

Postoperative radiotherapy in Stage IB squamous cell cervical cancer

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Summary

Objective: The purpose of the study was to evaluate postoperative whole pelvic radiation for high-risk patients with FIGO Stage IB cervical cancer.

Methods: One hundred and forty-eight patients with Stage IB squamous cell carcinoma of the cervix underwent radical hysterectomy and pelvic lymphadenectomy. The low-risk group included patients without unfavorable prognostic factors who were treated only by surgery. The high-risk group included women with pelvic node metastases, with positive or close surgical margins, clinical tumor size > 4.0 cm, depth of stromal invasion > 1/3 the cervical wall, grade 3 tumor and presence of lymphovascular space involvement. High-risk patients received whole pelvic radiotherapy between two and four weeks after surgery.

Results: Seventy patients (47.3%) were low risk and 78 patients (52.7%) were high risk. Locoregional recurrences were diagnosed in nine cases (12.8%) in the surgery group and in 11 patients (14.1%) assigned to radiotherapy. The incidence of distant metastases was 2.8% in the surgery group and 6.4% in the surgery and radiotherapy group. Overall survival at five years was 88.6% in the low-risk group and 84.7% in the high-risk group.

Conclusion: Five-year overall survival, locoregional and distant metastases were similar in the low-risk and high-risk groups of patients, thus emphasizing the value of whole pelvic radiation in patients with unfavorable prognostic factors in Stage IB cervical cancer.

Key words: Stage IB cervical cancer; High-risk patients; Postoperative pelvic radiation.

Introduction

Uterine cervical cancer is the most common gynecological cancer worldwide with a yearly incidence of 500,000 cases [1]. It is an important health problem for women in developing countries. Risk factors for cervical cancer include early onset of sexual activity, multiple sexual partners, lower socio-economic group and history of sexually transmitted disease. Human papilloma virus has been implicated as the major causative agent in this disease. Squamous cell carcinoma is the most common type accounting for 80-85% of cases. At the FIGO Congress in Montreal 1994, the Gynecologic Oncology Committee made some changes in the staging for cervical cancer. Stage IB comprises patients with microscopic stromal invasion more than 5.0 mm or with horizontal spread more than 7.0 mm and a clinically visible lesion confirmed to the cervix. Stage IB1 presents clinical lesions no greater than 4.0 cm in size and Stage IB2 clinical lesions greater than 4.0 cm in size [2]. Signs range from an abnormal cervical smear to a cervix with exophytic or crater-like type lesions. Symptoms include abnormal vaginal bleeding, postcoital spotting and vaginal discharge. Primary treatment may consist of radical hysterectomy and bilateral pelvic lymphadenectomy. Postoperative radiotherapy is recommended for patients with unfavorable prognostic factors [3].

The purpose of this study was to evaluate postoperative whole pelvic radiation for high-risk patients with Stage IB cervical cancer.

Patients and Methods

One hundred and forty-eight patients were included in the study mean age 42.6 ± 11.4 years. Initial evaluation included medical history, Pap smears and pelvic examination. When cytology showed malignant cells in patients with no visible tumor we performed diagnostic cone biopsy. In patients with clinically visible lesions confined to the cervix, diagnosis was confirmed by a directed punch biopsy. Preoperative evaluation included physical examination, complete blood count, blood chemistry tests, chest radiography, intravenous pyelogram, cystoscopy and sigmoidoscopy. All patients were treated by Wertheim hysterectomy and pelvic lymphadenectomy. The diagnoses of squamous cell cervical cancer were made by a pathologist. Women with adenocarcinoma, adenosquamous and small cell carcinoma were excluded from the study.

The low-risk group included patients without unfavorable prognostic factors who were treated only by surgery. The high-risk group included women with pelvic node metastases, with positive or close surgical margins, clinical tumor size > 4.0 cm, depth of stromal invasion > 1/3 the cervical wall, grade 3 tumors and presence of lymphovascular space involvement. High-risk patients received radiotherapy between two and four weeks after surgery.

Postoperative radiotherapy was administered to the pelvic region according to a standardized protocol. The total dose was 40-50 Gy in 20-25 fractions using 2 Gy daily fractions, five days a week. Radiation was delivered by anteroposterior and posteroanterior parallel ports.

Patients were evaluated by physical examination, Pap smear, blood counts, blood chemistries and chest radiography every three months for the first two years, every six months during the next three years and then annually. Computed tomography (CT) scans with contrast were done at six months and then yearly.

Results

From 1985 to 1999, 148 patients with FIGO Stage IB squamous cell cervical cancer were primarily treated by radical surgery. Seventy patients (47.3%) were low risk and 78 patients (52.7%) were high risk (Table 1). For the low-risk group of patients no future therapy was applied, while high-risk patients received postoperative whole pelvic radiation. The median interval between the operation and the first radiotherapy session was 24 days. During radiotherapy the patients were treated with medication or dietary measures, or both, for treatment-related symptoms.

Locoregional recurrences in the pelvis or vagina were diagnosed in nine cases (12.8%) in the surgery group and in 11 patients (14.1%) assigned to radiotherapy. Distant metastases involved the abdomen or lung, or both locations. The incidence of distant metastases was 2.8% in the surgery group and 6, 4% in the surgery and radiotherapy group (Table 2). The difference was not statistically significant. Local relapses were treated by surgery and patients with distant metastases received adjuvant chemotherapy with cisplatin-based regimens.

Overall survival at five years was 88.6% in the low-risk group and 84.7% in the high-risk group of patients (Table 3). The difference was not statistically significant.

Table 1. — *Pathologic findings.*

Prognostic factors	Number of cases	%
Low-risk group	70	47.3
High-risk group	78	52.7
Total	148	100.0

Table 2. — *Recurrences of the irradiated and nonirradiated group of patients.*

Site of recurrence	Surgery only (no. = 70)	Pelvic radiation (no. = 78)
Local	9 (12.8%)	11 (14.1%)
Distant	2 (2.8%)	5 (6.4%)
Total	11 (15.6%)	16 (20.5%)

Table 3. — *Five-year survival of patients according to treatment in relation to good and poor prognostic factors.*

Prognostic factors	Number of cases	Pelvic radiation	5-year survival (%)
Low-risk	70	No	88.6
High-risk group	78	Yes	84.7

Discussion

An algorithm for the management of Stage IB cervical cancer included radical hysterectomy and pelvic lymphadenectomy. Patients with lymph node metastases were treated with postoperative adjuvant pelvic radiation [4]. Positive surgical margins, tumor diameter, depth of stromal invasion, grade of tumor and lymphovascular space involvement were also risk factors for recurrences. The Gynecology Oncology Group (GOG) study in 1990 reported clinical tumor size, depth of invasion and lym-

phovascular space involvement as independent prognostic factors. Patients with negative lymph nodes in Stage IB cervical cancer had 25% of high-risk factors [5]. Another GOG study in 1999 suggested that postoperative pelvic radiation reduced risk of recurrence rate in patients with at least two risk factors: large tumor diameter, > 1/3 stromal invasion and lymphovascular space involvement [6]. Women with lymph node metastases post Wertheim hysterectomy who were given adjuvant treatment had a better survival rate than those undergoing surgery in multivariate analysis. Of patients without pelvic lymph node metastases but with parametrial extension, tumor size > 4 cm, full thickness of cervical stromal invasion and DNA index more than 1, three had significantly better five-year recurrence-free survival rate if they received postoperative radiotherapy [7]. Ayhan *et al.* reported that tumor size larger than 4 cm, lymphovascular space involvement and vaginal involvement were independent prognostic factors in lymph node negative invasive cervical cancer. Depth of stromal invasion, parametrial, endometrial and myometrial involvement, however, were not independent prognostic factors [8]. Pieterse *et al.* found statistically significant differences in five-year survival and five-year disease-free survival between the high-risk group treated with radiotherapy and the group without radiotherapy after radical hysterectomy with pelvic lymphadenectomy [9]. Similar results have been reported by other investigators [10, 11].

In our study the low-risk group of 70 patients had no unfavorable prognostic factors and were treated by surgery only. The high-risk group of 78 women had one or more risk factors: pelvic node metastases, positive or close surgical margins, tumor size > 4.0 cm, stromal invasion > 1/3 the cervical wall, grade 3 tumors and presence of lymphovascular space involvement. High-risk patients received postoperative radiotherapy. Eleven (15.6%) women in the low-risk group had cancer recurrences, nine (12.8%) local, and two (2.8%) distant. High-risk patients included 16 (20.5%) cancer recurrences, 11 (14.1%) local and five (6.4%) distant. The five-year overall survival rate in the low-risk surgery group only and high-risk surgery and radiotherapy group was similar, 88.6% and 84.7%, respectively, thus emphasizing the value of whole pelvic radiation in patients with unfavorable prognostic factors in Stage IB squamous cell cervical cancer.

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