



## Obstetric outcomes of patients undergoing total laparoscopic radical trachelectomy for early stage cervical cancer



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### HIGHLIGHTS

- TLRT is a useful technique associated with an excellent pregnancy rate (52%).
- Increased incidence of pPROM during pregnancy remains a major concern.
- CAM development had no predictor except Nugent's BV or cervical granulocyte elastase.

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### ABSTRACT

**Objective.** To assess the obstetric outcomes of our total laparoscopic radical trachelectomy (TLRT) cases for early stage cervical cancer.

**Materials and methods.** A total of 56 patients who underwent TLRT between December 2001 and August 2012 were reviewed retrospectively using clinicopathological, surgical, and follow-up data from patients' medical records.

**Results.** We performed this operation on 56 patients during the study period. The mean age of these 56 patients was 31.9 years (range 22–42 years). Fifty-three patients' fertility was preserved without requiring post-operative adjuvant treatment. Twenty-five women attempted to conceive, of whom 13 succeeded for a total of 21 pregnancies (52% pregnancy rate). Ten of these 21 pregnancies were the result of assisted reproductive technologies. Of those, 5 resulted in first trimester miscarriages, 2 in second trimester miscarriages, and 13 in live births. Ten pregnancies reached the third trimester. Preterm premature rupture of membranes (8/13, 61.5%) was the most common complication during pregnancy. The rate of preterm delivery was 47.6%. Three patients delivered at 22–28 weeks of gestational age. Two of these babies showed permanent damage: one has cerebral palsy; the other has developmental retardation. One pregnancy is ongoing.

**Conclusion.** TLRT is a useful technique associated with an excellent pregnancy rate in fertility-preserving surgery to treat early stage cervical cancer.

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### Introduction

Cervical cancer continues to be an important gynecologic malignancy [1]. As it has in other developed countries, the incidence of cervical cancer among women in their 20s and 30s has increased also in Japan. Many women are starting families much later in life. Therefore, fertility preservation therapy for cervical cancer has received a great deal of attention [2]. Since Dargent performed a vaginal radical trachelectomy (VRT) in 1986 with laparoscopic pelvic lymphadenectomy as a fertility-sparing technique for patients with cervical cancer, the VRT procedure has been shown to be an effective treatment for early stage cervical cancer [3,4]. However, this procedure yields insufficient resection of the cardinal

ligament. It can engender difficulties in patients with locally adverse conditions including young nulliparous women and those with a history of conization [5]. Smith et al. reported a new surgical technique in 1997, abdominal radical trachelectomy (ART), to overcome problems encountered with VRT [6]. The salient shortcoming of ART is that it entails a large abdominal incision. Minimally invasive approaches to radical trachelectomy are now emerging in the gynecologic oncology literature. Nick et al. reported recently that robotic radical trachelectomy, in contrast to laparotomy, is associated with significantly less blood loss and shorter postoperative hospital length of stay [7].

At our hospital, we performed the VRT procedure according to the Dargent's original method in our first three cases. However, in December 2001, we introduced our total laparoscopic radical trachelectomy (TLRT), a technique in which resection of the cardinal ligament was modified to type III.

Radical trachelectomy (RT) is now an accepted treatment for early stage cervical cancer in women who wish to preserve fertility. Many

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authors have reported oncologic and obstetric results [4,6–11], but few reports describe cases with successful pregnancy after TLRT. The first report of TLRT was that by Cibula et al. published in 2005 [12]. Only five pregnancies after TLRT are described in these reports: two first-trimester miscarriages, one preterm delivery, one term delivery, and one ongoing [5,12–14].

Therefore we reviewed our experiences using this surgical technique and analyzed our patients' outcomes. Herein, we report the largest series of TLRT and pregnancies after TLRT to date.

## Patients and Methods

A total of 56 patients who underwent TLRT between December 2001 and August 2012 were reviewed retrospectively using clinicopathological, surgical, and follow-up data from patients' medical records. Fertility and perinatal information was obtained by telephone.

In principle, the indications for TLRT included external-growth type tumors, both adenocarcinoma and squamous cell carcinoma (SCC), with diameter of less than 25 mm in which a free surgical margin of 10 mm or greater was secured. Written informed consent was obtained from all patients following sufficient explanation of the risks of recurrence, post-operative complication, miscarriage, premature delivery, and severe perinatal prognosis. This study, which was approved by our ethical committee, was performed in conformity with the Declaration of Helsinki.

Before TLRT were started, we did vaginal cuff closure. An incision on the vaginal wall is made circumferentially. Once separated from remainder of the vagina, the vaginal cuff is closed over the cervix to cover it by suturing, so that we can prevent scattering of the cervical tumor cells into the pelvic cavity. All other procedures were done under laparoscopic control. Resection of the cardinal ligament was conducted according to our conventional radical hysterectomy procedure (Piver type III). The ascending branches of the uterine arteries were preserved. Permanent cerclage was performed during the operation in all cases. We initially used Tetrone tape for the cerclage, but the suture thread was exposed and discharged into the vagina after surgery in two patients. For that reason, we now use #2 Ethibond suture.

After TLRT, we recommended contraception for 6 months. Pregnancy management was not uniform because different attending doctors examined the patients. All pregnant cases were delivered by caesarean section.

Fisher's exact test was performed for comparison and *t*-tests were used to compare the cervical length at the early pregnant stage and immediately before delivery between subjects with and without premature rupture of the membrane. Statistical tests, based on two-sided probabilities, were done using software (SAS, ver. 8.2; SAS Institute, Inc., Cary, NC, USA).  $P < 0.05$  was considered statistically significant.

## Results

Fifty-six patients underwent this procedure during December 2001 to August 2012 (VRT patients are not included). The median follow-up period was 60 months (range 4–138 months). The mean age of these 56 patients was 31.9 years (range 22–42 years). The clinical stages included 4 patients at stage Ia2 and 52 patients at Ib1. Histologically, the tumors were diagnosed as SCC in 42 patients, adenocarcinoma in 12 patients, and adenosquamous carcinoma in 2 patients (Table 1). Lymphovascular space invasion (LVSI) was found in 14 cases. The median operative time is 349 min (range 215–640 min). The median blood loss is 300 ml (range 75–1540 ml). The median length of hospital stay is 17.5 days (range 7–47 days), which is longer in Japan than in Western countries because Japan has a universal health insurance system. Most patients were discharged only after complete recovery. The rate of intraoperative complications is 3.57% (2/56: injury to the right common iliac vein and the left external iliac artery). These two cases were managed laparoscopically without transfusion. The total number of lymph nodes was 32.1 (range 14–55). The rate of residual disease in the surgical specimen was 62.5% (35/56).

**Table 1**  
Patient and tumor characteristics.

Characteristics	Number of patients
Age (mean range), years	31.9 (22–42)
FIGO stage	
Ia2	4
Ib1	52
LVSI <sup>a</sup>	14
Histological type	
Squamous cell carcinoma	42
Adenocarcinoma	12
Adenosquamous carcinoma	2

<sup>a</sup> Lymphovascular space invasion.

Three patients received total laparoscopic hysterectomy and chemotherapy after TLRT for high-risk features on final pathology. Fertility was preserved in 53 patients (Table 2). One patient had recurrence in the right obturator cavity and died two years after TLRT. The recurrence rate was 1.8% (1/56).

Of the 53 patients, 26 patients were married; 47 were nulliparous. Also, 25 patients had actively attempted conception. Of those 25 patients, 13 patients had conceived for a total of 21 pregnancies: 11 spontaneously and 10 assisted by reproductive technology. These figures indicate the pregnancy rate of 52% (13/25). One of these 13 patients, because of high risk of tumor recurrence, had received adjuvant chemotherapy immediately after her operation. The patient had one cycle of intra-arterial infusion of carboplatin (300 mg/body) and five cycles of intravenous carboplatin after undergoing TLRT. The dosage of intravenous carboplatin was unobtainable. Four years later, she conceived through artificial insemination from her husband and developed PROM because of CAM at 26 weeks and 4 days into her first pregnancy. Consequently, the baby had cerebral palsy. The next year, she became pregnant spontaneously, underwent Saling procedure (total cervical occlusion) [16], and was able to have elective cesarean section at term.

## Infertility

Thirteen patients (13/25, 52%) had undergone assisted reproductive technology, 8 of whom (8/13, 61.5%) conceived for a total of 10 pregnancies. Table 3 shows the respective conception methods. The main causes of infertility were the following: cervical stenosis (3/13, 23%), hormonal dysfunction (1/13, 7.6%), endometriosis (1/13, 7.6%), male factor (1/13, 7.6%), and unknown etiology (7/13, 53.8%). Three patients had two live babies. It is particularly interesting that they conceived with the help of assisted reproductive technology (1 artificial insemination from husband, 2 in vitro fertilization – embryo transfer) for their first pregnancies, but their second pregnancies were spontaneous.

Three patients among those patients who had undergone assisted reproductive technology had cervical stenosis. Two had cervical dilation before conceiving with assisted reproductive technology. The remaining patient, with no symptoms, had no cervical dilation or further reproductive assistance. We had five patients of cervical stenosis in all. The remaining two patients did not attempt to conceive. The cervical stenosis rate was 8.9% (5/56).

**Table 2**  
Fertility characteristics.

Fertility characteristics	Number of patients
TLRT	56
Fertility spared	53
Married as of time of surgery	26
Nulliparous	47
Attempting conception	25
Nulliparous	21
Conceived	13

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