

Fertility-Sparing Surgery in Early-Stage Cervical Cancer: Indications and Applications

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Key Words

Trachelectomy, fertility-sparing surgery, cervical cancer, sentinel node mapping.

Abstract

This article describes the surgical and pathologic findings of fertility-sparing radical trachelectomy using a standardized surgical technique, and reports the rate of posttrachelectomy outcomes. The authors analyzed a prospectively maintained database of all patients with FIGO stage IA1–IB1 cervical cancer admitted to the operating room for planned fertility-sparing radical abdominal trachelectomy. Sentinel node mapping was performed through cervical injection. Between November 2001 and May 2010, 98 consecutive patients with FIGO stage IA1–IB1 cervical cancer and a median age of 32 years (range, 6–45 years) underwent a fertility-sparing radical trachelectomy. The most common histology was adenocarcinoma in 54 patients (55%) and squamous carcinoma in 42 (43%). Lymph-vascular invasion was seen in 38 patients (39%). FIGO stages included IA1 (with lymph-vascular invasion) in 10 patients (10%), IA2 in 9 (9%), and IB1 in 79 (81%). Only 15 (15%) needed immediate completion radical hysterectomy because of intraoperative findings. Median number of nodes evaluated was 22 (range, 3–54), and 16 (16%) patients had positive pelvic nodes on final pathology. Final trachelectomy pathology showed no residual disease in 44 (45%) cases, dysplasia in 5 (5%), and adenocarcinoma in situ in 3 (3%). Overall, 27 (27%) patients needed hysterectomy or adjuvant pelvic radiation postoperatively. One (1%) documented recurrence was fatal at the time of this report. Cervical adenocarcinoma and lymph-vascular invasion are common features of patients selected for radical trachelectomy. Most patients can undergo the operation successfully with many having no residual invasive disease; however, nearly 27% of all selected cases will require hysterectomy or postoperative chemoradiation for oncologic

reasons. Investigation into alternative fertility-sparing adjuvant therapy in patients with node-positive disease is needed. (*JNCCN* 2010;8:1435–1438)

Fertility-sparing radical vaginal or abdominal trachelectomy in select young women with stage I cervical cancer has become an acceptable alternative to radical hysterectomy in many gynecologic oncology practices worldwide.^{1–8} The abdominal operation also has broadened the use of radical trachelectomy beyond the laparoscopic/vaginal approaches initially described and popularized by Dargent et al.^{9,10} Since 2001, the authors began offering fertility-sparing radical trachelectomy procedures through the vaginal approach to select women with stage I cervical cancer who have a strong desire to preserve reproductive function. In 2004, the authors began performing radical abdominal trachelectomy in pediatric patients who were not candidates for the vaginal approach.¹¹ This experience broadened their inclusion criteria to offer this important operation to many patients interested in fertility preservation. Currently, the authors use both approaches, vaginal or abdominal, and select candidates for either laparoscopic/vaginal approaches or the abdominal approach based on lesion characteristics and patient anatomy to provide the most adequate oncologic resection with the best hope of preserving reproductive function and fertility. This article reports the surgical and pathologic findings of fertility-sparing radical trachelectomy using a standardized surgical technique, and reports on the rate of posttrachelectomy outcomes.

Methods

After Institutional Review Board approval, the authors analyzed a prospectively maintained database of all patients with FIGO stage IA1 (with lymph-vascular inva-

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sion)—IB1 cervical cancer admitted to the operating room for planned fertility-sparing radical trachelectomy. The authors previously described their surgical technique for fertility-sparing abdominal trachelectomy in detail.^{12,13} All patients had standard preoperative imaging with either CT of the abdomen and pelvis or MRI of the pelvis and all had clinical stage I disease without any evidence of metastasis. Sentinel node mapping was performed through cervical injection of blue dye with or without Technetium, as previously described.¹⁴ Pathologic parameters were gathered from the final pathology report. Tumor diameter was estimated clinically when a visible lesion was noted or from final pathology based on the longest dimension of the lesion. At the authors' institution, all gynecologic specimens are reviewed by specially trained gynecologic pathologists. Standard statistical analysis was performed.

Results

Between November 2001 and May 2010, 98 consecutive patients with FIGO stage IA1–IB1 cervical cancer of median age 32 years (range, 6–45 years) underwent surgery with the intent to perform a fertility-sparing radical trachelectomy.

The most common histology was adenocarcinoma in 54 patients (55%) and squamous carcinoma in 42 (43%). Lymph-vascular invasion was seen in 38 patients (39%). FIGO stages included IA1 (with lymph-vascular invasion) in 10 patients (10%), IA2 in 9 (9%), and IB1 in 79 (81%). Only 15 (15%) needed immediate completion radical hysterectomy because of intraoperative findings. Of the remaining 83 patients, 47 (57%) underwent a laparoscopic/vaginal approach, and 36 (43%) an abdominal approach. The median number of lymph nodes evaluated was 22 (range, 3–54); and 16 (16%) patients had positive pelvic nodes on final pathology.

Final trachelectomy pathology showed no residual disease in 44 patients (45%), dysplasia in 5 (5%), and adenocarcinoma in situ in 3 (3%). Overall, 27 patients (27%) needed hysterectomy or adjuvant pelvic radiation postoperatively. One (1%) documented recurrence was fatal at the time of this report; in addition, one patient died of pulmonary complications during pregnancy and one from an automobile accident; both patients were clinically disease-free at last medical evaluation before death.

Pregnancy outcomes for the entire cohort included 14 healthy deliveries (2 patients had 2 children each); 2 additional patients are currently pregnant. Among 4 miscarriages (2 in first trimester and 2 in early second trimester), the second-trimester miscarriages occurred in patients in whom no cerclage was placed or who had a cerclage that eroded and had to be removed before conception. Therefore, the authors' group's policy is to routinely place a permanent McDonald-type cerclage at trachelectomy using a #0 permanent suture such as GoreTex or Ethibond. Three patients elected to terminate pregnancy in the first trimester.

Discussion

As gynecologic oncologists continue to investigate new approaches to treat cervical cancer and preserve reproductive potential, they are faced with the challenge of performing a technically feasible procedure that is both oncologically sound in principle and available to patients who may be candidates. The authors' initial data indicated that cervical adenocarcinoma and lymph-vascular invasion are common features in patients selected for radical trachelectomy. Most patients can undergo the operation successfully; however, nearly 27% of all selected cases will require either immediate radical hysterectomy (because of intraoperative findings such as positive lymph nodes or positive endocervical resection margin), or posttrachelectomy chemoradiation for high-risk features, namely positive pelvic lymph nodes on final pathology.

Routine sentinel node mapping is useful in triaging patients intraoperatively for completion hysterectomy, when tumor is detected at frozen-section. However, until lower false-negative rates are achieved, pelvic lymphadenectomy with parametrectomy remains the gold standard in this disease.

Future challenges include better preoperative selection of patients and the investigation of alternative fertility-sparing adjuvant therapy in patients with node-positive disease. The authors' current selection criteria for fertility-sparing radical trachelectomy are listed in Table 1. Patients are selected for a laparoscopic vaginal approach (Dargent operation) if they are good candidates for vaginal surgery and have stage IA1 lesions with lymphovascular invasion, stage IA2 lesions, or select stage IB1 lesions (< 2 cm),^{14,15}

Table 1 Suggested Clinical Eligibility Criteria for Radical Trachelectomy

1.	Confirmed invasive cervical cancer: excluding small cell neuroendocrine tumors and adenoma malignant tumors
2.	FIGO stage IA1 with LVI, IA2, and IB1
3.	Age < 45 years and strong desire to preserve fertility
4.	No clinical evidence of impaired fertility
5.	Lesion size ≤ 4 cm
6.	Chest radiograph with no evidence of metastasis. At physician's discretion, preoperative appropriate imaging protocol
7.	4–6 weeks postconization with adequate resolution of acute inflammation

particularly those with superficial invasion in which the bulk of tumor is found to be a shallow flat wide lesion on conization or loop electrosurgical excision procedure. Patients who are not candidates for vaginal surgery, or have lesions found to be deeply invasive on conization or with an estimated clinical size of 2 to 4 cm, are triaged to the abdominal approach. The robotic approach mimicking the resection outlined by the abdominal approach is becoming more common in many practices, although most results are from small case reports or series. However, this approach will undoubtedly become more popular in experienced hands and will provide yet another surgical approach for fertility preservation.

Two main categories of fertility-sparing adjuvant therapy are currently available for patients with node-positive disease: surgical procedures without the need for radiation, and systemic chemotherapy without radiation. Surgical procedures for intraoperative management of detected node-positive disease, such as the laterally extended parametrectomy (LEP) procedure described by Ungar and Palfalvi,¹⁶ may be an option in select cases. This procedure was introduced by the Budapest team for the treatment of patients with early-stage cervical cancer with pelvic lymph node metastases. The procedure was used without any adjuvant treatment in 31 patients with stage IB cervical cancer, in whom pelvic lymph node metastases were confirmed with intraoperative histology. With a mean follow-up of 60 months, 25 of 29 patients were alive and disease-free at the end of the study period. Kaplan-Meier 5-year cumulative proportion survival was 85%. These results suggest that pelvic lymph node metastases can be cured with surgery alone. The LEP procedure seems to be a treatment alternative to chemoradiotherapy for patients with early-stage cervical cancer and pelvic lymph node metastases, and deserves further investigation.

Moreover, whether all patients with positive

nodes need postoperative chemoradiation based on the Intergroup trial,¹⁷ as opposed to postoperative chemotherapy, is an intriguing question. In 1996, Curtin et al.¹⁸ reported on the clinical efficacy of adjuvant chemotherapy alone versus chemotherapy plus whole pelvic radiation therapy after radical hysterectomy and node dissection for cervical cancer in patients at high-risk for recurrence. They conducted a prospective multicenter randomized phase III trial in patients with stage IB–IIA cervical cancer undergoing radical hysterectomy and node dissection. Risk factors included deep cervical invasion, tumor 4 cm or larger, parametrial involvement, nonsquamous histology, and/or pelvic lymph node metastasis. Chemotherapy consisted of cisplatin and bleomycin, alone (n = 44) or in combination with whole pelvic radiotherapy (n = 45). Of the patients who underwent chemotherapy alone, 9 (20%) experienced recurrence, compared with 10 (22%) of those who underwent chemotherapy and radiation (*P* = not significant). Patterns of recurrence were statistically similar between the treatment arms, even among the subgroup of patients with 3 or more risk factors. The results of this limited trial led the investigators to conclude that multimodality treatment with chemoradiation was not a superior adjuvant therapy for patients at high-risk of recurrence after radical hysterectomy and node dissection for early cervical cancer.

Using the authors' criteria, radical abdominal trachelectomy may have a broader applicability for patients thought to be poor candidates for radical vaginal trachelectomy. However, this group of patients will inherently have a higher chance of needing additional therapy. The role of adjuvant chemotherapy alone for select high-risk patients after radical trachelectomy and lymphadenectomy instead of chemoradiation deserves further investigation to improve the potential fertility preservation in this select group of patients.

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