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Surgical and Pathologic Outcomes of Fertility-Sparing Radical Abdominal Trachelectomy for FIGO Stage IB1 Cervical Cancer

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Abstract

Objectives—To describe the surgical and pathologic findings of fertility-sparing radical abdominal trachelectomy using a standardized surgical technique, and report the rate of post-trachelectomy adjuvant therapy that results in permanent sterility

Methods—A prospectively maintained database of all patients with FIGO stage IB1 cervical cancer admitted to the operating room for planned fertility-sparing radical abdominal trachelectomy was analyzed. Sentinel node mapping was performed via cervical injection of Technetium and blue dye.

Results—Between 6/2005 and 5/2008, 22 consecutive patients with FIGO stage IB1 cervical cancer underwent laparotomy for planned fertility-sparing radical abdominal trachelectomy. Median age was 33 years (range 23–43). Histology included 13 (59%) with adenocarcinoma and 9 (41%) with squamous carcinoma. Lymph-vascular invasion was seen in 9 (41%) cases. Only 3 (14%) needed immediate completion radical hysterectomy due to intraoperative findings (2 for positive nodes, 1 for positive endocervical margin). Median number of nodes evaluated was 23 (range 11–44); and 6 (27%) patients had positive pelvic nodes on final pathology – all received postoperative chemoradiation. Sixteen (73%) patients agreed to participate in sentinel node mapping which yielded a detection rate of 100%, sensitivity of 83%, specificity of 100% and false negative rate of 17%. Eighteen of 19 (95%) patients who completed trachelectomy had a cerclage placed, and 9/22 (41%) patients had no residual cervical carcinoma on final pathology. Median time in the operating room was 298 minutes (range 180–425). Median estimated blood loss was

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Conflict of interest statement

YS has received research support from Plasma Surgical, has served as a consultant for Covidien and a speaker for Genzyme. All other authors have no conflicts of interest to declare.

250 ml (range 50–700), and median hospital stay was 4 days (range 3–6). No recurrences were noted at the time of this report.

Conclusions—Cervical adenocarcinoma and lymph-vascular invasion are common features of patients selected for radical abdominal trachelectomy. The majority of patients can undergo the operation successfully; however, nearly 32% of all selected cases will require hysterectomy or postoperative chemoradiation for oncologic reasons. Sentinel node mapping is useful but until lower false negative rates are achieved total lymphadenectomy remains the gold standard. Investigating alternative fertility-sparing adjuvant therapy in node positive patients is needed.

Keywords

abdominal trachelectomy; fertility-sparing surgery; cervical cancer; sentinel node mapping

Introduction

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 throughout the world [1–8]. The abdominal operation also has broadened the utilization of radical trachelectomy beyond the laparoscopic and vaginal approaches initially described and popularized by Dargent [9–10]. Since 2001 we have been offering fertility-sparing radical trachelectomy procedures via the vaginal approach to select women with stage I cervical cancer that have a strong desire to preserve reproductive function. In 2004 we performed radical abdominal trachelectomy in pediatric patients who were not candidates for the vaginal approach [11]; this experience broadened our inclusion criteria to offer this important operation to many of our patients interested in fertility preservation. Currently we use both approaches - vaginal or abdominal - and select patients to laparoscopic/vaginal approaches versus 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. The objectives of this report are to describe the clinical characteristics of patients selected for this operation (including their surgical and pathologic findings), and to report the rate of post-trachelectomy adjuvant therapy that results in permanent sterility.

Methods

Following Institutional Review Board approval, we analyzed a prospectively maintained database of all patients with FIGO stage IB1 cervical cancer admitted to the operating room for planned fertility-sparing radical abdominal trachelectomy. We have previously described our surgical technique for fertility-sparing abdominal trachelectomy in detail [12–13]. All patients had standard preoperative imaging with either computerized tomography of the abdomen and pelvis or magnetic resonance imaging of the pelvis and all had clinical stage IB1 disease without any evidence of metastasis. Sentinel node mapping was performed via cervical injection of Technetium and blue dye 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 our institution, all gynecologic specimens are reviewed by specially trained gynecologic pathologists. Standard statistical analysis was performed.

Results

Between 6/2005 and 5/2008, 22 consecutive patients with FIGO stage IB1 cervical cancer underwent laparotomy for planned fertility-sparing radical abdominal trachelectomy. The median age was 33 years (range, 23–43) with a median body mass index (BMI) of 24.5 (range, 17.2–35.5). Only 2 of 22 (9%) patients had children from previous pregnancies and the remaining patients were nulliparous.

Histology included 13 (59%) adenocarcinomas and 9 (41%) squamous carcinomas. Lymph-vascular invasion was seen in 9 (41%) cases. Only 3 (14%) needed immediate completion radical hysterectomy due to intraoperative findings (2 for positive nodes, 1 for positive endocervical margin detected at frozen-section). Eighteen of 19 patients (95%) patients in whom the trachelectomy was completed had a permanent cerclage placed using #0 Ethibond.

The median number of nodes evaluated was 23 (range 11–44); 6 (27%) patients had positive pelvic nodes on final pathology including the 2 cases that underwent immediate radical hysterectomy. Sixteen (73%) patients agreed to participate in sentinel node mapping and all of these had successful mapping with a median of 5 sentinel nodes identified intraoperatively (range, 1–9). Overall sentinel node mapping yielded a sensitivity of 83%, specificity of 100% and false negative rate of 17% (1/6 cases). The 6 cases that had positive pelvic nodes on final pathology all had successful sentinel node mapping with identification of sentinel nodes intraoperatively that were sent for frozen-section as well. The intraoperative frozen-section of sentinel nodes detected disease intraoperatively in 2 of 6 (33%) cases and resulted in immediate completion radical hysterectomy. Disease was missed in 3 of 6 (50%) cases, and was detected only on final pathology. In addition, one patient had 8 completely negative sentinel nodes with the only positive node being a “non-sentinel” node in the parametria; this node was undetected as a sentinel node and identified only on final pathology in the parametria of the abdominal trachelectomy specimen.

The median length of the right parametria as measured by the pathologist was 3.5cm (range, 0.5–6cm), and the median length of the left parametria was 3.5cm (range, 1.5–7.9cm). The mean diameter of tumor was 16mm (range, 9–25mm). Overall 9 patients (41%) had no residual cervical carcinoma on final pathology, but 7 (32%) patients unfortunately ended up with either radical hysterectomy (n=3) or post-trachelectomy chemoradiation (n=4) due to high-risk pathologic features, primarily positive pelvic nodes.

The median time in the operating room was 298 minutes (range, 180–425), with a median estimated blood loss of 250 ml (range, 50–700), and median hospital stay was 4 days (range, 3–6). With a median follow-up of 12 months (range, 1–35 months), no recurrences were noted at the time of this report.

Complications included post-trachelectomy stenosis of the neo-cervix in 4 of 19 (21%) patients, infected pelvic lymphocyst requiring interventional radiology drainage in 2 of 22

(9%) patients, cerclage erosion through the vagina 1 of 19 (5.3%) patients, leg lymphedema in 1 of 22 (4.5%) patients, and amenorrhea in 1 of 19 (5.3%) patients.

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. From our initial data, we realized that cervical adenocarcinoma and lymph-vascular invasion are common features of patients selected for radical abdominal trachelectomy. The majority of patients can undergo the operation successfully; however, nearly 32% of all selected cases will require either immediate radical hysterectomy (due to intraoperative findings such as positive lymph nodes or positive endocervical resection margin), or post-trachelectomy chemoradiation for high-risk features, namely positive pelvic lymph nodes on final pathology. The routine utilization of sentinel node mapping is useful in triaging patients intraoperatively for completion hysterectomy – when tumor is detected at frozen-section. However, based on our data and until lower false-negative rates are achieved, total lymphadenectomy 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 node positive patients. Our current selection criteria for fertility-sparing radical abdominal trachelectomy are listed in Table 1. Patients are selected to 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 (<2cm) [14], particularly those with superficial invasion where the bulk of tumor is a shallow flat wide lesion on conization or LEEP. Patients who are not candidates for vaginal surgery or have deeply invasive lesions on conization or lesions with clinical size estimated at 2–4cm are triaged to the abdominal approach.

Current fertility-sparing adjuvant therapy options for node positive patients falls under 2 main categories: one is surgical options without the need for radiation; the other is systemic chemotherapy without radiation. Surgical options for intraoperatively management of detected node positive cases such as the laterally extended parametrectomy (LEP) procedure described by Ungar and Palfalvi [16] may be an option in select cases. This operation was introduced by the Budapest team for the treatment of early stage cervical cancer patients with pelvic lymph node metastases. The procedure was used without any adjuvant treatment in 31 stage IB cervical cancer patients, where pelvic lymph node metastases were proven by 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 by surgery alone. The LEP procedure seems to be a treatment alternative to chemoradiotherapy for early-stage cervical cancer patients with 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. The clinical efficacy of adjuvant chemotherapy alone versus chemotherapy plus whole pelvic radiation therapy in patients post-radical hysterectomy and node dissection for cervical cancer at high-risk for recurrence was reported by Curtin in 1996 [18]. A prospective multicenter randomized phase III trial in patients with Stage IB-IIA cervical cancer undergoing radical hysterectomy and node dissection was conducted. Risk factors include deep cervical invasion, tumor ≥ 4 cm, parametrial involvement, nonsquamous histology, and/or pelvic lymph node metastasis. Chemotherapy consisted of cisplatin and bleomycin, alone or in combination with whole pelvic radiotherapy. Forty-four patients received chemotherapy alone versus 45 patients treated with chemotherapy and external radiation. Nine of 44 (20%) patients receiving chemo alone recurred compared to 10/45 (22%) patients receiving chemo and RT (P=ns). Patterns of recurrence were statistically similar between the two treatment arms, even among the subgroup of patients with ≥ 3 risk factors. This led the investigators to conclude that multimodality treatment with chemoradiation did not prove a superior adjuvant therapy for patients at high-risk of recurrence after radical hysterectomy and node dissection for early cervical cancer in this limited trial.

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

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Table 1

Suggested clinical eligibility criteria for radical abdominal trachelectomy

1.	Confirmed invasive cervical cancer: squamous, adenocarcinoma, or adenosquamous
2.	FIGO Stage IA2 to 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 X-ray with no evidence of metastasis. At attendings discretion, preoperative MRI of pelvis + abdomen, or appropriate imaging protocol
7.	4–6 weeks post conization with adequate resolution of acute inflammation