## ORIGINAL ARTICLE

# Importance of uterine cervical cerclage to maintain a successful pregnancy for patients who undergo vaginal radical trachelectomy

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Received: 5 July 2013/Accepted: 14 October 2013/Published online: 31 October 2013 © Japan Society of Clinical Oncology 2013

#### Abstract

*Background* We have performed 36 vaginal radical trachelectomies (RTs) for patients with early invasive uterine cervical cancer and experienced 10 deliveries. Pregnancy after RT has far higher risks of prematurity and complications such as preterm premature rupture of the membrane (pPROM) and chorioamnionitis. We report the significance of transabdominal cerclage in the follow-up of pregnancy after vaginal RT.

*Methods* Our operative procedure is based on that of Dargent et al. We amputated the cervix approximately 10 mm below the isthmus. For the removal of the parametrium, we cut at the level of type II hysterectomy. A nylon suture is also placed around the residual cervix. Pregnancy courses after vaginal RT were studied in 9 patients (10 pregnancies) with respect to cervical length and several infectious signs.

*Results* Obstetric prognosis after RT was improved with our follow-up modality. Four patients who were followed up with this modality were able to continue their pregnancies until late in the third trimester. However, it was not effective for four patients who showed cervical incompetence due to slack cerclage. They suffered from pPROM without any infectious signs and uterine contraction. Though we performed transabdominal uterine cervical cerclage for one patient in her 19th week of pregnancy, it was unsuccessful.

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Department of Obstetrics and Gynecology, School of Medicine, Sapporo Medical University, Minami 1-jo, Nishi 16-chome, Chuou-ku, Sapporo, Hokkaido 060-8543, Japan e-mail: ishioka@sapmed.ac.jp *Conclusions* Cervical cerclage placed at the time of RT played an important role in preventing dilatation of the uterine cervix and the subsequent occurrence of pPROM. Transabdominal cervical cerclage should be performed earlier in pregnancy or before pregnancy in patients who have experienced problems with cervical cerclage.

**Keywords** Radical trachelectomy (RT) · Uterine cervical cancer · Transabdominal cervical cerclage

## Introduction

Vaginal radical trachelectomy (RT) has become a useful and oncologically safe treatment modality for patients with early invasive uterine cervical cancer who want to preserve their fertility in Japan and other countries in the last decade [1–5]. We have performed 36 vaginal RTs and experienced 10 pregnancies so far. However, management of pregnancy after RT is still a challenge not only for gynecological oncologists but also for obstetricians. This operation is completely different from laser conization from the standpoint of targeting lesions and postoperative invasiveness [2, 6]. Pregnancy after RT has far higher risks of prematurity and complications.

As we have reported previously, preterm labor and the subsequent occurrence of preterm premature rupture of the membrane (pPROM) due to the lack of mechanical support of the residual cervix and chorioamnionitis (CAM) caused by disruption of the endocervical glands and reduced secretion of mucus can easily occur in these patients [2, 6–8]. Therefore we take great care to prevent uterine cervical infection and ensure bed rest under hospitalization for such patients [1, 2, 6, 8]. Thanks to this follow-up modality, most patients were able to continue their pregnancies until

the late third trimester, and it was possible to perform a scheduled cesarean section.

Recently, however, we have encountered difficult cases in which we could not prevent the occurrence of pPROM even with this follow-up modality. These patients had various problems with cervical cerclage, which seem to have an impact on pregnancy after vaginal RT. Here we report on the significance of cervical cerclage in the followup management of pregnancy after vaginal RT.

### Patients and methods

Thirty-six patients with early-stage invasive uterine cervical cancer who wanted to preserve their fertility underwent vaginal RT with pelvic lymphadenectomy between January 2003 and December 2012 at our hospital. They were periodically followed-up at our hospital and eight of them became pregnant (twice for one patient) during the same period (Table 1). In addition, one pregnant patient who had undergone vaginal RT at another hospital was referred to our hospital for the follow-up of pregnancy. The pregnancy courses of these nine patients were studied retrospectively.

As we reported previously, our operative procedure for vaginal RT was based on that of Dargent et al. [9]. The procedure began with a pelvic lymphadenectomy. Then we performed vaginal RT. We usually amputated the cervix approximately 10 mm below the isthmus. For the removal of the parametrium, we cut at the level of Type II hysterectomy. After the trachelectomy, a nylon suture was placed around the residual cervix and a Sturmdorf suture was placed to cover the surface of the cervix. Our vaginal RT was performed according to the preoperative criteria for RT proposed by Plante et al. [10]. These consist of the desire to preserve fertility, lesion size  $\leq 2$  cm, International Federation of Gynaecologists and Obstertricians (FIGO) stage Ia1 with vascular space involvement, stage Ia2 or stage Ib1, squamous histology or adenocarcinoma, no involvement of the upper endocervical canal as determined by colposcopy or magnetic resonance imaging (MRI), and no evidence of lymph node metastasis. We usually recommended pregnancy 6 months after the operation. Prior ethical approval for the treatment was also obtained from the institutional review board at our institution.

We followed-up pregnant patients after case 3 according to the treatment modality proposed in a previous report (Table 2) [6]. Briefly, we recommended them to be admitted to our hospital early in the second trimester in spite of there being no signs of threatened abortion. Daily vaginal disinfection with povidone iodine, bed rest, and administration of ritodrine and an ulinastatin vaginal suppository were continued until delivery. Cervical length was measured almost every day using transvaginal ultrasonography. Furthermore, as markers of genital tract inflammation, examination of the Nugent score, granulocyte elastase and oncofetal fibronectin levels in vaginal secretion, as well as serum C-reactive protein (CRP), and general blood examination results were checked routinely. Thus, the basis of follow-up was the early detection and prevention of uterine cervical infection. Scheduled cesarean section was usually performed at 34 weeks of gestation. The decision to operate at this stage (34 weeks) of gestation was taken by obstetricians and neonatologists after receiving detailed informed consent from the patients and their families, due

Table 1 Clinical characteristics of patients who underwent vaginal RT

Case	Age	Pregnancy after operation (months)	Stage	Histology	Admission (weeks)	Delivery (weeks)	CAM	Weight of baby (g)	Recurrence
1	33	8	1B1	Adeno.	17	32 (PROM)	+	1991	_
2	33	6	1B1	SCC	20	24 (PROM)	+	588	_
3	28	30	1B1	SCC	14	34	_	1862	_
4	24	21	1B1	SCC	14	34	_	2138	_
5	32	26	1A2	SCC	14	34	_	2527	_
6	32	16 weeks pregnant <sup>a</sup>	1B1	SCC	15	34 (PROM)	_	2112	_
7 <sup>b</sup>	39	62	1B1	SCC	14	26 (PROM)	+	878	_
8	34	80	1B1	Adeno.	14	19 (PROM)	+	n.a	_
9	35	31	1B1	SCC	15	19 (PROM)	+	n.a	_
10	32	51	1B1	Adeno.	10	19 (PROM)	+	n.a	_

Adeno adenocarcinoma, PROM premature rupture of the membrane, SCC squamous cell carcinoma

<sup>a</sup> Case 6 underwent vaginal RT after 16 weeks of pregnancy

<sup>b</sup> Case 7 is the second pregnancy of case 1

to consideration of the maternal physical and mental conditions resulting from long-term bed rest, and to avoid the sudden occurrence of PROM.

For case 10, we performed transabdominal cerclage (abdominal Shirodkar operation) after the dilatation of residual uterine cervix was detected. Briefly, after laparotomy, the vesicouterine peritoneum was incised and the bladder was pushed down. The uterine vessels were palpated at the side of the uterus, and an avascular space was identified between these vessels and the uterus. Then a Teflon strap was placed under the vessels via a needle and tied slowly and firmly. The effects of cerclage were confirmed through ultrasonography (Fig. 1).

 Table 2
 Follow-up modality of pregnant patients who underwent vaginal RT

Prevention and early detection of uterine cervical infection

Daily vaginal disinfection with povidone iodine

- Prophylactic daily administration of an ulinastatin vaginal suppository
- Routine checks for bacterial vaginosis, and maintenance of normal vaginal flora

Examination of Nugent score, the granulocyte elastase level and oncofetal fibronectin level in vaginal secretion, serum CRP, and general blood examination

#### Tocolysis

Admission and bed rest from early in the second trimester of pregnancy

Administration of ritodrine

Measurement of cervical length using transvaginal ultrasonography

# Results

Table 1 shows the characteristics of pregnant patients who underwent vaginal RT. We have experienced 10 pregnancies in 9 patients thus far. All the patients remained free of disease after delivery and have regular cycles of menstruation now. As we previously reported, two earlier patients (cases 1 and 2) suffered from pPROM at 24 and 32 weeks of gestation, respectively, and their placentas showed the existence of CAM.

Thereafter, however, four patients (cases 3–6), who were followed-up according to our new follow-up modality described in Table 2 were able to continue their pregnancies without any problems until late in the third trimester, and we were able to perform scheduled cesarean section, including for a patient who had undergone vaginal RT during her pregnancy (Fig. 2a).

Recently we encountered several difficult cases. Case 7 was the second pregnancy after vaginal RT (the first pregnancy was case 1), and case 8 became pregnant 7 years after the operation. Both of them seemed to have trouble with the uterine cervical cerclage. They suffered from pPROM after sudden dilatation of the cervical canal at 26 and 19 weeks of gestation, respectively, even though we treated them according to our new follow-up modality. The placentas of these patients showed the existence of severe CAM. As shown in Table 3, the Nugent score, oncofetal fibronectin level, and CRP were almost within normal ranges or almost negative until the sudden occurrence of pPROM. Elastase level was elevated for case 7. However, the elastase level does not seem to be very sensitive for the





Fig. 2 Changes of uterine cervical length during the pregnancy under our follow-up modality. **a** Changes of uterine cervical length in cases 3-6, who were able to continue pregnancy until the scheduled cesarean section. **b** Changes of uterine cervical length in cases 7-10, who showed cervical incompetence due to slack cerclage

 Table 3
 Results of various infectious markers measured just before

 pPROM in patients who had problems with cervical cerclage

Case	Bacterial vaginosis <sup>a</sup>	Elastase level (µg/ml)	Oncofetal fibronectin	Serum CRP
7	-	+(13.5)	-	-
8	_	_	_	-
9	_	_	_	_
10	-	+ (4.2)	-	-

<sup>a</sup> Existence of bacterial vaginosis was determined by use of the Nugent score. A score of 7–10 is consistent with presence of bacterial vaginosis. Scores <7 are considered to show absence of bacterial vaginosis

detection of cervical infection. Although no gradual decrease in the uterine cervical length was detected, we found loosened cervical cerclage in both patients at the time of cesarean section (Fig. 2b). For case 7, it had been necessary to enlarge the uterine cervical canal to excrete lochia at the time of the first cesarean section. For case 8, the extended period of time after the initial operation might have resulted in degradation of the nylon sutures. Furthermore, we could not find the nylon sutures of the uterine



Fig. 3 Transabdominal cerclage for case 10. **a** A Teflon strap was placed under uterine arteries via a needle and tied slowly and firmly. **b** The uterine cervical canal was dilated and the bag of water about 5 cm in diameter was seen. **c** Dilated cervical canal shrunk dramatically after the cerclage. The bag of water was no longer seen

cervical cerclage for case 9 and case 10 when they visited our hospital.

Case 9 underwent vaginal RT with uterine cervical cerclage at our hospital in 2007. It was considered that the nylon suture had separated spontaneously. Case 10 was referred from another hospital. The patient had not undergone cervical cerclage of the uterine cervix. Although neither infectious signs nor uterine contraction was detected, both patients were admitted to our hospital at 14 weeks of gestation, after which they were also followed up according to our modality. Both of them also suffered from sudden dilatation of the cervical canal and the subsequent occurrence of pPROM at 19 weeks of gestation (Fig. 2b). As shown in Table 3, the Nugent score, oncofetal fibronectin level, and CRP were within normal ranges or almost negative until the sudden occurrence of pPROM, though slight elevation of elastase level was seen in case 10. No gradual decrease in the uterine cervical length was detected in either of them. The placentas of these patients also showed the existence of severe CAM.

When we detected dilatation of the uterine cervical canal for case 10, we performed transabdominal cerclage of the residual uterine cervix (abdominal Shirodkar operation) as described under "Patients and methods" (Fig. 1). On laparotomy, we found that she did not have enough residual cervix. Therefore we had to perform cerclage on a higher part of the residual uterine cervix equivalent to the lower part of the uterine body (Fig. 3a). This portion has thicker uterine muscle than the lower uterine cervix so it was impossible to obtain perfect closure of the residual cervix. Nevertheless, the dilatation of the cervical canal was reduced dramatically (Fig. 3b, c). Unfortunately, leakage of amniotic fluid started after the operation, and the fetus died the day after the operation. We then performed laparotomy, followed by extraction of the Teflon thread and cesarean section.

#### Discussion

This report demonstrates that cervical cerclage placed at the time of RT plays an important role in prevention of dilatation of the residual uterine cervical canal and the subsequent occurrence of pPROM. Cervical cerclage is usually performed as a treatment for cervical atony [11]. The mechanisms by which this treatment modality is effective are the strengthening of mechanical support of the uterine cervix and the prevention of dilatation of the cervical canal. Considering the fact that the placentas of all 4 patients who showed cervical incompetence due to slack cerclage suffered from severe CAM, it is likely that adequate cerclage prevents cervical infection, probably by preventing cervical dilatation. Pregnancy after conization is also reported to have a high risk of preterm birth [12], although the effects of cerclage for these patients are still controversial [13, 14]. Cerclage after conization is not inevitable. However, in patients who undergo RT, this procedure might be the key to preventing pPROM. Kim et al. [15] also recently reported similar results.

As we described above, we take thorough measures not only to prevent uterine cervical infection, but also periodically check the bacterial vaginosis (BV) scores, elastase levels, and oncofetal fibronectin levels, as well as conducting blood tests for the early detection of uterine cervical infection for pregnant patients after RT. Why, then, could we not detect the progress of silent infection in these patients? Although the placentas of these patients showed the existence of severe CAM, all the infectious markers checked were almost within normal ranges at the time pPROM occurred. Silent intrauterine infection that could not be detected by our routine examinations might have already existed. New strategies for the early detection of silent intrauterine infections are thus necessary. Various inflammatory cytokines such as interleukin-6, -8, and TNF- $\alpha$  are reported to play prominent roles in the occurrence of preterm labor [16, 17]. Furthermore, it has been reported recently that the expression of various microRNAs affects the responses to bacterial pathogens [18]. Such molecular markers might be new tools for the detection of silent intrauterine infection.

How can we prevent cervical incompetence due to slack cerclage and reduce the occurrence of pPROM in these patients? Of course, it would be best to become pregnant soon after RT if possible. Materials other than nylon sutures must be taken into consideration [19]. However, once slack cerclage is detected, we believe repeat cervical cerclage is the best and only policy for these patients. As we described in a previous report, it seems to us that transvaginal uterine cervical cerclage is very difficult or almost impossible because the residual cervix is too short to place such a cerclage [6]. We believe that the transabdominal uterine cervical cerclage originally proposed by Benson and Durfee [20] might be the best policy for these patients. This operative procedure was originally introduced to treat cervical incompetence in patients with a short cervix as a result of obstetric injury and large conization. However, as this operative procedure requires laparotomy for the placement of the cerclage, it is more invasive than transvaginal cerclage. Lee et al. [21] reported the success of this procedure for a patient pregnant with twins. We also performed transabdominal cerclage for a pregnant patient who already showed dilatation of the residual cervix. However, our treatment was not successful. There were various difficulties in this case.

There are several problems in performing this operation for patients who have undergone RT. First there is the question of when this operation should be performed. Although we performed transabdominal cerclage in the 19th week of pregnancy in one patient, it should be performed earlier in the pregnancy if possible. The uterus in the second trimester seemed to be too large to perform effective transabdominal cerclage. As we usually amputate the cervix approximately 10 mm below the isthmus, it is impossible to obtain enough space to perform cerclage when we dissect the bladder downward. Therefore we have to make the cerclage in the higher part of the residual uterine cervix, or lower part of the uterine body. In such cases, it seems to be impossible to obtain tight closure because the higher parts of the uterine cervix have thicker uterine muscle than the lower parts. In our case, as we described under "Results", it was impossible to perform perfect reclosure of the residual cervix, although the dilatation of the cervical canal was reduced.

This cerclage operation should have been performed earlier in the pregnancy or before pregnancy. When we perform the operation early in pregnancy, the risk of abortion should be taken into account. However, if we perform this cerclage before the pregnancy, we have to hasten conception. Because the suture for cerclage is a foreign body, it can cause intraabdominal problems such as peritonitis and adhesion to other organs. No definitive guidelines exist as to how long intraabdominal sutures can be maintained without any problems. Therefore, we have to monitor the patients very carefully after recerclage. We believe that observation for one year after the operation might be practical as the first step of the study. If a pregnancy is not achieved within 1 year after recerclage, the suture should be removed to prevent problems. If it is not possible to detect any intraabdominal problems, it might be possible to prolong the duration of observation.

Thus the follow-up care of pregnant patients after RT is still a challenge for obstetricians. It is not easy to prevent the occurrence of pPROM. Cooperation between gynecologic oncologists and obstetricians is important in order to improve the prognosis for successful pregnancy in patients after RT.

**Conflict of interest** The authors declare that they have no conflict of interest.

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