A female infant weighing 2640 g was delivered, with Apgar scores of 9 and 10 at 1 and 5 min, respectively. The blood loss during the operation was 200 ml. Postoperative recovery was uneventful.

Case 2

A 30 year-old nulliparous woman was diagnosed with stage Ib1 adenocarcinoma of the uterine cervix by colposcopy at a local hospital. She

Table I. Clinical characteristics of pregnant patients underwent VRT.

No	Age	Parity	Histology	Staging	VRT time, year	Cervix length resected by VRT (cm)	Conception time, year
1	33	0	SCC	Ia1	2005	2.0	2009, 2010
2	31	0	SCC	Ib1	2006	1.8	2007, 2011
3	34	0	SCC	Ib1	2006	2.0	2009
4	28	1	SCC	Ib1	2006	1.8-2.2	2008, 2009
5	29	0	SCC	Ia1	2006	1.0	2011
6	37	1	SCC	Ib1	2007	1.5	2007
7	31	0	SCC	Ib1	2008	1.2	2010
8	24	0	SCC	Ib1	2010	1.5-2.0	2011
9	30	0	Adeno	Ib1	2010	2.5	2010, 2011
10	29	0	SCC	Ia1	2011	2.0	2011
11	34	0	SCC	Ib1	2011	2.5	2012
12	24	0	SCC	Ia1	2012	2.8	2013

Parity is expressed as "number of deliveries" before VRT; Adeno: adenocarcinoma of uterine cervix; SCC: squamous cell carcinoma of uterine cervix.

Table II. Fertility outcome of patients after VRT.

Patient	Gestational age	Complication	Pregnancy outcome	Body weight
1	1 st trimester	Miscarriage	Miscarriage	
2	1 st trimester	Ectopic pregnancy	Ectopic pregnancy	
	38+6	None	CS	3000 g
	39	None	CS	3150 g
3	36	PPROM, PB	CS	2900 g
4	32	PPROM, PB	CS	1500 g
	1 st trimester	None	Abortion	
5	1 st trimester	None	Abortion	
6	37+2	None	CS	3100 g
7	37	None	CS	2640 g
8	35.4	PPROM, PB	CS	2350 g
9	1 st trimester	Miscarriage	Miscarriage	
	37	None	CS	3250 g
10	30	PPROM, PB	CS	1460 g
11	37.4	None	CS	3290 g
12	2 nd trimester	Miscarriage	Miscarriage	

PPROM: preterm premature rupture of membrane; PB: preterm birth; CS: cesarean section.

was admitted to our hospital for fertility-sparing treatment. VRT was performed in January 2010, and cervical cerclage was not done. The excised uterine cervix (2.5 cm) and lymph nodes were negative for cancer as determined by pathological examination. Nine months after the operation, the patient conceived naturally. At 8 weeks of gestation, the patient suffered a blighted ovum, which was treated by medical abortion. Ten months later she became pregnant again. She was followed with serial speculum examination of the cervix in the clinic. Her cervix demonstrated no changes as the pregnancy progressed. She was given precautionary intramuscular dexamethasone at 31 weeks. Fetal fibronectin was negative. A vaginal swab was taken at 36 weeks for Group B Streptococci, which was negative. At 37 weeks of gestation, a planned CS was performed. Intra-abdominal examination revealed a partially absent lower uterine segment and utero-vesical fold. We entered the uterus through a transverse incision on the upper part of the uterus, due to increased veins in the lower part. A male infant weighing 3250g was delivered, with Apgar scores of 10 and 10 at 1 and 5 min, respectively. The blood loss during the operation was 150 ml. Postoperative recovery was good.

Case 3

A 30 year-old nulliparous woman was diagnosed with stage Ib1 squamous cell carcinoma of the uterine cervix by colposcopy at a local

hospital. She was admitted to our hospital and VRT was performed in September 2006. A cervical cerclage was inserted during the procedure. The excised uterine cervix (1.8 cm) and lymph nodes were negative for cancer as determined by pathological examination. She had the cerclage removed in a local hospital in February 2007 and became pregnant the same year. At 16 weeks of gestation, a transabdominal ultrasound revealed a cervical length of 1.0 cm. Cervical cerclage was inserted at this time at our hospital. The patient subsequently returned to her hometown. At 38 weeks of gestation, a planned CS was performed. A female infant weighing 3000 g was delivered without any complications, and she recovered uneventfully after. The patient subsequently got pregnant in 2012 for the second time. No cerclage was inserted during this pregnancy. This delivery was also done by CS at 39 weeks.

Discussion

Pregnancy Rate and Fertility Outcome

VRT has become a feasible fertility-preserving treatment for young patients with early-stage invasive cervical cancer. VRT has 5-year disease-free survival rates and overall survival rates of 95% and 97% respectively⁴. These rates are comparable to those of radical hysterectomies for similarly sized lesions. In the literature, variable pregnancy rates post-VRT are variable have been

reported⁵. In our present study, the pregnancy rate is 36.4%, which is lower than the reported rate by Plante et al. (46.4%-63%)⁶.

There was only one patient who experienced second trimester miscarriage whose cervix length was 2.8 cm. All of the other nine patients who reached the second trimester did not have loss of pregnancy and reached the third trimester, although two patients delivered at 30 weeks and 32 weeks.

VRT and Cervical Cerclage

Our department started performing VRTs in 2003. In the first three years, we cervical cerclage insertion was performed as part of the VRT procedure. However, none of the 16 patients conceived during this period. After 2006, two patients had their cervical cerclage removed in a local hospital and subsequently conceived, delivering at 38 and 36 weeks. It is possible that cervical cerclage may cause stenosis or narrowing of the cervix that could hamper conception. Therefore, from that point onward cervical cerclage insertion during VRT was no longer performed.

Decreased mechanical support for the pregnancy from a partially absent cervix was considered to be a significant risk for preterm delivery. Theoretically, partially cervical cerclage can prevent incompetence of the cervix⁷. Kim et al⁸ reported 10 cases of cervical stenosis and 2 cases of cerclage erosion associated with cerclage in the 35 cases they studied of women who attempted to conceive after radical trachelectomy.

In our case series, only one woman received cerclage placement at VRT, removed prior to conception, and inserted again at 16 weeks because the cervical length was less than 1 cm. The same patient got pregnant four years later naturally and carried to term without cervical cerclage. The very early preterm delivery rate in our study was 20% (2/10), similar to a recent review by Plante (25%)⁶.

Based on the findings from our current study, it may not be recommended to perform routine cervical cerclage either before or during pregnancy. Further study and evidence using a larger population would be required to definitively qualify the value of routine cervical cerclage.

Prevention of Preterm Birth and PPROM

Premature birth and PPROM are the most important complications of pregnancy after VRT. The rate of preterm delivery rate was 25%-28%, which represents an increased risk

of four-fold as compared with the normal population. The mechanism is likely to be due either to cervical incompetence or to increased incidence of infection. The impaired production of mucus can facilitate the access of microorganisms to the choriodecidual space and the uterine cavity, leading to preterm birth and PPROM⁹. In order to prevent preterm birth and PPROM, it has been recommended that regular measurements of the cervical length, observing for funneling, and administration of daily progesterone pessaries from 12 weeks of gestation be done, and intramuscular corticosteroids administered if preterm labor is threatened¹⁰. Bed rest early in pregnancy and administration of oral ritodrine and daily vaginal administration of povidone-iodine and ulinastatin vaginal suppository have also been suggested as effective means to prevent preterm birth^{11,12}. However, all these suggestions were empirical without any evidence from randomized controlled studies. Extrapolating from non-VRT pregnancies, cervical length (< 25 mm) and positive fetal fibronectin are useful predictors for preterm labor. Furthermore, while daily progesterone has been shown to be beneficial, cervical cerclage has not been proven so.

However, progesterone pessaries are not readily available in many areas of China and are not affordable for long-term use for many patients. In our practice serial speculum examination was usually performed to check cervical length from 20 weeks, and vaginal swabs were taken to screen for vaginal infections. Use of progesterone pessaries was limited to those patients with a shortened cervix. Ritodrine and corticosteroids are reserved for patients with threatened preterm delivery. We believe that these amendments to protocol may be useful for the management of patients in developing countries with minimal access to resources or economic constraints.

The Procedure of the Cesarean Section

Some authors have suggested that CS after VRT should be performed through a classical (vertical) incision in order to prevent lateral extension into the uterine vessels. However, this may pose a higher risk of intraoperative bleeding. Ishioka^{11,12} believed that a high transverse uterine incision is a safer option for patients post-VRT. We have performed this operation safely through a transverse section on the upper part of the uterus for all ten patients. No cases of postpar-

tum hemorrhage or lateral extension of the uterine incision occurred. The reported time of delivery for those women who reached term gestational age is variable. Some authors suggested early classical CS around 34 weeks in case onset of uterine contractions led to uterine rupture and hemorrhage. Others performed most CS deliveries shortly after 37 weeks of gestation following evaluation of fetal lung maturity. In the present study, four CS were performed at 30, 32, 35 and 36 weeks respectively because of either preterm labor or PPRM. The remaining five patients delivered by CS between 37 and 38 weeks. No cases of uterine rupture or hemorrhage occurred. Therefore, we suggest that elective CS should be performed at 37 weeks of gestation with careful monitoring until delivery.

Conclusions

VRT is an effective fertility-preserving treatment for young patients with early-stage cervical cancer and has reasonable oncology and fertility outcomes, but the obstetrical management of pregnancy following VRT is still controversial. Interdisciplinary cooperation between the gynecologic oncologist, the maternal fetal medicine specialist and neonatologist is very important in the management of pregnancy and delivery. Based on the current findings from our research, CS shortly after 37 weeks of gestation through a high transverse uterine incision is a safe and feasible method of delivery.

Declaration of Funding Interests

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Conflict of Interest

The Authors declare that there are no conflicts of interest.

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