### **ORIGINAL ARTICLE**



# Radical Vaginal Trachelectomy with Laparoscopic Pelvic Lymphadenectomy for Fertility Preservation in Young Women with Early-Stage Cervical Cancer

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**Abstract** The primary objective of this study was to describe our experience with the conservative treatment of early-stage cervical cancer (stages IA1, IA2, and IB1) with radical vaginal trachelectomy (RVT) and laparoscopic pelvic lymphadenectomy. This retrospective observational case series included 36 patients with early cervical cancer. Radical trachelectomy and laparoscopic pelvic lymphadenectomy were performed as described by D. Dargent in 32 of these cases. Oncologic, reproductive, and obstetric outcomes were observed subsequently over a median period of 42 (24-96) weeks. A total of 32 RVTs were preformed with a mean operating time of  $117\pm22.8$  (77– 167) minutes and an average blood loss of 486 mL (150-800 mL). All obtained resection margins were negative for cancer. Lymphovascular space invasion was noted in 11 (30.55 %) of the cases. No recurrences occurred during the study period. Seven (17.8 %) patients were able to become pregnant postoperatively, five of whom delivered healthy infants near term. Radical vaginal trachelectomy with laparoscopic pelvic lymphadenectomy appears to be a safe therapeutic option for fertility preservation in young women with early cervical cancer.

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**Keywords** Cervical cancer · Radical vaginal trachelectomy · Laparoscopic pelvic lymphadenectomy · Pregnancy

#### Introduction

Romania ranks first in Europe in terms of both the incidence and the mortality of cervical cancer, which are 34.9 and 14.2 per 100,000 women, respectively [1]. Cervical cancer affects women of all ages, but 40 % of all early-stage cervical cancer diagnoses (stages IA1 to IB1) are made in women under the age of 45 [2]. The classical treatment of early-stage cervical cancer is represented by radical abdominal hysterectomy (which signifies the complete removal of the uterus en bloc with the parametria and the upper portion of the vagina) together with concurrent pelvic lymphadenectomy [3].

The idea to preserve the reproductive function of young patients with early-stage cervical cancer can be attributed to the Romanian doctor E. Aburel, who described a technique called abdominal subfundal trachelectomy in 1954 [4, 5]. In 1986, Daniel Dargent applied the same technical principle to the development and implementation of a vaginal trachelectomy and laparoscopic pelvic lymphadenectomy. This dual approach provided a significant improvement in recovery times and is currently considered the optimal route for radical trachelectomy [6]. The popularity of the Dargent technique increased after the first reports of postoperative pregnancies carried successfully to term were published in 1994 [7, 8]. Several centers adopted and modified the procedure [9, 10] so that a total of 992 radical vaginal trachelectomies and 436 subsequent pregnancies with a delivery rate of 67.2 % were reported in 2012 [11, 12].

Radical trachelectomy has recently proven to be amenable to various adjustments regarding the extent of cervical or parametrial resection and the elected route (vaginal or



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abdominal). The oncologic outcomes of these variations seem to be on par with those of radical abdominal hysterectomy, especially when prognostic variables such as lymphovascular space invasion (LVSI) or deep stromal penetration (DSP) are taken into account [13]. Furthermore, the administration of neoadjuvant chemotherapy may allow for the extension of the indication of fertility-preserving surgeries in patients with tumors larger than 2 cm [14].

#### **Materials and Methods**

The study included 36 patients with early-stage cervical cancer (i.e., stages IA1, IA2, and IB1), who were treated between 2006 and 2013 using the Dargent technique: radical vaginal trachelectomy with laparoscopic pelvic lymphadenectomy and sentinel lymph node identification.

Cervical lesion assessment was carried out using a combination of pap smears, HPV genotyping, colposcopy, vaginal ultrasonography, and MRI. The diagnosis was confirmed by careful assessment of specimens obtained through cervical conization in 20 cases and targeted biopsy in 16 cases.

The selection criteria for conservative surgical treatment were as follows:

- Age under 40 years
- The patient's firm desire for fertility-preserving surgery or for the preservation of her uterus and/or menstrual function
- A histological diagnosis of early-stage squamous cell carcinoma or adenocarcinoma of the cervix in the following stages:
- Tumors stage IA1 with lymphovascular invasion
- Tumors stage IA2 or
- Tumors stage IB1 no larger than 2 cm in any direction

All the patients received psychological counseling and gave their informed consent before surgery, and all interventions were conducted under general anesthesia. The patients were also informed about the possibility of intraoperative conversion to radical vaginal hysterectomy in case of detection of metastasis in the sentinel lymph node. This occurred in four cases and proved to be the main exclusion criterion from this study. Patients with small cell carcinoma of the cervix were also excluded.

### **Operative Technique**

The operation began by injecting blue dye in the four cardinal points of the cervix. Laparoscopy was performed after 20–30 min in order to identify the sentinel lymph node bilaterally.



After placement of the 10-mm optic trocar, three working ports were created, through which two 5-mm trocars were placed laterally and a 10-mm trocar was placed suprapubically. The parietal peritoneum was sectioned parallel to the external iliac vessels between the round ligament and the common iliac artery. The paravesical and pararectal fossa were exposed, and the ureter was identified. The identification and removal of the sentinel lymph node and its analysis by frozen section were carried out in all cases. Laparoscopic excision of the main pelvic lymphatic groups (external iliac, obturator, interiliac, iliolumbar) was then performed bilaterally regardless of sentinel lymph node involvement. All the removed lymph nodes were submitted to a postoperative histopathological and imunohistochemical analysis. An abdominal drain was placed in all cases.

### Vaginal Stage

The vaginal stage debuted by preparing the vaginal cuff. The initial approach to the cervico-isthmic aspect was obtained after posterior colpoceliotomy followed by sectioning and ligating the uterosacral ligaments at their insertion on the cervix. The anterior plane was developed by opening the vesicouterine space and dissecting the bladder pillar, which allowed the identification of the terminal portion of the ureters and their subsequent removal from the operative field beneath Breisky retractors. In this way, the ureters were displaced cranially in order to expose the uterine vessels. The lateral plane was developed by sectioning the parametrium 2 cm away from the cervix and dividing the cervico-vaginal branches while preserving the main uterine artery. The cervix was resected at 1 cm below the isthmus. A prophylactic cerclage was performed on all the patients at the level of the isthmus using non-resorbable suture material (USP 1 Prolene, Ethicon). The last phase of the operation consisted of the anastomosis of the vagina and the uterine stump using two Sturmdorf sutures.

## **Results**

A total of 32 radical vaginal trachelectomies with laparoscopic pelvic lymphadenectomy were performed from the 36 proposed cases. In four cases, the sentinel lymph node was positive on frozen section, which required a conversion to radical vaginal hysterectomy.

The preoperative histopathological diagnosis was based on specimens obtained after loop electrosurgical excision or cold knife conization for all patients with cervical cancer stages IA1 and IA2 and targeted biopsy for stage IB1 (Table 1). Eight cases (22.2 %) required a repeated conization in order to



 Table 1
 Diagnostic methods and histological parameters

Stage ( <i>N</i> /%)	Diagnosis		Histological type		Differentiation			LVSI
	Cone biopsy/LEEP	Targeted biopsy	SCC	ADK	G1	G2	G3	
IA1 (4/11.1)	4/100	_	4/100	_	_	4/100	=	4/100
IA2 (13/36.1)	13/100	_	13/100	_	1/7.6	12/92.3	_	3/23.07
IB1 (19/52.7)	3/15.78	16/84.21	17/89.47	2/10.52	3/15.78	16/84.21	_	4/21.05
Total (36/100)	20/55.5	16/44.4	34/94.4	2/5.55	4/11.1	32/88.8	0/0	11/30.55

All values are expressed as number/percentage

ADK cervical adenocarcinoma, LEEP loop electroexcision biopsy, LVSI lymphovascular space invasion, SCC cervical squamous cell adenocarcinoma

ensure a correct histopathological diagnosis, due to the fact that the initial specimens had positive resection margins after previous interventions. The patients diagnosed with cervical cancer stage IA1 were evaluated histologically by determining the level of lymphovascular invasion and immunohistochemical staining using prognostic markers Ki-67, p16, and E-cadherine. Infection with a high-risk strain of HPV infection was confirmed in 28 cases (77.7 %).

The mean age of the patients was 33 years (24–40 years,  $SD\pm4.2$ ). The main indication for radical vaginal trachelectomy (RVT) was preservation of fertility in 33 cases (91.6 %). The desire to preserve the integrity of one's body image in the absence of interest in fertility preservation was expressed by three women (8.3 %).

The average operating time was 117±22.8 (77–167) minutes. Actual work time did not take the time needed to switch between the laparoscopic and the vaginal approach into account (Table 2). The average intraoperative blood loss was 486 mL (150–800).

Pelvic lymphadenectomy and the identification of the sentinel lymph nodes were performed in all cases. The sentinel lymph nodes were identified bilaterally in all but two cases, where this step could not find the sentinel node on the left side of the pelvis.

The histopathological examination of lymph nodes as paraffin-embedded specimens revealed micrometastasis in one case (2.7 %) where the sentinel lymph node was negative at frozen section. Postoperative radiotherapy was recommended under these circumstances. Histopathological examination of the parametria and the resection margins of the specimens

 Table 2
 Mean operative time for all stages of the procedure

Laparoscopie	c time	Vaginal time	Total time	
(minutes)			(minutes)	(minutes)
Right side	Left side	Total		
40.5±8.9 (22–65)	40.1±10.2 (25–60)	80.6±19.1 (47–125)	37±6.5 (25–50)	117.6±25.6 (77–167)

obtained after radical trachelectomy was negative for cancer in all cases. The designated oncological safety limit was set at 8–10 mm from the resection margins.

Intraoperative complications (Table 3) were represented by lower urinary tract injuries occurring during trachelectomy (9.37 % of all complications of RVT). These were represented by two inadvertent cystotomies and one ureteral thermal injury. The two bladder injuries were recognized and directly repaired intraoperatively during the vaginal stage. The ureteral injury was discovered 7 days after surgery. The patient presented with persistent vaginal discharge (biochemically confirmed to be urine), accumulation of fluid in the pelvis, diffuse abdominal pain, and general malaise. The case was solved laparoscopically by reimplantation of the right ureter.

Early postoperative complications included the appearance of lymphocele, as well as of suprapubic or vulvar edema, and were therefore related to the laparoscopic lymphadenectomy. They occurred in 15.62 % of patients.

Late postoperative complications included dysmenorrhea and abnormal vaginal bleeding. Various degrees of incomplete cervical stenosis were suspected in patients presenting with the former complaint. Cervical canal dilatation under local anesthesia was performed in those cases. All patients with spontaneous or post-coital vaginal bleeding were examined

 Table 3
 Intra- and postoperative complications

Type of complication	Number (% of all RVTs)				
Intraoperative complications					
Inadvertent cystotomy	2 (6.25)				
Ureter injury	1 (3.12)				
Early postoperative complications					
Lymphocele	2 (6.25)				
Vulvar edema	1 (3.12)				
Suprapubic edema	2 (6.25)				
Long-term complications					
Dysmenorrhea	4 (12.5)				
Vaginal bleeding	9 (28.12)				
Abnormal uterine bleeding	2 (6.25)				



colposcopically and diagnosed with endocervical ectropion. Punctate electrocoagulation was then performed.

Oncological follow-ups were done over a period of 24–96 months with an evaluation every 3 months during the first year and then every 6 months for the next 5 years. During the follow-up, we performed clinical examination and Pap smear on all the patients. The most frequently noticed postoperative change in cytology was the presence of endometrial cells, endometrial stromal cells, and tubal metaplasia cells. The median duration of follow-up was 42 months (24–96). The survival rate after RVT was 100 % in this case series, and none of the patients have presented with any signs of tumor recurrence so far.

All patients received oral contraception over 1 year after RVT. Pregnancy was desired by 28 patients. Within this group, seven (17.8 %) patients obtained pregnancies, two of which ended in two missed abortions during the first trimester. Four of the pregnancies were obtained naturally approximately 2 years after RVT. One pregnancy was obtained after in vitro fertilization 5 years after RVT (Table 4).

All pregnancies presented a high obstetrical risk and were monitored accordingly. The monthly assessments, preventive therapies, and lifestyle recommendations each patient received were developed by Knight [15] and adapted to our protocol and included the following:

- Sterile speculum examination to evaluate the cervical stump
- Transvaginal ultrasonography with sterile gel to assess the length of the uterine isthmus and the position of the cerclage sutures
- · Bacteriological examination of vaginal discharge
- Fetal monitoring and ultrasound assessment of placental insertion
- No digital examination
- No sexual contact (between 14 and 36 weeks of gestation)

- No gymnastics or other physical activities
- Progesterone 200 mg ×3/day administered intravaginally from the detection of pregnancy until 37 weeks of gestation
- Emergency admissions at any sign of vaginal bleeding or painful uterine contractions
- Delivery by cesarean section between 37 and 39 weeks of gestation

#### **Discussions**

The first radical trachelectomy was performed by the authors of this study in 2006 done at the request of a 33-year-old patient with squamous cervical cancer stage IB1 who wished to preserve her fertility [16]. As the popularity of this technique increased among patients with early cervical cancer, the authors realized that some women also wished to preserve their menstrual function and their bodily integrity. The current global experience of almost 20 years with surgical conservative techniques in early-stage cervical cancer has demonstrated that carefully selected cases have similar results compared with radical surgery in terms of perioperative complications, 5-year survival, and recurrence rates. [13] These data encouraged us to focus on these particular cases in our study. The inclusion of patients under 40 years of age was also in agreement with the data obtained from literature [17, 18].

The preoperative assessment estimated the tumor volume, the degree of stromal invasion, the distance from the internal cervical os, the extracervical extension, and the possibility of lymph node invasion. Protocols validated by several studies were used to interpret the data obtained by vaginal ultrasonography and MRI [19, 20].

The macroscopic aspect of the sentinel lymph node and the resection margins of the cervix were carefully visually

 Table 4
 Obstetric outcomes of pregnancies after RVT

Case Nr.	Time of conception (years after RVT)	Type of conception	Evolution	Treatment	Time of delivery	Mode of delivery	Newborn weight (g)	Complications
1	2	Spontaneous	Normal	PGS	39 weeks	CS	3150	=
2	2	Spontaneous	Missed abortion at 10 weeks	PGS+SL	-	_	_	_
3	2	Spontaneous	Missed abortion at 9 weeks	PGS+SL	_	_	-	_
4	2	Spontaneous	Normal	PGS	38 weeks	CS	3000	Lower segment laceration
5	2	Spontaneous	Normal	PGS	39 weeks	CS	3250	_
6	2	Spontaneous	PUCs in the second trimester	PGS+SL	38 weeks	CS	2900	_
7	5	IVF	Normal	PGS+SL	38 weeks	CS	2950	-

CS cesarean section, IVF in vitro fertilization, PGS progesterone, PUC premature uterine contractions, RVT radical vaginal trachelectomy, SL spasmolytics



inspected intraoperatively in order to identify metastasis. The intraoperative decision to proceed with RVT was conditioned by the absence of metastasis in the sentinel lymph node and the absence of the tumor cells in the resection margins. The extemporaneous evaluation of the sentinel lymph node and of the trachelectomy specimen represented an indicator for the necessity of an immediate conversion to radical vaginal hysterectomy.

Histopathological examination was focused on the detection of micrometastasis in the resected lymph nodes. The risk of discovering micrometastasis in cases with a negative sentinel lymph node at standard staining (hematoxylin and eosin) can be up to 20 % when immunohistochemistry is added and 42.8 % at reevaluation with RT-PCR for the expression of CK19 [21, 22]. Therefore, systemic pelvic lymphadenectomy regardless of sentinel lymph node involvement was considered necessary in all cases with early cervical cancer.

The conversion rate to radical vaginal hysterectomy due to the presence of lymph node metastasis in this series was 11.1 % (four cases). This ranks just below the 12–17 % conversion rate described by other authors [23].

RVT reduces the spontaneous pregnancy rate by about 25–30 % by reducing the length of the cervix or by causing cervical stenosis. The authors attempted to minimize this effect by preserving 1 cm of cervical tissue up to the level of the internal cervical os [24].

The histopathological examination of the resection margins performed extemporaneously and postoperatively on embedded specimens demonstrated the absence of tumor invasion in all the cases. However, some authors consider that the resection margins should be evaluated only when there is a visible lesion in the cervix [25].

The main focus of conservative surgery for early cervical cancer is the preservation of the reproductive function without prejudice to the oncological radicality of the procedure. RVT does not guarantee a future pregnancy or an evolution that does not imply any risk for miscarriage or preterm delivery. Patients should be counseled thoroughly about these possible outcomes in the preoperative setting. In this case series, two (6.25 %) patients had miscarriages in the first trimester of pregnancy and required surgical evacuation of the uterine contents by dilation and curettage. This outcome ranks under the rates of miscarriage after RVT described in the literature [21, 26, 27].

Out of seven pregnancies obtained after RVT during this study, five (71.4 %) were delivered by elective cesarean section at 38–39 weeks of pregnancy. All neonates weighed over 2900 g. The prophylactic cerclage of the residual uterine body was recommended by other authors as well [26] and proved to be an efficient way of reducing the risk of miscarriage, ascending infections, and premature rupture of membranes. The number of obtained pregnancies was consistent with our patients' desire for postoperative fertility. From this point of

view, the data obtained in this study (15.7 %) were similar to the data in literature [3, 28].

From this point of view, the most intriguing case in this series was that of a 29-year-old patient who obtained a pregnancy after 5 years of infertility and was diagnosed with cervical carcinoma stage IB1 at 13 weeks of gestation. The patient strongly desired to keep the pregnancy in spite of all the associated risks and elected a conservative treatment for cervical cancer. Radical vaginal trachelectomy with laparoscopic pelvic lymphadenectomy were performed with good postoperative outcomes for the mother and fetus. The pregnancy evolved uneventfully, and the patient was monitored monthly until term, when she was delivered of a healthy infant via cesarean section.

## **Conclusions**

Radical vaginal trachelectomy with pelvic laparoscopic lymphadenectomy is an alternative therapeutic option in selected patients with early-stage cervical cancer who desire preservation of fertility and/or body image. It is far less invasive than abdominal trachelectomy and is similarly efficient from an oncological viewpoint.

**Conflict of Interest** The authors declare that they have no competing interests

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