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Case Report

# Simple Vaginal Trachelectomy for Small Volume Cervical Cancer: Case Report and Review of the Literature

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## Abstract

The radical hysterectomy with pelvic lymphadenectomy is the standard treatment for stages IA2-IB1 cervical cancer. In the literature, there is an ongoing debate whether less radical surgery (conization, simple trachelectomy or simple hysterectomy) can be a valuable option in selected patients with early-stage small volume cervical cancer. We report here a case of an elderly patient (80 years of age) with an early-stage IB1 small volume cervical cancer where a simple vaginal trachelectomy was the only possible surgical approach, due to a completely obliterated abdomen related to previous extensive surgery and radiation therapy. In response to this case, a literature search was performed on PUBMED and MEDLINE of all studies published as original articles in English up to June 2017, using the search terms cervical cancer, early-stage and trachelectomy. We reviewed the recent literature on less radical surgery in cervical cancer as well as ongoing trials.

***Keywords:*** *Cervical Cancer; Small Volume; Trachelectomy; Conization; Radical Hysterectomy; Gynaecological Oncology*

## Introduction

Worldwide cervical cancer is the third most common cancer (after breast and colorectal cancer) in women, with an estimated 500.000 new cases and 275.000 related deaths annually [1]. Almost 85% of the cases occur in undeveloped countries, accounting for 15% of all cancers in women. In developed countries cervical cancer accounts for 3.6% of new cancers, with an incidence of 14 cases per 100.000 women [2]. The median age of cervical cancer diagnosis worldwide is between 40 and 60 years. Cervical cancer is rarely diagnosed in patients older than 75 year, accounting for only 8.6% of new diagnosis of cervical cancer.

Chronic persistent infection with carcinogenic genotypes of sexually transmitted human papilloma virus (HPV) is the causative agent of virtually all cases of cervical cancer. Several other etiologic cofactors (sexual behavior, parity, cigarette smoking, humoral immunity) influencing the risk of persistence of carcinogenic HPV infection and progression to cancer, are involved. Since the introduction of Pap smear screening, the rate of squamous cell carcinomas has slightly declined, while the rate of adenocarcinomas (accounting for approximately 15%) has risen.

The radical (abdominal) hysterectomy with pelvic lymphadenectomy is the standard treatment for International Federation of Gynecology and Obstetrics (FIGO)-stages IA2-IB1 cervical carcinoma. It is effective at treating early-stage cervical cancer, but results in infertility. Forty percent of all stage I cervical cancers are diagnosed before the age of 40 [3]. As more women are delaying pregnancy, preservation of fertility and reproductive function is become a major concern.

In women who desire preservation of fertility a cervical conization is a surgical option in selected patients with very early lesions (stage IA1). The concept of a uterine corpus-sparing radical trachelectomy was initiated to treat early stage cervical cancer patients with

a desire to preserve fertility, who are identified having a low risk of recurrence and lymph node involvement, and with small volume lesions. The radical trachelectomy removes the cervix with contiguous parametria and upper vaginal cuff (with the aim of a tumour free margin of 2 cm), and preserves the uterine corpus and adnexae. Two approaches have been proposed, abdominal or vaginal. The abdominal approach was first described by Aburel in the treatment for in situ carcinoma of the cervix in the 1950s. In the radical abdominal trachelectomy the uterine viability is maintained by the collateral circulation from the utero-ovarian ligaments [4]. The vaginal approach, introduced in the 1990s was more popular. Daniel Dargent introduced the radical vaginal trachelectomy in 1994 with the purpose to treat early cervical cancer (less than 2 cm) and to preserve uterine morphology and reproductive function. It is a modification of the radical vaginal hysterectomy (Schauta procedure), except that the uterine arteries are not ligated but only the descending branch. First, a laparoscopic pelvic lymphadenectomy is performed. The trachelectomy specimen is removed by vaginal approach [5].

However, radical surgery (with removal of the parametria) is associated with significant adverse effects regarding urinary and sexual function. The importance of a parametrectomy in patients with early-stage small volume tumours have been questioned. We report a case of an elderly patient with an early-stage IB1 small volume cervical cancer where a simple vaginal trachelectomy was the only possible surgical approach. An abdominal approach for a radical hysterectomy or trachelectomy with pelvic lymphadenectomy was not possible due to a completely obliterated abdomen, related to previous extensive surgery with bowel resection, colostomy and radiation therapy to the abdomen, pelvis and perineum for colorectal cancer.

Less radical surgery for early-stage cervical cancer in selected patients had been proposed to reduce morbidity while maintaining oncologic outcomes. . A literature search was performed on PUBMED and MEDLINE of all studies and reviews published as original articles in English up to June 2017, using the search terms cervical cancer, early-stage and trachelectomy. We summarized the current literature and ongoing trials on less radical surgery to better inform clinical practice.

## Case Presentation

An 80-year old woman, G1P1, was referred from a local hospital to our tertiary hospital with a new diagnosis of cervical cancer. She had an extensive operative history. In 1998 she underwent an ano-rectal amputation, left-sided colostomy and lymphadenectomy, with subsequent chemo-radiotherapy for a rectal carcinoma. In 1999 she had a left nephrectomy because of an atrophic kidney. She was diagnosed in 2006 with breast cancer and treated with mastectomy and axillary clearance, followed by radiotherapy and hormonal treatment. In 2013 she underwent a laparotomy with drainage of a retrocolic abcess. A right hemicolectomy was performed due to bowel injury, caused by adhesiolysis of multiple adhesions. She presented at the gynecology clinic of a local hospital with discrete post-menopausal bleeding. Clinical examination revealed a small uterus fixed in the pelvis due to previous surgery and radiotherapy with a small and fibrotic cervix. A zone of fibrosis extended to the vaginal mucosa posteriorly. A suspect, irregular, fragile zone was visible on the anterior lip of the cervix. The patient underwent a colposcopy and diagnostic hysteroscopy. Visualisation was difficult due to bleeding of the tissue. Loop cone biopsy showed between 9 and 12 o'clock squamous cell carcinoma with absence of the basement membrane, 5 mm in depth and a width of 11 mm, and CIN 3/squamous carcinoma in situ, respectively. There was no evidence of lymphovascular invasion (LVSI). A hysteroscopy showed a normal cavity with atrophic endometrial tissue. Magnetic Resonance Imaging (MRI) revealed contrast enhancement in the endocervical canal, possibly due to the loop cone biopsy, without extension towards the vagina, parametrium or the uterus. There was no evidence of pelvic adenopathy. A Positron Emission Tomography-Computer Tomography (PET-CT) showed no suspicious metabolic active lesions. Based on these findings the diagnosis of a cervical carcinoma, small volume (5 mm in depth and 11 mm in width) FIGO-stage IB1 was made. At our multidisciplinary meeting a standard radical abdominal hysterectomy with pelvic lymphadenectomy was proposed, by a median laparotomy because of the previous surgery and the presence of a left sided colostomy. Whilst opening the anterior abdominal wall we noticed several loops of small bowel being morbidly adherent and stuck to the rectus sheet and muscle. Opening of the abdominal cavity would entail resection of several loops of small bowel without being certain to enter the pelvis easily. Therefore, the procedure was converted to the only possible surgical approach, a vaginal trachelectomy. During the vaginal approach, the parametria revealed to be fibrotic and fragile due to previous surgery and radiotherapy for her rectal carcinoma. A simple vaginal trachelectomy was performed,

with a vaginal cuff of 1 - 2 cm. The vaginal access was also difficult due to a narrow vagina, partially due to previous radiotherapy. An episiotomy and an anterior vaginal valve improved only slightly the visibility. Intraoperative frozen section showed free surgical margins. Definitive anatomopathological examination of the simple trachelectomy specimen showed only residual CIN 3. The postoperative course was uncomplicated and the patient was discharged 5 days after the operation. No further treatment was indicated.

## Discussion

The radical hysterectomy with pelvic lymphadenectomy is the standard treatment for early-stage cervical carcinoma (IA2-1B1). The concept of a uterine corpus-sparing radical trachelectomy was initiated to treat patients with low-risk early stage cervical cancer, who want to preserve fertility.

The ideal patients for Dargent's operation are those in whom tumor size is small and is confined to the cervix, with no evidence of direct spread to either the parametrium or uterine corpus and a low risk of nodal metastasis. The eligibility criteria for a radical vaginal trachelectomy include the following: women less than 40 years of age who have a strong desire to preserve fertility, no clinical evidence of impaired fertility, lesion size less than 2 cm, FIGO stages IA-IB1, no involvement of the upper endocervical canal.

There is evidence in the literature that a radical trachelectomy can be performed safely in selected patients with a desire to preserve fertility. The first large series (n = 72) to review the oncological results and complication rate of vaginal radical trachelectomy was published by Plante., *et al*. in 2004 [6]. Subsequent studies have demonstrated the safety and feasibility of a radical trachelectomy [7-10]. Average recurrence rate after radical vaginal trachelectomy is approximately 5%. The sites of recurrence were the parametrium, para-aortic nodes and pelvic side wall, rarely the recurrences were located in the remaining stump (isthmus) of the uterus. Studies that compared the outcome of patients undergoing radical vaginal trachelectomy or radical hysterectomy showed no significant differences in oncological outcome and recurrence rate, after adjusting for age, tumor size, histology, LVSI and pelvic node metastases [11-13]. Blood loss, transfusion rate and hospital stay were significantly shorter in patients treated with trachelectomy. They concluded that a vaginal radical trachelectomy seems to be the procedure of choice for women with small early stage cervical cancer (tumors measuring 2 cm or less) wishing to preserve fertility.

The most important risks of recurrence after less radical surgery for early stage cervical cancer are thought to be tumor size > 2 cm, the presence of LVSI, and deep stromal invasion. There is an on-going debate concerning fertility-preserving surgery in patients with an unfavourable histology (e.g. adenocarcinoma, neuroendocrine carcinoma) [14]. The management of women with cervical adenocarcinoma is controversial, particularly for those with small tumours. Dargent reported that adenocarcinoma is an important factor for recurrence, but the series of Plante., *et al*. could not confirm this. However, Plante suggested that patients with an unfavourable histology should be treated by aggressive chemo-radiation therapy rather than surgery. An ovarian recurrence of adenocarcinoma in a stage Ib1 patient after radical vaginal trachelectomy was reported [15]. Reade., *et al*. reviewed the published literature on the treatment and outcomes of patients with early cervical adenocarcinoma [16]. They refer to small series supporting the safety of conisation and follow-up of FIGO stage IA1 cervical adenocarcinoma. They summarized the surgical and pathological outcomes of 18 small series of patients with early stage cervical adenocarcinoma. Overall, 337 patients with stage IA1, 118 patients with stage IA2 and 105 patients with stage IB1 cervical adenocarcinoma underwent conservative or radical treatment (58%, 81% and 87% radical treatment in stage IA1, IA2 and IB1 respectively). There was no parametrial involvement in patients with stage IA1 and IA2 cervical adenocarcinoma, and only 1% in stage IB1 cervical adenocarcinoma. Recurrence rate and lymph node metastasis in stage IA1, IA2 and IB1 was 1%, 1%, 6% and 1%, 0%, 1%, respectively. Suggesting the oncologic outcome and prognosis of early adenocarcinoma is similar to that of squamous cell carcinoma, the group of Read., *et al*. believes that adenocarcinoma histology should not be a contraindication to fertility-sparing surgery. There is a lack of evidence about the management of rare forms of cervical cancer (clear cell carcinoma, adenosquamous type, glassy cell carcinoma). These histological types can be more aggressively and risky for recurrence. A conservative surgical approach in this kind of aggressive histological subtype needs further evaluation.

However, radical trachelectomy requires the removal of parametrial tissue and may lead to autonomic nerve damage. The overall risk of intra-operative complications is approximately 4% and include injury to adjacent bowel, bladder, ureters or surrounding vascular structures. Postoperatively, the most common side effects are lower urinary tract dysfunction, sexual dysfunction (dyspareunia) and colorectal motility disorders. Additionally, because of the high rate of no residual disease on trachelectomy specimens (after conization), Shepherd., *et al*. suggested that a less aggressive surgery might be an alternative in patients with early stage cervical cancer [7]. That opened an active debate in literature on less radical approach for small volume cervical cancer. Radical trachelectomy preserves reproductive function, but removes the parametrial tissues, carrying the risk of peri-operative morbidity associated with parametrectomy. The value of removal of the parametria in cases of early cervical cancer is questioned. To assess the incidence and factors predictive of parametrial involvement Covens., *et al*. reported prospectively 842 patients with stage 1A1-IB1 cervical cancer who underwent a radical hysterectomy [17]. The incidence of parametrial involvement in patients (n = 536) with negative lymph nodes, tumor size 2 cm or smaller and stromal invasion 10 mm or less was 0.6%. The factors predictive of parametrial involvement were age, tumor size, LVSI, advanced tumor grade, depth of invasion and the presence of pelvic lymph node metastases. Wright., *et al*. reviewed retrospectively 594 patients with invasive cervical cancer who underwent a radical hysterectomy [18]. Parametrial metastases were documented in 64 patients (10.8%). High-risk histology, advanced grade, deep cervical invasion, LVSI, large tumor size, advanced stage, uterine or vaginal involvement, and pelvic or para-aortic lymph node metastases were risk factors associated with parametrial invasion. In women with negative lymph nodes, no LVSI and tumors smaller than 2 cm, the incidence of parametrial disease was only 0.4%.

A recent retrospective study performed by Baiocchie., *et al*. confirmed that patients with a tumor size less than 2cm and no LVSI are unlikely to have parametrial involvement, unless lymph node metastasis or deep stromal invasion is present [19]. A series of 345 patients with stage Ia2 to Ib2 that underwent radical surgery between January 1990 and October 2016 in a tertiary Cancer Center were analysed. Parametrial invasion was present in 4.6% of patients and was associated to perineural invasion, tumor size >2cm, depth of invasion > 10 mm, lymph node metastasis and the presence of LVSI.

Several groups have documented favorable oncologic outcomes for patients with early cervical cancers treated with simple hysterectomy or simple trachelectomy. In overall, the series published in literature are small and retrospective.

Reade., *et al*. listed an overview of 16 small series, published between 1994 and 2012, of patients that underwent simple hysterectomy or simple trachelectomy for the treatment of ≥ IA2 cervical cancer [16]. A total of 341 patients are included in these studies. Criteria to select patients for less radical surgery varied between the studies, but mostly included tumor size (≤ 2 cm) and histopathologic features (squamous cell carcinoma (SCC), adenocarcinoma (AC), no lymph-vascular space invasion, negative lymph nodes). In follow up, 17 out of 270 (6.3%) of these patients had recurrence and 5 out of 334 (1.5%) of these patients died from the disease. One of the largest series (n = 125) mentioned was a randomized controlled trial comparing simple hysterectomy plus removal of the upper 1/3 of the vagina to type III radical hysterectomy in patients with FIGO stages IB1-IIA1 (≤ 4 cm) cervical cancer [20]. Patients with SCC or AC histologies were enrolled from 1981 to 1986 at a single Italian center, and all patients received bilateral pelvic lymphadenectomy. Sixty-two patients were randomized to class I surgery and 63 to class III. Adjuvant radiotherapy was associated if positive or close (≤3 mm) surgical margins, LVSI close to the resection margins or lymph node metastases. No significant differences were observed regarding pathologic findings and adjuvant treatment. Morbidity rates were higher after class III surgery (84% versus 45%). Recurrences occurred in 24% (n = 15) of patients undergoing the simple hysterectomy and 13% (n = 8) of patients undergoing radical hysterectomy, not statistically significant (p = 0.11). Fifteen-year overall survival rate was 90 and 74% respectively (p = 0.11) and 76 and 80% when cervical size is ≤ 3 cm (p = 0.88).

Pluta., *et al*. published a pilot study of 60 patients (50 SCC and 10 AC patients) in stages IA1 (n = 3), IA2 (n = 11) and IB1 (n = 46) cervical cancer that underwent laparoscopic sentinel lymph node (SLN) identification using frozen section [21]. Negative SLN patients (n = 55) underwent complete pelvic laparoscopic lymphadenectomy and vaginal hysterectomy. FS positive patients (n = 5) underwent radical hysterectomy with low para-aortic lymphadenectomy. Median follow-up was 47 months. There were no recurrences in both groups.

In a prospective study of Biliatis., *et al*. 62 patients with FIGO stage 1B1 cancer and estimated tumour volume of less than 500 mm (3) in a loop biopsy were included [22]. For women who had completed their family, a simple hysterectomy and bilateral pelvic node dissection was offered (n = 35). For women who wished to preserve their fertility, a LLETZ specimen showing completely excised cervical tumor followed by laparoscopic bilateral pelvic node dissection (n = 27). After a median follow up of 56 months (16-132) no recurrence was noted.

Plante., *et al*. published very recently a prospective study on 35 women with stage 1A1, IA2 and IB1 cervical cancer that underwent a simple vaginal trachelectomy with laparoscopic sentinel lymph node mapping +/- pelvic node dissection [23]. 37% of women were diagnosed with an adenocarcinoma, 54% had squamous histology and 9% had other histologic findings. Lymph nodes were negative on final pathology in all patients except 2 cases with isolated tumor cells. 63% of patients had either no residual disease on the trachelectomy specimen or residual dysplasia. The recurrence-free survival at 48 months was 96.7%.

Ramirez., *et al*. reviewed the existing literature on the conservative management of cervical cancer [24]. They summarized several small, retrospective studies in selected patients exploring less radical surgical options including simple hysterectomy, simple trachelectomy and cervical conization with sentinel lymph node biopsy and/or pelvic node dissection. In total eight studies of conservative surgical treatment for early-stage cervical cancer, performed between 2008 and 2013 are described. To date, 260 women with early-stage cervical cancer (stage IA1 with LVSI, IA2 and IB1) managed conservatively are reported. Of these patients, 75.8% were diagnosed with squamous cell carcinoma and 22.7% had a diagnosis of adenocarcinoma. Stage IB1 was the most frequent (80.4%). All patients underwent a conservative management with routinely a sentinel node identification or complete pelvic lymphadenectomy. Oncological outcome was very favourable. Follow-up time in the series published to date ranged from 1 to 168 months. At the time the reports were published, 2 patients had relapsed and 1 patient had died of recurrent disease.

Kokka., *et al*. published a Cochrane Review to evaluate less invasive surgical options for stage IA2 disease, such as simple hysterectomy, simple trachelectomy or conisation, with or without pelvic lymphadenectomy, to avoid complications of more radical surgical methods [25]. They searched the literature for randomized controlled trails (RCTs) that compared radical with less radical approaches, regarding overall survival, progression-free survival, quality of life and adverse effects. They concluded that in the literature there are no relevant studies to evaluate the effectiveness and safety of the different surgical procedures. The results of ongoing trials will hopefully allow an assessment of the role of less radical surgery in small volume early-stage cervical cancer.

Currently, two prospective trials and one randomized controlled trial are evaluating less radical surgery (conization or simple hysterectomy) in patients with early-stage cervical cancer.

The MD Anderson Cancer Center set up a prospective, international, multi-institutional cohort study (ConCerv) to evaluate the safety and feasibility of conservative surgery in women with early-stage cervical cancer. It is an early phase trial to evaluate the safety and feasibility of performing conservative surgery in women with early-stage cervical cancer with favorable pathologic characteristics. Inclusion criteria are tumors without LVSI and negative margins on conization. Patients with a desire of fertility undergo only cervical conization and pelvic lymph node dissection with lymphatic mapping. Other patients undergo a simple hysterectomy and pelvic lymph node dissection with lymphatic mapping.

The Gynecologic Oncology group protocol 278 (GOG-278) is conducting a prospective trial to evaluate the impact of non-radical surgery on bladder, bowel, and sexual function and to examine the incidence and severity of lymphedema after non-radical surgery. To identify candidates for less radical surgery lateral margin status and depth of invasion (≤ 10 mm) on conization were evaluated.

The Gynecologic Cancer Intergroup (Plante and colleagues) is conducting a randomized controlled trial (SHAPE trial) comparing outcomes of radical hysterectomy and simple hysterectomy in patients with low-risk cervical cancer. Patients with a tumor size > 20 mm, stromal invasion ≥ 50% on post-conization MRI and depth of invasion (> 10 mm) on conization were excluded from the less radical surgery group.

Lee., *et al*. have set up a retrospective analysis in 125 stage IB1 cervical cancer to evaluate whether the criteria used in these three ongoing studies accurately identify low-risk patients for parametrial involvement (PMI) with acceptable false negativity [26]. Additionally, they suggested a new, simplified criterion for less radical surgery: no demonstrable lesions on post-conization MRI in microscopic stage IB1 cervical cancer (MRI-invisible tumor vs MRI-visible tumor). All patients in the study population underwent a conization followed by radical hysterectomy. The rate of pathologic PMI was 5.6% (7/125) in the studied population. In 11 (8.8%) patients that satisfied the ConCerv criteria and 14 (11.2%) patients that met the GOG-criteria, no parametrial involvement (PMI) was detected. In 78 patients that satisfied the SHAPE criteria, one patient had PMI. Of the 74 patients in the MRI-invisible group, only one patient had PMI. The study concluded that the criteria used in the three ongoing studies and the new MRI criterion could identify candidates for less radical surgery with acceptable false negativity in microscopic Stage IB1 disease. However, in this study only patients with microscopically diagnosed IB1 cervical cancer, who had no clinically visible lesions, were evaluated. As tumor size is one of the most important factors for predicting PMI, patients with visible lesions may have a higher risk of PMI. In a previous study, performed by the same research group, a low risk group for parametrial involvement in macroscopic IB1 lesions was identified based on preoperative MRI parameters [27]. In total, 190 Stage IB1 cervical cancer patients with clinically visible lesions who had undergone Type C2 radical hysterectomy and preoperative MRI were included in this study. Patients were identified as being either low-risk (tumor size ≤ 25 mm and no evidence of PMI, n = 127) or high-risk (tumor size >25 mm and/or findings indicating PMI, n = 63) based on MRI parameters. The study concluded that patients with a cervical tumor smaller than 25 mm, without evidence of PMI on MRI had a minimal risk of PMI (0 out of 127 patients had PMI) and are possible candidates for trials on less radical surgery.

In the case presented, a simple vaginal trachelectomy (only surgical approach possible) was performed in an elderly patient with early stage small volume cervical cancer, because an abdominal approach and performing a radical hysterectomy was not possible due to an obliterated abdomen related to previous extensive surgery with bowel resection, colostomy and pelvic radiotherapy. The cervical loop cone biopsy, macroscopically suspicious for an invasive lesion, revealed after review of the pathology slides a squamous carcinoma, measuring 5 mm in depth and 11 mm in width, making it an early FIGO-stage IB1 cervical cancer. As this patient had a cervical squamous carcinoma smaller than 2 cm without LVSI, the risk of parametrial involvement was very low (0 - 0.6% in above studies), and therefore a potential candidate for less radical surgery. However, preferentially a pelvic lymph node assessment by sentinel node procedure or lymphadenectomy is performed in early-stage cervical cancer. The incidence of lymph node involvement in (non-bulging) early stage cervical cancer is around 7% in stage IA2 and around 20% in stage IB1. The risk of parametrial involvement was 6% in patients with negative pelvic lymph nodes, compared to 48% in patients with lymph node metastases [18]. In our case, a pelvic lymphadenectomy was not feasible due to an obliterated abdomen and left-sided colostomy. Due to previous surgery and radiotherapy for her rectal carcinoma, the parametria were fibrotic hard and fragile and the uterus was fixed in the pelvis. Therefore only a simple vaginal trachelectomy with vaginal cuff resection could be performed.

## Conclusion

A simple vaginal trachelectomy can be a reasonable alternative for treating selected patients with small volume cervical cancer, where an abdominal approach is not possible and who had previous pelvic radiotherapy. Initially it was performed to preserve fertility in younger, selected patients, but the procedure can also be considered in elderly patients with small cervical cancers. It is a less invasive procedure than a radical hysterectomy and can be more safely performed in elderly patients with severe co-morbidities. Whether a simple or a radical trachelectomy is performed, depends on the tumor and patient characteristics. The current literature demonstrates that less radical surgery can be performed in selected patients with low-risk cervical cancer. Three large prospective trials are still ongoing to evaluate the safety and feasibility of less radical surgery in selected patients with small volume cervical cancer.

## Declaration of Interest

There are no financial interest or any other conflicts of interests for any of the authors.

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**Volume 5 Issue 3 August 2017**