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GYNECOLOGIC ONCOLOGY

Long-term fertility, oncological, and quality-of-life outcomes after trachelectomy in early stage cervical cancer

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Abstract

Purpose Our aim was to evaluate fertility-sparing surgery of early stage cervical cancer after the introduction of vaginal trachelectomy (VT) and pelvic lymph node dissection (PLND). The objectives were to assess surgical, long-term oncological, fertility, and obstetric outcomes together with self-assessed quality of life (QoL).

Methods All women ≤ 40 years diagnosed with early stage cervical cancers IA1–IB1 and ≤ 2 cm treated by VT and PLND between 2000 and 2014 were included. All successful fertility-sparing surgeries were identified. Medical records were reviewed and analyzed for surgical, oncological, fertility, and obstetric outcomes. Postal questionnaires were collected to further evaluate and validate the fertility and obstetric outcomes and QoL was assessed using the QLQ-C30 and QLQ-CX24 instruments.

Results Thirty-nine patients fulfilled the inclusion criteria, where 28 patients (71.8%) had successful VT performed with preserved fertility according to the oncological guidelines. Mean follow-up after VT was 95.0 months (range 26.5–182.4). There were 2 recurrences (7.1%) registered. All together, 24 pregnancies were identified and 17 children born; 76.5% after gestational week (gw) ≥ 34 + 0 and 23.5% preterm (gw < 34 + 0). The questionnaires revealed an overall high level of self-assessed QoL with global health status scores of 91.7 (median) and physical, role, emotional, cognitive, and social functioning all had median scores of 100 and a low incidence of "symptom experience scores" of urogynecological morbidity, although 38.9% experienced lymphedema.

Conclusions Early stage cervical cancers treated by VT and PLND are associated with acceptable long-term oncological outcomes, relatively high rate of successful pregnancies, and a high long-term QoL.

Keywords Cervical cancer · Fertility-sparing surgery · Trachelectomy · Outcome · Quality of life

Introduction

Cervical cancer affects women of all ages. About 500 000 new cases are discovered worldwide each year, and approximately 25% of women diagnosed are under the age of 40 [1]. In Sweden, the cervical cancer incidence of 11.3/100.000 women is lower than in many other countries [2]. Fertility-sparing therapy options are important to young women if their oncological safety can be secured. Besides the obvious trauma of a cancer diagnosis and fear of cancer recurrence, many other perspectives should be considered when cancer affects the reproductive organs in women of fertile age, including the wish to conceive, fear of subsequent impaired fertility, and sexual health and quality of life (QoL).

Early stage cervical cancer is traditionally treated by radical hysterectomy (RH) and lymph node dissection. Women of fertile age may today be offered fertility-sparing surgery consisting of radical trachelectomy (RT) and pelvic lymph node dissection (PLND) [3]. The trachelectomy procedure was introduced by Dargent in the early 1990s [4]. Studies have shown similar survival and cancer recurrence rates between trachelectomy and RH cohorts in comparable early

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stage cervical cancer [5–7]. Since the introduction of trachelectomy, the procedure has been performed in different ways. Both abdominal and vaginal approaches are being used as well as various surgical techniques such as conventional laparotomy, laparoscopy, and robotic-assisted laparoscopy, and various combinations [8–11]. Furthermore, the least radical surgery is referred to as simple vaginal trachelectomy (SVT), where the ureters are not dissected free, but part of the parametrium and the upper part of the vagina resected. The exact definition concerning radical versus simple trachelectomy is lacking, but both are referred to as trachelectomies and recommended as a fertility sparing option by the European Society for Medical Oncology (ESMO) in early stage cervical cancers [12–14]. There is no general consensus regarding preferred surgical approach.

Nevertheless, one should emphasize that the main purpose for performing a trachelectomy in a woman of fertile age is to preserve fertility. Therefore, it is of great importance to, besides studying oncological safety, also evaluate the obstetric outcome and fertility issues as well as quality of life (QoL). Although trachelectomy may preserve fertility and may seem less radical than hysterectomy, it could still result in significant life-impairing morbidity. Very few studies have investigated QoL in patients treated by trachelectomy, and to our knowledge, there are no existing long-term studies. There are studies suggesting impaired QoL, urogynecological morbidity and lymphedema after treatment [15] as well as sexual dysfunction [16, 17].

Our aim was to evaluate the long-term results of VT and PLND performed in early stage cervical cancers at a university hospital setting, where primary cervical cancer care is centralized. Our primary objective was to establish the total number of successful trachelectomies. Secondary outcomes were tumor characteristics, additional treatments, complications, and long-term oncological, fertility, and obstetric outcomes together with QoL.

Materials and methods

Study design

This is a cohort study of all early stage cervical cancers in women ≤ 40 years, treated by VT and PLND in the western Sweden health care region (population 1.8 million). In this region, cervical cancers are centralized to Sahlgrenska University Hospital. The study was conducted from the introduction of VT in 2000 to 2014 and performed at Sahlgrenska University Hospital. To identify all study patients, we conducted a computerized search using surgical codes related to trachelectomy, conization, and hysterectomy. We chose selection criteria of women ≤ 40 years to identify a cohort treated with fertility sparing surgery with a fair chance of pregnancy. According to our national oncological guidelines [18], the recommended criteria to perform VT and PLND in cervical cancer were: tumor stage IA1 with lymph vascular space invasion, stages IA2–IB1 with a tumor size ≤ 20 mm (mm), and absence of high–risk histology. We defined successful VT as removal of the cervical cancer with adequate margins and an intact uterus. Expert gyne-oncological referral pathologists assessed the tumor margins. Adequate margins were defined as at least 5-mm margin from tumor to resected area. If during surgery, the frozen section of the top part of the trachelectomy specimen was found to have inadequate margins or metastasis in the pelvic lymph glands, an RH was performed in the same procedure. Furthermore, if the final postoperative pathological review considered the trachelectomy specimen to have inadequate margins or occurrence of lymph gland metastasis, an RH was recommended in a second surgery according to our national oncological guidelines. Patients were preoperatively thoroughly informed about the protocol and guidelines. We thoroughly reviewed all medical records for background factors and surgical, oncological, and obstetric outcomes. Peri- and post-operative adverse events were registered and graded according to the Clavien–Dindo classification scale [19]. To establish complete postoperative follow-up, cervical cancer recurrences, and dysplasia, we conducted a cross-check with the Swedish database "cytburken", which records the majority of Papanicolaou tests taken in Sweden (www.cytburken.se) [20]. We supplemented the retrospective analysis with postal questionnaires, adding information about fertility, obstetric, and QoL outcomes. The regional ethical review board of Gothenburg (D no.: 089–15) approved the study.

Study cohort

All women ≤ 40 years who fulfilled the inclusion criteria were included in the study. The cohort represents the total number of VT and PLND performed in women diagnosed with cervical cancer stage IA1 with lymph vascular space invasion or stage IA21–IB1 and tumor size ≤ 20 mm in the western Sweden health care region during the study period. The study cohort was followed until January 27 2017 or until death or lost to follow up.

Postal questionnaires

The postal questionnaires consisted of two parts. The first part, designed by the authors, contained questions about fertility and obstetrical outcomes. The second part consisted of two validated self-assessed QoL questionnaires (QLQ-C30 and QLQ-CX24) from the European Organization for Research and Treatment of Cancer (EORTC). The QLQ-C30 questionnaire has 30 questions evaluating symptoms applicable to a broad spectrum of cancer patients, global

health status (GHS), five multi-item functioning scales (physical, role, emotional, social, and cognitive functioning), three multi-item symptom scales (fatigue, pain, and nausea/vomiting), and six single-item symptom scales (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) [21]. The subpart QLQ-CX24 is a cervical-cancer-specific questionnaire, containing 24 questions about symptoms that could result from cervical cancer treatment. It consists of four functioning scales: two multi-item scales (body image and sexual/vaginal functioning) and two single-item scales (sexual activity and sexual enjoyment). There are also five symptom scales, four single-item scales (lymphedema, peripheral neuropathy, menopausal symptoms, and sexual worry), and one multi-item scale (symptom experience) [22]. All scale and item scores were transformed to a 0–100 scale, following the scoring manual of the EORTC [23]. A high score on the GHS/QoL represents a high QoL, higher scores on functioning scales represent high or healthy levels of functioning, and high scores on symptom scales represent high levels of symptoms or problems.

The questionnaires, study-information, a written consent form, and a postage-paid return envelope were posted from March to August 2016 to all study patients living in Sweden with successfully performed VT and without cancer recurrences. Non-responders were sent a new questionnaire after 6 weeks and a final reminder was sent after a further 4 months.

Statistical analyses

Due to the size of our study cohort, we were limited to descriptive and basic statistics. We used Microsoft Excel® for MAC 2011 version 14.7.1 and SPSS, IBM® SPSS statistics version 23.

Results

Patients and tumor characteristics

A flow chart of the study population is shown in Fig. 1. Thirty-nine patients fulfilled the inclusion criteria and had VT and PLND performed, whereas 28 (71.8%) patients had successful surgeries with preserved fertility. In 27 of these surgeries, VT and PLND were performed in the same surgical session: and one VT was performed at another hospital with PLND and cerclage performed at Sahlgrenska University Hospital. The VTs performed were slightly heterogeneous concerning surgical techniques. The first surgeries could be considered as radical VTs as in complete ureter dissection and parametrial removal. However, in the majority of patients, the ureters were not dissected free, thereby could be considered as SVT. The PLNDs were performed by

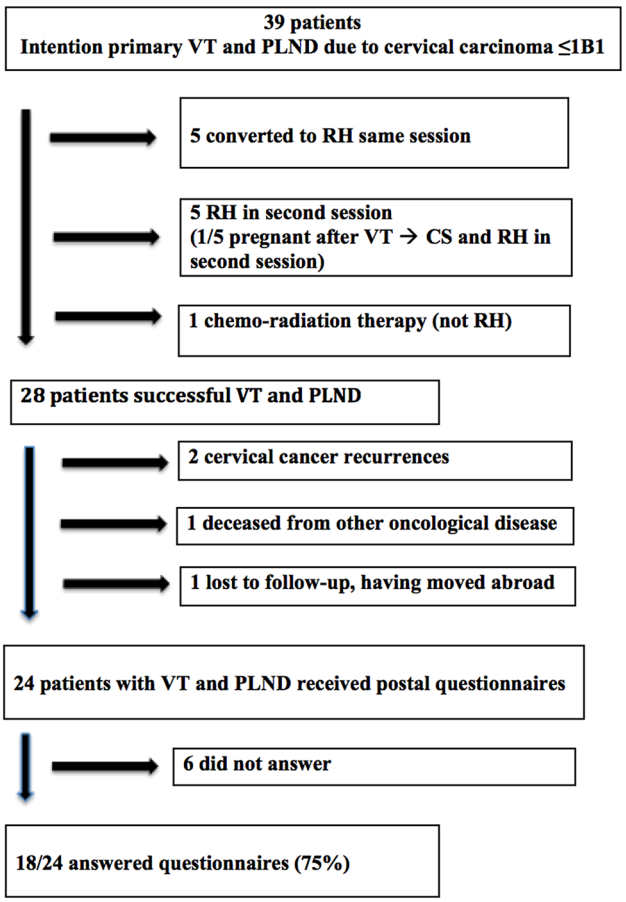

Fig. 1 Flow chart showing study cohort, successful VT. *VT* vaginal trachelectomy, *PLND* pelvic lymph node dissection, *RH* radical hysterectomy, *CS* cesarean section

laparoscopy (16 patients), robotic-assisted laparoscopy (10 patients), and abdominal surgery (2 patients).

Eleven (28.2%) out of the initial 39 patients were converted to radical hysterectomies or oncological therapies following our oncological recommendations (Fig. 1). One patient had a lymph node metastasis and received concomitant chemo-radiation without further surgery. Ten patients were treated with RH, five in the same surgical session as VT and five in a second surgery. This was due to that the pathological review revealed inadequate margins in frozen sections during surgery or in the final pathological assessment and in one patient due to the finding of lymph node metastasis during surgery. There were frozen sections performed in the majority of cases but not in the complete cohort due to organizational issues.

The very first successful VT did not include cerclage at the time due to inexperience, but a cerclage was installed a few years after the primary VT. Patients and tumor characteristics are shown in Table 1.

The mean follow up of the entire study cohort was 95.0 months (range 26.5–182.4), defined as the time from VT

Table 1 Patient and tumor characteristics, successful VT

Patient characteristics	Total ($n=28$)	NED ($n=26$)	Recurrence ($n=2$)
Age at surgery, mean (range)	30.0 (24–37)	30.0 (24–37)	30.5 (26-–35)
BMI, mean (range)	22.9 (19.4–32.9)	22.6 (19.4–32.9)	25.1 (19.8–30.5)
Not stated, *n* (%)	8 (28.6)	8 (30.8)	0
Parity before surgery			
Yes, *n* (%)	11 (39.3)	9 (34.6)	2 (100)
No, *n* (%)	17 (60.7)	17 (65.4)	0
Stage			
1A1 + LVSI, *n* (%)	1 (3.6)	1 (3.8)	0
1A2, *n* (%)	10 (35.7)	10 (38.5)	0
1B1, *n* (%)	17 (60.7)	15 (57.7)	2 (100)
Histology			
SCC, *n* (%)	20 (71.4)	19 (73.1)	1 (50)
AC, *n* (%)	8 (28.6)	7 (26.9)	1 (50)
Grade			
1, *n* (%)	5 (17.9)	5 (19.2)	0
2, *n* (%)	10 (35.7)	9 (34.6)	1 (50)
3, *n* (%)	10 (35.7)	9 (34.6)	1 (50)
Not stated, *n* (%)	3 (10.7)	3 (11.5)	0
LVSI			
Yes/strong suspicion, *n* (%)	8 (28.6)	7 (26.9)	1 (50)
No, *n* (%)	13 (46.4)	13 (50)	0
Not stated, *n* (%)	7 (35)	6 (23.1)	1 (50)
Tumour size			
0–5 mm, *n* (%)	6 (21.4)	6 (23.1)	0
> 5–10 mm, *n* (%)	17 (60.7)	16 (61.5)	1 (50)
> 10–15 mm, *n* (%)	4 (14.3)	3 (11.5)	1 (50)
> 15–20 mm, *n* (%)	1 (3.6)	1 (3.8)	0
Lymph nodes, mean (range)	22 (8–45)	22 (8–45)	11
Not stated, *n* (%)	6 (21.4)	5 (19.2)	1 (50)
Cancer in trachelectomy specimen			
Yes, *n* (%)	7 (25)	5 (19.2)	2 (100)
No, *n* (%)	21 (75)	21 (80.8)	0
Follow-up months, mean (range)	95.0 (26.5–182.4)		
Months to recurrence, mean (range)			8 (4–12)
Last PAP test			
No dysplasia, *n* (%)		24 (92.3)	
Dysplasia, *n* (%)		2 (7.7)	

VT vaginal trachelectomy, *NED* no evidence of disease, *SCC* squamous cell carcinoma, *AC* adenocarcinoma, *LVSI* lymph vascular space invasion, *PAP test* Papanicolaou test

to the end of the study period. The questionnaires had a response rate of 75% (Fig. 1). The mean time from VT to responding to the questionnaire was 92.1 months (range 16.7–172.2). Analysis of responders and non-responders (including the patient who was lost to follow-up), showed no differences in baseline characteristics. However, 6/7 of non-responders had stage IB1, versus 50% of responders (9/18). Statistical analysis was not performed due to the limited numbers of patients.

Complications and oncological outcomes

Adverse events, long-term complications, and symptoms are presented in Table 2. There were no intra-operative complications. Two patients (7.1%) had recurrences within 4 and 12 months, respectively, with an approximately 5-year progression free survival (PFS) of 93%. Both recurrences were located locally, in the residual cervical tissue and received further surgical and oncological therapies

Table 2 Adverse events and long-term complications in successful VT

Adverse events	$n = 28$ (%)	Clavien-Dindo scale
Intra-operative complications	0	
Post-operative blood transfusion	3 (10.7%)	2
Surgical intervention, general anaesthesia	2 (7.1%)	3b
Readmission and intravenously antibiotics < 30 days	4 (14.3%)	2
Lymphedema	9 (32.1%)	
Nerve sensory loss > 30 days post-surgery	9 (32.1%)	
Cervical stenosis/dysmenorrhea	4 (14.3%)	
Cerclage erosion/problems	3 (10.7%)	

VT vaginal trachelectomy. Information obtained from patients' medical records

with successful outcomes and showed no evidence of disease (NED) during the follow-up period.

The patient with recurrence within 4 months was initially diagnosed with a macroscopic cervical tumor, where biopsies showed adenocarcinoma and lymph vascular space invasion (LVSI) not stated. Imaging with MRI revealed a cervical tumor measuring 16 × 12 × 10 mm and accordingly stage IB1. A trachelectomy was performed with histopathology showing an adenocarcinoma, 12 × 10 × 11 mm in size and adequate oncological margins (minimum 13 mm from tumor to resected area). The other patient with recurrence, which was diagnosed 12 months after surgery, had a squamous cell carcinoma (SCC) with LVSI. The tumor size in the initial diagnostic cone was 9 × 4 mm and stage IB1. The pathological assessment after trachelectomy revealed a small SCC tumor with one mm invasion and adequate margins. However, there was a large amount of carcinoma in situ in the specimen, but this was also assessed as radically removed. The remaining patients with successful VT had a mean follow-up period of 97.5 (26.9–182.4) months without cancer recurrence. All patients included had postoperative normal PAP-tests registered in a Swedish database [20].

Fertility and obstetric outcomes

The total pregnancy outcome is presented in Table 3. There were 24 pregnancies found in 17 study patients and 17 children born. The most common obstetric complication registered was preterm premature rupture of the membrane (PPROM) affecting five patients (29.4%). PPROM with chorioamnionitis (verified by pathology examination) was found in the placentas of the three most premature born children. Five patients were found to have infertility issues and one patient had an ongoing infertility investigation. The infertility issues are summarized and are shown in Table 3.

Quality of life

The results of the questionnaire were converted to 0–100 scales according to the EORTC instructions [23]. The response rates and results of the QLQ-C30 and QLQ-CX24 are presented in Tables 4 and 5. Overall, a high level of self-assessed QoL was reported. Global health status (GHS) scores were 91.7 (median) and 85.6 (mean). Physical, role, emotional, cognitive, and social functioning all had median scores of 100. Symptom experience scale, consisting of 11 items/symptoms on pain, intestinal, and urogynecological morbidity was reported to be low (median = 1.5: mean = 2.9). All symptoms asked for had a median of 0; however, a few symptoms had a higher mean value, indicating still existing symptoms or problems in some patients. Lymphedema was reported by 7/18 (38.9%) and 4 out of the 18 (22.2%) reported sexual worry (worry that sex would hurt). Moreover, 3 out of the 18 (16.7%) reported peripheral neuropathy and 5/18 (27.8%) said that their body image was affected by their cancer diagnosis or treatment.

Discussion

Our study shows an acceptable level of successful VTs with strict oncologic criteria, tolerable long-term oncological safety, satisfactory fertility, and obstetric outcomes, and an overall high level of long-term QoL. To our knowledge, our study has the longest validated follow-up time on QoL after VT.

Fertility was preserved in 71.8% of the patients scheduled for VT. This is somewhat lower than reported in some previous international studies. However, we consider this to be acceptable in a retrospective cohort including patients from the very beginning of the use of a novel fertility sparing surgical technique. Plante and co-workers showed successful VT in 89% of 140 patients [24] and similar results were shown by Rob et al. [1]. A recent meta-analysis showed

Table 3 Fertility and obstetrical outcomes in successful VTs

Outcome	$N=29$, *n*/total[a]	(%)
Patients pregnant after VT	17/29	(58.6)
Patients giving birth after VT	13/29	(44.8)
Pregnancies		
Total pregnancies	24/24	(100)
Total achieved after VT	22/24	(91.7)
Patients unknowingly pregnant at time of VT[b]	2/24	(8.3)
Conception		
Spontaneously	19/24	(79.2)
IVF	5/24	(20.8)
Children born (live birth rate), total	17/24	(70.8)
gw ≥ 37 + 0	7/17	(41.2)
gw ≥ 34 + 0	13/17	(76.5)
gw 28 + 0 to 33 + 6	2/17	(11.8)
gw < 28 + 0	2/17	(11.8)
Spontaneous miscarriages (reported)[c]	3/24	(12.5)
First trimester	2/24	(8.3)
Second trimester	1/24	(4.2)
Legal abortion	3/24	(12.5)
Missing data (most likely legal abortion)	1/24	(4.2)
Infertility issues	6/29	(20.7)
Partly cervical/uterine factor	3/29	(10.3)
Male factor	1/29	(3.4)
Infertility prior to VT	1/29	(3.4)
On-going investigation	1/29	(3.4)

Information obtained from patients' medical records and questionnaires

VT vaginal trachelectomy, *PLND* pelvic lymph node dissection, *IVF* in vitro fertilization, *gw* gestational week

[a]*N* 29: 28 patients with successful VT + PLND and one patient who had insufficient margins in the trachelectomy specimen, but who became pregnant post-VT and chose to continue the pregnancy. She was delivered in gw 33 + 3 with cesarean section and RH performed in same session

[b]Two patients were unknowingly pregnant at time of VT: one chose to continue pregnancy and gave birth at term and one chose elective pregnancy termination

[c]The first successful VT patient did not initially receive a cerclage and suffered two miscarriages, one in the first and one in the second trimester, before a cerclage was placed

a success rate of 91.7% after RT and 92.5% after cervical conization [25]. Due to the fairly low number of patients and heterogeneity in surgical approaches, even in the previously published studies, it may be difficult to properly validate the data and further studies are needed to more exactly explore the outcome. Nevertheless, our recurrence rate was 7.1%, which is similar to the previous studies that reported recurrence rates of 4.8% [24], 5.5% [7], and 8.5% [6]. A recent meta-analysis showed an altogether low recurrence rate of 2.3% after RT, ranging from 0 to 33% in analyzed studies [25]. However, there are different ranges in follow-up in the published studies and we believe that our study adds important information about long-term recurrences.

Our results on preserved fertility and recurrence may be explained by our small cohort size and our inclusion of all patients from the very beginning of VT treatments at one center. The small cohort size should be considered in relation with the low incidence of cervical cancers in Sweden due to long-term prevention programs and subsequent low number of eligible patients [2]. However, Sweden has highly centralized treatment for gynecologic cancers and its full coverage quality registries gives valid and reliable results. The western Sweden health care region treats the second largest numbers of cervical cancers in Sweden and our results indicate that trachelectomy treatments in this type of population and centralized setting are oncological safe.

Twenty-four pregnancies resulted in a 70.8% live birth rate, which is comparable to the previous studies [24, 26], and highlighting a promising pregnancy rate after VT. Patients treated with trachelectomy tend to have an increased risk of infertility issues [1, 26] and a well-known increased risk of premature delivery and complications during pregnancy [26], as was also seen in our study. Three out of five patients with PPROM presented with chorioamnionitis. Although our study was small, it may reinforce earlier conclusions about the increased risk of ascending infections during pregnancy after trachelectomy or at least after VT [1, 26].

To our knowledge, this is the first study to investigate long-term QoL by validated questionnaires (QLQ-C30 and QLQCX-24) in cervical cancer patients treated by trachelectomy. The mean follow-up time in our study was more than 7 years after surgery. Our cohort reported high long-term QoL, evaluated as high GHS scores and also high scores on physical, role, emotional, cognitive, and social functioning with a median at the maximum value of 100, indicating very good functioning. Our cohort also reported fairly low values of pain and intestinal, and urogynecological morbidity, indicating a low incidence of long-term symptoms or problems in this area. The scores indicate good overall long-term sexual and vaginal function after VT, but also a relatively high prevalence of lymphedema. It has to be taken into account that our cohort, in majority, may be considered as simple vaginal trachelectomies, and therefore, it may affect the QoL outcomes and the high GHS scores.

There are very few studies on QoL after trachelectomy. Froeding et al. reported a prospective evaluation of QoL in 18 patients with cervical cancer treated by radical VT and PLND [15, 16]. Their cohorts are comparable to ours, because they also treated women of childbearing age with fertility sparing surgeries and evaluated QoL, using identical QoL measurement as us. Moreover, they also investigated QoL outcomes in an age-matched control

Table 4 Long-term QoL after successful VT

	Median	Minimum	Maximum	Mean	SD
Functional scales					
Global health status (GHS)	91.7	50.0	100.0	85.6	(17.3)
Physical	100.0	86.7	100.0	98.5	(4.3)
Role	100.0	50.0	100.0	92.6	(14.3)
Emotional	100.0	8.3	100.0	90.7	(21.7)
Cognitive	100.0	50.0	100.0	93.5	(14.2)
Social	100.0	0.0	100.0	88.9	(25.6)
Symptom scales					
Fatigue	0.0	0.0	66.7	11.7	(18.5)
Nausea and vomiting	0.0	0.0	50.0	2.8	(11.8)
Pain	0.0	0.0	33.3	3.7	(9.1)
Single-item scales					
Dyspnea	0.0	0.0	33.3	7.4	(14.3)
Insomnia	0.0	0.0	33.3	1.9	(7.9)
Appetite loss	0.0	0.0	33.3	1.9	(7.9)
Constipation	0.0	0.0	0.0	0.0	(.0)
Diarrhea	0.0	0.0	33.3	1.9	(7.9)
Financial difficulties	0.0	0.0	33.3	1.9	(7.9)

EORTC QLQ-C30 scores ($n = 18$)

Questionnaires were responded in 92.1 (mean: range 16.7–172.2) months postoperatively. Scores transformed to 0–100 scales according to EORTC. In GHS/QoL, a high score represents a high QoL. In functional scales, a higher number represents a higher or healthy level of functioning. In symptom or single-item scales, a higher number represents greater symptomatology or problems

QoL quality of life, *SD* standard deviation, *VT* vaginal trachelectomy

Table 5 Long-term symptoms and sexual/vaginal functioning after successful VT

	Median	Minimum	Maximum	Mean	SD
Functional scales					
Body image	100	0.0	100	84.6	(28.6)
Sexual activity	66.7	0.0	100	51.9	(28.5)
Sexual enjoyment ($n = 16$)[a]	100	0.0	100	81.2	(29.7)
Sexual/vaginalfunctioning ($n = 16$)[a]	91.7	66.7	100.0	92.2	(9.8)
Symptom scales					
Symptom experience	1.5	0.0	9.1	2.9	(3.5)
Lymphedema	0.0	0.0	100	22.2	(32.3)
Peripheral neuropathy	0.0	0.0	33.3	5.6	(12.8)
Menopausal symptoms	0.0	0.0	33.3	3.7	(10.8)
Sexual worry	0.0	0.0	100	13.0	(28.3)

EORTC QLQ-CX24 scores ($n = 18$)

Symptom experience entails grading of local urogynecological or intestinal symptoms or pain. Questionnaires were answered in 92.1 (mean: range 16.7–172.2) months postoperatively. Scores were transformed to 0–100 scales according to EORTC. In global health status/QoL, a high score represents a high QoL. In functional scales, a higher number represents a high/healthy level of functioning. In symptom or single-item scales, a higher number represents greater symptomatology or problems

VT vaginal trachelectomy, *SD* standard deviation

[a]As instructed, two patients who were not sexually active did not answer questions about sexuality

group, containing premenopausal women without any prior cancer disease and no previous hysterectomy [15, 16]. They compared the QoL outcomes in the radical VT and RH cohorts with those in the healthy control group. The radical VT and RH groups were evaluated by QoL questionnaires (QLQ C-30 and CX-24) preoperatively, and after 3, 6, and 12 month post-surgery and reported a significant risk of bladder dysfunction, persistent lymphedema,

and impaired QoL 1 year post-VT [15], but also significant sexual dysfunction [16].

Our cohort reported higher mean values on all functioning scales at mean 92.1 months postoperatively, compared to Froeding's VT group 12 months postoperatively [13]. Our cohort had a mean GHS value of 85.6 compared with Froeding's mean value of 69, which in Froeding's study was significantly lower than their healthy controls (mean 87). Fleming et al. reported a persistent decline in emotional well being after trachelectomy that persisted up to 4 years postoperatively [23]. Since our cohort more than 7 years postoperatively reported similar GHS values as Froeding´s healthy control group, this may indicate women treated by VT have a GHS that improves over time, and may even reach that of healthy women. Our higher GHS values compared to Froeding´s group may be a result of less radical surgery, and improved QoL as a result of this. This is an essential finding in our study.

A low incidence of urogynecological symptoms and high sexual/vaginal functioning (mean 92.2) was also seen in our study. Our patients reported that "sexual activity" score was slightly higher than Froeding's healthy control group, and their "sexual enjoyment" was similar to Froeding's VT group 12 months postoperatively, which in Froeding´s study was not significantly different from their healthy control group [16]. We could also see an improvement in "sexual worry", with our cohort reporting a mean value of 13, and Froeding's VT group 38.5 at 12 months postoperatively [16]. This may indicate that sexual worry declines with time after surgery, which is also an important finding. Taken together, our results indicate that women treated by VT have an overall high level of long-term sexual and vaginal functioning. However, some patients will experience local vaginal problems and worry that their sexual activity will be affected. Lymphedema was reported by 38.9% in our cohort, presented as a QLQ-mean value of 22.2, which is slightly higher than Froeding's value of 16.7 [15]. It must be emphasized, however, that patients need to be properly informed and there must be a well-functioning healthcare structure to provide these women with appropriate treatment options.

The somewhat different outcomes between Froeding's study and ours may be explained by our long-term follow-up and our less radical vaginal surgical approach. There is a lack of updated international consensus concerning the differences in the surgical trachelectomy procedures. This emphasizes the importance of an international standardization and classification system of the surgical procedures performed for trachelectomies worldwide, which would allow valid comparisons and studies to evaluate this young and important patient group.

A main strength of our study is our presentation of the entire spectrum of outcomes patients may experience and their long-term QoL after VT for early stage cervical cancer. To our knowledge, we have the longest validated follow-up time of QoL after VT. The study's weaknesses are the small cohort size, heterogeneous surgical approaches, lack of a control group, lack of baseline values of QoL prior treatment, and the wide range of follow-up. However, our results are essential, because they contribute to enhance knowledge of treatment outcomes in a fairly small, but important cohort of women of fertile age with early stage cervical cancers.

In conclusion, our study highlights problems that may occur after VT with PLND in young women with early cervical cancers. We found acceptable oncological safety, a slight degree of infertility, but a promising obstetric outcome. Furthermore, high long-term QoL, low incidence of urogynecological morbidity, and high sexual/vaginal functioning are important findings. However, the treatment is associated with a fairly high risk of chronic lymphedema, suggesting the need for early treatment for lymphedema and using the sentinel node concept [27] or a less surgical approach. Our study also suggests that some morbidity continues to improve over time and may even reach levels comparable to healthy women. It should be noted that this improvement might take time. VT may be safely offered to young women with early cervical cancers, providing that they are also given correct and continuous information about the post-treatment issues addressed in our study.

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Compliance with ethical standards

Conflict of interest C. Malmsten declares that she has no conflict of interest. P. Hellberg declares that he has no conflict of interest. K. Bergmark declares that she has no conflict of interest. P. Dahm-Kähler declares that she has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The regional ethical review board of Gothenburg (D no.: 089–15) approved the study.

Informed consent The patients responding to the questionnaires gave their informed consent.

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