

Surgical, Oncological and Obstetric Outcomes After Radical Abdominal Trachelectomy for Early-Stage Cervical Cancer at a Single Tertiary Center.

Marlene Kranawetter

Medical University of Vienna

Christoph Grimm (✉ Christoph.grimm@meduniwien.ac.at)

Medical University of Vienna

Helena M Obermair

University of Notre Dame Australia <https://orcid.org/0000-0002-0217-6574>

Valentina Paspalj

Medical University of Vienna

Alexander Reinthaller

Medical University of Vienna <https://orcid.org/0000-0002-7205-0985>

Eva Langthaler

Medical University of Vienna

Stephan Polteraer

Medical University of Vienna <https://orcid.org/0000-0002-9649-4505>

Research Article

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Abstract

Purpose

Radical trachelectomy is a viable option to preserve fertility for young patients with early cervical cancer. The aim of this study was to report surgical, oncological and obstetric outcomes of patients treated with radical abdominal trachelectomy at our institution.

Methods

A retrospective chart analysis and telephone survey for all patients with early stage cervical cancer treated with a radical abdominal trachelectomy and pelvic lymphadenectomy between 2007 and 2019 at the Department of Obstetrics and Gynaecology at the Medical University of Vienna, Austria was performed.

Results

Radical abdominal trachelectomy with pelvic lymph-node dissection was attempted for 22 patients. Four cases required conversion to radical hysterectomy due to positive resection margins and two cases required primary chemo-radiotherapy due to positive lymph nodes. Sixteen successfully abdominal radical trachelectomies preserving fertility were performed with two of these patients treated with neo-adjuvant chemotherapy. With a median follow-up time of 21.5 (6.5- 57.25) months, one patient (4.5%) had disease recurrence and subsequently died from cervical cancer. Six patients attempted to conceive, with a resulting four pregnancies with a live birth rate of 75%.

Conclusion

Abdominal radical trachelectomy is a safe procedure for women with early stage cervical cancer who desire fertility preservation. Surgery should be performed at a high volume gynaeco-oncological center.

Introduction

Cervical cancer is the fourth most common cancer in women worldwide, and is often first detected in women of child-bearing age.¹ Cervical cancer is most commonly detected at an early stage, particularly in developed countries with formal screening programs.² As the average child-bearing age increases, the number of women with cervical cancer who wish to conceive also has increased.³ Therefore fertility-sparing treatment of early cervical cancer has become a major issue. Fertility-sparing surgery has important implications for the psychosocial welfare of patients, who often experience feelings of depression and grief associated with loss of fertility.⁴

Radical trachelectomy was first described by Dargent in 1994 using a vaginal approach⁵ and later in 1997 complemented by Smith using an abdominal approach.⁶ Subsequently the procedure has been used in several tertiary cancer centers, demonstrating fertility preservation and oncologic safety.⁷⁻⁹

Radical trachelectomy is a therapeutic option for women who are of reproductive age and still wish to conceive, diagnosed with early stage squamous cell or adenocarcinoma, with limited endocervical extension and no evidence of lymph node metastasis on initial staging.¹⁰ During the procedure pelvic lymph nodes are typically removed, followed by the removal of the cervix, parametria and the upper vagina. For early-stage cervical cancer, radical trachelectomy has equivalent oncologic outcomes to radical hysterectomy.^{11,12} Obstetric outcomes reported in the literature to date are limited and inconsistent.^{13,14}

There is little information about the performance of radical trachelectomy in Germany and Austria¹⁵⁻¹⁷ and only few tertiary care centers in Central Europe perform the procedure. This study reports the surgical, oncologic, and obstetric outcomes of a series of patients treated with radical abdominal trachelectomy at the Department of Obstetrics and Gynaecology, Medical University of Vienna, Austria over 12 years.

Methods

In this retrospective analysis, all consecutive patients with early stage cervical cancer and the desire to preserve fertility, treated with radical trachelectomy between September 2007 and April 2019 at a single academic institution (Medical University of Vienna) were included. Institutional review board approval was obtained from the Ethics Committee of the Medical University of Vienna (1641/2018).

Women of reproductive age, diagnosed with early stage cervical cancer and the wish to preserve fertility were discussed at a multidisciplinary tumour board to consider fertility preserving therapy.

In our institution all patients had lymphadenectomy followed by radical trachelectomy through an open, abdominal approach. In 4 cases laparoscopic lymph node dissection was performed prior to laparotomy. Sentinel lymph node dissection was performed in 5 patients. Two patients with neoadjuvant chemotherapy had pelvic laparoscopic lymph node staging before neoadjuvant chemotherapy was initiated. A radical abdominal trachelectomy according to Querleu-Morrow type C1 radical hysterectomy^{18,19} was performed and the cervix, parametrium and vaginal cuff were excised. A non-resorbable cerclage was positioned and the residuum of the cervix, was then sutured to the vagina. All patients underwent follow-up at our institution and patients lost to follow-up were actively contacted. Clinico-pathological data were assessed by chart review.

Descriptive statistics such as mean, median, frequencies, and percentages were used to present patient's characteristics. Categorical variables were described as median/range for metric variables without normal distribution described as mean (standard deviation=SD), using SPSS version 20.0 (IBM Corporation, New York, USA).

Results

Patients' characteristics are shown in Table 1. The median age at first diagnosis of cervical cancer was 33 (27.7- 35.2) years. According to the 2009 International Federation of Gynecology and Obstetrics (FIGO) staging guidelines, 86.4% (n=19) of disease was diagnosed at FIGO stage 1B1 and 13.6% (n=3) at FIGO stage 1B2. In the present manuscript the 2018 FIGO classification system is used.²⁰ Based on the revised classification, we had one (4.5%) patient with FIGO stage 1A1, three (13.6%) patients at FIGO stage 1A2, seven (31.8%) patients at FIGO stage 1B1, nine (41.0%) at FIGO stage 1B2 and two (9.1%) patients at FIGO stage 1B3. The median tumour size of all cases was 20mm (10.5- 26.5). 77.3% (n=17) of cases were diagnosed as squamous cell carcinomas, 22.7% (n=5) of cases as adenocarcinomas. Three (13.6%) patients well differentiated carcinomas, 13 (59.1%) patients intermediate and six (27.3%) patients undifferentiated carcinomas. Two (9.5%) patients, with an initial tumour size of 34mm and 40mm received neoadjuvant chemotherapy with 6 cycles of weekly platinum based combination-chemotherapy. All patients had a surgical evaluation of pelvic lymph nodes prior to radical trachelectomy. In 4 cases laparoscopic lymph node dissection was performed, all other cases had open lymph node dissection. Patients with neoadjuvant chemotherapy underwent lymph node dissection prior to initiation of neoadjuvant chemotherapy. Frozen section analysis of lymph node specimens was performed for 5 patients. A median number of 17.5 (15.0- 33.5) lymph nodes were resected. Radical abdominal trachelectomy was attempted in 22 patients. Two (9.1%) patients required primary chemo-radiotherapy due to positive lymph nodes and no radical trachelectomy or hysterectomy was performed. Successful abdominal radical trachelectomy was performed in 16 (72.7%) patients. Four (19%) cases required radical hysterectomy due to positive endocervical resection margins. Median width of resected parametria was 30mm (15.75- 38.75), and parametrial nodes were ascertained in 7 (31.8%) patients. There was no infiltration of the parametria or the parametrial lymph nodes for any patients. Median length of surgery, length of hospital stay and complications are shown in Table 1. No severe intraoperative complications were observed. Postoperatively, three patients experienced Clavien- Dindo grade III complication. Two patients required drainage of lymphatic cysts and one patient required drainage of a pelvic abscess.

With a median follow-up time of 21.5 (6.5- 57.25) months, one patient (4.5%) had pelvic wall recurrence. At initial diagnosis this patient had a 1B2 (25mm diameter) adenocarcinoma, with negative lymph nodes (0/43). She had not conceived, recurred 85 months after primary surgery and finally died 127 months after radical abdominal trachelectomy. At the time of recurrence, she received palliative chemo-radiotherapy subsequently followed by therapy with an immune-check-point inhibitor.

Obstetric outcomes are shown in Table 2. Only 6 (37.5%) out of the 16 patients, who had a successful radical trachelectomy, attempted to conceive. Reported reasons for patients not trying to conceive included fear of cancer recurrence and fear of preterm delivery (Table 2). Four (25.0%) of the six patients who tried to conceive subsequently became pregnant. Three patients conceived spontaneously and one patient underwent successfully in vitro fertilization and embryo transfer. One patient experienced a first trimester miscarriage. Three pregnancies were delivered by Caesarean section in the third trimester, two

patients by scheduled Caesarean section at 38 weeks gestation and one patient by emergency Caesarean section at 35 weeks` gestation due to acute vaginal bleeding, the cause of which remained unclear. Of the three patients with live births, two patients experienced vaginal bleedings during the first trimester, in one case most likely caused by a decidual polyp. One patient experienced urinary retention in the second trimester, requiring an indwelling urinary catheter for few days. Symptoms resolved at the end of the second trimester.

Figure 1 shows ultrasound images of a pregnant patient with cervical length measurements and cerclage position.

Discussion

This study describes the outcome of patients with early stage cervical cancer who underwent abdominal radical trachelectomy. It is the first report about a series of abdominal radical trachelectomies in Austria. In Germany reports on this technique are also limited and most cases were reported using a vaginal approach. In our cohort patients experienced overall good surgical and oncological outcome and four pregnancies with three live births were observed. Interestingly, many patients in our cohort did not try to conceive despite having fertility- sparing management for cervical cancer.

Globally fertility- sparing trachelectomy for early cervical cancer is still a rarely used procedure. A recent published survey by Matsuo et al. in the United States described 815 cases of trachelectomies performed in 89 centers over ten years (2001 to 2011). The vast majority of centers included in this survey (76.4%) had a limited surgical volume of just one case per year.²¹ Even though the technique of abdominal radical trachelectomy is similar to abdominal radical hysterectomy, it remains a challenging surgical technique and a certain learning curve has to be considered.²² A higher surgical volume is associated with reduced perioperative morbidity and pooling cases of radical trachelectomies in high volume gynecologic centers is highly recommended.²¹ The Medical University of Vienna is the largest center for gynecologic oncology in Austria. The surgical volume performed at our institution is comparable to top-decline centers in the United States (>2 cases per year).²¹ A nationwide survey of all trachelectomies performed in Austria is not available. The median surgical time (285 min vs 250 min), intraoperative and postoperative complication rate of our institution is comparable to previous internationally reported outcomes.²²

After results were released from the prematurely closed Laparoscopic Approach to Cervical Cancer (LACC) trial, the surgical approach for radical hysterectomy for the management of early cervical cancer now clearly favors an open abdominal approach.²³ For radical trachelectomy no such data are available and different surgical approaches are used. A current study, the International Radical Trachelectomy Assessment study (IRTA study) is evaluating the oncological safety of open compared to minimally invasive radical trachelectomy.²⁴ Existing data show oncological safety irrespective of the surgical approach for trachelectomy.²⁵ In a recent systematic review, Nezhat et al. found a cancer recurrence rate of $3.6 \pm 7.1\%$ in patients with abdominal radical trachelectomy (n=1060) within a median follow up

period of 33 months. In this study we report one (6.7%) recurrence of disease within a follow up period of 34.7 months, which is comparable to existing literature. Providing a careful patient selection, radical abdominal trachelectomy is a safe oncological procedure.

Another aim of this study was to evaluate pregnancy rates and obstetric outcomes after abdominal radical trachelectomy. The largest report on reproductive outcomes after fertility sparing surgery had been published by Nezhat et al. in 2020.²⁵ In this systematic review including 3000 patients receiving fertility sparing surgery, 1047 pregnancies were observed with a significant difference in the clinical pregnancy rate in patients who underwent vaginal radical trachelectomy compared to abdominal radical trachelectomy ($67.5\% \pm 20.0\%$ vs. $41.9\% \pm 19.4\%$). The authors argued, that the vaginal approach might cause fewer intra- abdominal and pelvic adhesions with a subsequent reduction in tubal factor infertility.²⁵ In our cohort we found a clinical pregnancy rate of 25%, consistent with this systematic review. The live birth rate reported by Nezaht et al. after abdominal radical trachelectomy was $65.7\% \pm 24.1$ compared to 75% in our cohort. In the present study, all patients had a cerclage placed at time of radical abdominal trachelectomy. Prospective data on advantages and disadvantages of cerclage placement during this procedure is not available, and the approach is usually based on surgeons' preference. With respect to complications during pregnancy, one patient experienced significant vaginal bleeding at 35 weeks` gestation. Due to suspected rupture of the cerclage she had an emergency Caesarean section at 35 weeks and gave birth to a healthy neonate. All other pregnancies in our cohort were not associated with any significant obstetric complications. Similarly to our cohort, Nezhat et al. reported a large numbers of patients who did not try to conceive post- trachelectomy (60% vs 62.5%, respectively). Given that only women with a strong desire to preserve fertility should be eligible for fertility preserving oncological management, the number of women not attempting to conceive post-trachelectomy seems extremely high. In our study we evaluated reasons for not trying to conceive which included fear of cancer recurrence and fear of preterm delivery. This reinforces the importance of extensive pre- therapeutic patient counselling and close follow up after initial therapy with multidisciplinary medical care (e.g. reproductive endocrinologist, clinical psychologist).

This study has some limitations. Due to the retrospective study design a certain reporting bias must be kept in mind and major conclusions cannot be drawn. Given the sample size of existing systematic reviews, the number of patients in our cohort is small and hast to be interpreted as an additional contribution to these reviews. Nonetheless, this is the first series describing radical abdominal trachelectomies and their outcomes in the German speaking area.

Abdominal radical trachelectomy is an oncologically safe procedure in well- selected cervical cancer patients. The procedure is well studied and can be seen as a standard treatment option in women, who fulfill clinicopathological criteria for fertility preservation and desire to preserve fertility. Radical abdominal trachelectomy should be performed exclusively at high volume gynecologic centers with extensive patient education being an essential component to clarify obstetric desires and risks.

Declarations

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Conflicts of interest:

Marlene Kranawetter received travel grant from Roche, PharmaMar and Tesaro outside of this work.

Christoph Grimm received fees as a consultant from AstraZeneca, Celgene, MSD, PharmaMar, Roche, GSK/Tesaro, Vifor Pharma, Clovis as a speaker from Amgen, AstraZeneca, MSD, PharmaMar, Roche, GSK/Tesaro and direct research funding from Meda Pharma, Roche Diagnostics outside of this project.

Helena Obermair has nothing to declare.

Valentina Paspalj has nothing to declare.

Alexander Reinthaller received fees for lectures, advisory boards or grants for research projects from Amgen, Astra Zeneca, Celgene, Clovis, GSK, MSD, PharmaMar, Roche, Roche Diagnostics, Tesaro and Vifor Pharma outside of this project.

Eva-Maria Langthaler has nothing to declare.

Stephan Polterauer received fees for lectures, advisory boards or grants for research projects from Astra Zeneca, Celgene, MSD, PharmaMar, Roche, Roche Diagnostics, Meda Pharma, Tesaro and Vifor Pharma outside of this project.

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Author Contribution

M Kranawetter: Protocol/project development, Data collection and management, Data analysis, Manuscript writing/editing

C Grimm: Protocol/project development, Data analysis, Manuscript writing/editing

HM Obermair: Data collection

V Paspalj: Manuscript writing/editing

A Reinthaller: Manuscript writing/editing

E Langthaler: Data collection

S Polterauer: Protocol/project development, Data management, Data analysis, Manuscript writing/editing

References

1. Siegel RL, Miller KD, Jemal A, Cancer statistics (2017) *CA: A Cancer Journal for Clinicians* **67**, 7–30 (2017)
2. Bethesda M (2019) SEER Cancer Stat Facts: Cervical Cancer. National Cancer Institute
3. Siegel RL, Miller KD, Jemal A (2019) Cancer statistics, 2019. *Cancer J Clin* **69**:7–34
4. Carter J et al (2005) Gynecologic cancer treatment and the impact of cancer-related infertility. *Gynecol Oncol* **97**:90–95
5. Dargent D, Martin X, Sacchetoni A, Mathevet P (2000) Laparoscopic vaginal radical trachelectomy: a treatment to preserve the fertility of cervical carcinoma patients. *Cancer* **88**:1877–1882
6. Smith JR et al (1997) Abdominal radical trachelectomy: a new surgical technique for the conservative management of cervical carcinoma. *Br J Obstet Gynaecol* **104**:1196–1200
7. Abu-Rustum NR, Sonoda Y (2007) Fertility-sparing radical abdominal trachelectomy for cervical carcinoma. *Gynecol Oncol* **104**:56–59
8. Cibula D et al (2009) Abdominal radical trachelectomy in fertility-sparing treatment of early-stage cervical cancer. *International journal of gynecological cancer: official journal of the International Gynecological Cancer Society* **19**:1407–1411
9. Rob L, Skapa P, Robova H (2011) Fertility-sparing surgery in patients with cervical cancer. *Lancet Oncol* **12**:192–200
10. Marchiole P et al (2007) Oncological safety of laparoscopic-assisted vaginal radical trachelectomy (LARVT or Dargent's operation): a comparative study with laparoscopic-assisted vaginal radical hysterectomy (LARVH). *Gynecol Oncol* **106**:132–141
11. Lanowska M et al (2011) Radical vaginal trachelectomy (RVT) combined with laparoscopic lymphadenectomy: prospective study of 225 patients with early-stage cervical cancer. *International journal of gynecological cancer: official journal of the International Gynecological Cancer Society* **21**:1458–1464
12. Xu L, Sun F-Q, Wang Z-H (2011) Radical trachelectomy versus radical hysterectomy for the treatment of early cervical cancer: a systematic review. *Acta obstetrica et gynecologica Scandinavica* **90**:1200–1209
13. Bentivegna E et al (2016) Fertility results and pregnancy outcomes after conservative treatment of cervical cancer: a systematic review of the literature. *Fertility sterility* **106**:1195–1211.e5
14. Pareja R et al (2015) Immediate radical trachelectomy versus neoadjuvant chemotherapy followed by conservative surgery for patients with stage IB1 cervical cancer with tumors 2cm or larger: A literature review and analysis of oncological and obstetrical outcomes. *Gynecol Oncol* **137**:574–580
15. Speiser D, Kohler C, Schneider A, Mangler M (2013) Radical vaginal trachelectomy: a fertility-preserving procedure in early cervical cancer in young women. *Deutsches Arzteblatt international* **110**:289–295

16. Speiser D et al (2017) Follow-up after radical vaginal trachelectomy (RVT): patients' problems and physicians' difficulties. *Archives of gynecology obstetrics* 296:559–564
17. Bader AA, Tamussino KF, Moinfar F, Bjelic-Radisic V, Winter R (2005) Isolated recurrence at the residual uterine cervix after abdominal radical trachelectomy for early cervical cancer. *Gynecol Oncol* 99:785–787
18. Querleu D, Morrow CP (2008) Classification of radical hysterectomy. *Lancet Oncol* 9:297–303
19. Querleu D, Cibula D, Abu-Rustum NR (2017) 2017 Update on the Querleu-Morrow Classification of Radical Hysterectomy. *Ann Surg Oncol* 24:3406–3412
20. Bhatla N, Aoki D, Sharma DN, Sankaranarayanan R (2018) Cancer of the cervix uteri. *Int J Gynaecol Obstet* 143 Suppl:22–36
21. Matsuo K et al (2020) Association between hospital surgical volume and perioperative outcomes of fertility-sparing trachelectomy for cervical cancer: A national study in the United States. *Gynecol Oncol* 157:173–180
22. Pareja R, Rendon GJ, Sanz-Lomana CM, Monzon O, Ramirez PT (2013) Surgical, oncological, and obstetrical outcomes after abdominal radical trachelectomy - a systematic literature review. *Gynecol Oncol* 131:77–82
23. Ramirez PT et al (2018) Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. *N Engl J Med* 379:1895–1904
24. Salvo G et al (2019) International radical trachelectomy assessment: IRTA study. *International journal of gynecological cancer: official journal of the International Gynecological Cancer Society* 29:635–638
25. Nezhat C, Roman RA, Rambhatla A, Nezhat F (2020) Reproductive and oncologic outcomes after fertility-sparing surgery for early stage cervical cancer: a systematic review. *Fertility sterility* 113:685–703

Tables

Table 1. Patients' characteristics

Parameter	N (%), median (IQR)
Number of patients	22 (100)
Age (years)	33 (27.7- 33.2)
BMI	21.4 (20.3- 22.9)
History of previous pregnancy	
Yes	1 (4.5)
No	21 (95.5)
FIGO stage (2018 system)	
1A1	1 (4.5)
1A2	3 (13.6)
1B1	7 (31.8)
1B2	9 (41.0)
1B3	2 (9.1)
Histology	
Squamous	17 (77.3)
Adenocarcinoma	5 (22.7)
Grading (G)	
G1	3 (13.6)
G2	13 (59.1)
G3	6 (27.3)
Tumor size (mm)	20 (10.5- 26.5)
Presence of LVSI	7 (31.8)
NACT	2 (9.1)
Type of Surgery	
Abdominal	22 (100)
Lymph Node Staging performed	22 (100)
Sentinel lymph node procedure	5 (22.7)
Lymph node positive	2 (9.1)
Number resected lymph nodes	17.5 (15.0- 33.5)

Trachelectomy abruption	6 (27.3)
Rate of conversion to chemo-radiation	2 (9.1)
Rate of conversion to hysterectomy	4 (19)
Width of resected parametria (mm)	30 (15.75- 38.75)
Resected parametrial lymph nodes	7 (31.8)
Surgical time (min)	285 (240- 301.25)
Length of hospital stay (days)	10 (8.75- 12.25)
Postoperative Complications	
Clavien-Dindo Classification	
Grade 1	15 (68.2)
Grade 2	4 (18.2)
Grade 3	3 (13.6)
Follow-up (months)	21.5 (6.5- 57.25)
Recurrence†	1 (4.5)
Local	1 (100)
Distant	0 (0)
Death from disease	1 (4.5)

FIGO: Fédération Internationale de Gynécologie et d'Obstétrique. NACT: neoadjuvant chemotherapy. LVSI: lymph vascular invasion. †only patients with completed abdominal radical trachelectomy

Table 2. Obstetric outcomes after radical abdominal trachelectomy

Parameter		N (%), median (IQR)
Number successful radical abdominal trachelectomy		16 (100)
Women attempting pregnancy	Yes	6 (37.5)
	No	8 (50.0)
	Unknown	2 (12.5)
Reason for not trying to conceive		
Recurrence of disease		1 (6.25)
No partner		1 (6.25)
Anxiety of premature birth		1 (6.25)
Anxiety of recurrence of cervical cancer		2 (12.5)
Pregnancy planned in near future		1 (6.25)
Follow up <6 months		1 (6.25)
Unknown		1 (6.25)
Clinical pregnancy rate		4 (25.0)
Conception	ART	1 (6.25)
	spontaneous	3 (18.75)
Cerclage	Yes	4 (25.0)
First trimester miscarriage		1 (6.25)
Second trimester deliveries		0 (0.0)
Third trimester deliveries		3 (18.75)
Birth procedure	Cesarean	3 (18.75)
Gestational age		37.0 (35- 38)

ART: Assisted reproductive technique

Figures



Figure 1

Successful pregnancy after radical abdominal trachelectomy. A cerclage was placed at time of trachelectomy.