The impact of pretreatment staging laparotomy on survival in locally advanced cervical carcinoma

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Summary

The purpose of this retrospective study was to determine the effect of pretreatment surgical staging on survival of patients with locally advanced cervical carcinoma. Two hundred and seventy-four women with cervical cancer stages IIB-IVA treated with primary radiotherapy comprised the study group. Eighty-nine patients underwent pretreatment staging laparotomy (group 1) and 172 patients underwent clinical staging (group 2). Thirteen patients underwent CT guided biopsy of paraaortic adenopathy. Paraaortic metastases were detected in 12.3% and intraabdominal metastases were found in 4.5% of patients in group 1.

Extended field radiotherapy and/or systemic chemotherapy were given in these cases. The median survival of patients in group 1 was statistically longer than that of patients in group 2, 29 months vs 19 months, respectively (p=.01). Multivariate analysis controlling for both stage and age showed pretreatment staging laparotomy is a significant predictor of survival (p=.03). Our data suggest that surgical staging may be beneficial in patients with locally advanced cervical carcinoma.

Key words: Cervical carcinoma; Surgical staging; Survival.

Introduction

Radiotherapy is the treatment of choice for locally advanced cervical cancer. The success of this treatment depends on the bulk of disease present, radiosensitivity of the tumor, and the likelihood that the disease is contained within the treatment field. In 1971, Van Nagell and associates [1] reported discrepancies between clinical and surgical staging in 45% of patients with stage II disease and 75% of patients with stage III disease. Similarly, Nelson and associates [2] reported that 16.1% and 46.4% of patients with stage II and III disease, respectively, had paraaortic metastases documented at pretreatment staging laparotomy. Thus, as many as 50% of patients with stage III disease may have metastatic disease outside of the standard pelvic radiation portal at the initiation of treatment. In order to identify these patients who may benefit from extended field radiation and/or systemic chemotherapy, a pretreatment staging laparotomy consisting of paraaortic lymph node biopsy and intraperitoneal exploration was introduced [3]. The ability of this procedure to provide information which may benefit patients with documented extrapelvic disease has been questioned. LaPolla and associates [4] estimated that only 2.5% of patients who undergo surgical staging will benefit from the procedure. In a similar study, Podczaski and associates [5] estimated only 4.6% of patients would derive benefit from the surgery in the form of prolonged disease-free survival. The purpose of the present study was to compare median survival of patients undergoing pretreatment laparotomy and extraperitoneal paraaortic lymph node sampling and patients undergoing clinical staging only. Special attention is given to the alterations in treatment caused by the findings at pretreatment laparotomy and the outcome of patients found to have extrapelvic disease.

Materials and Methods

Two hundred seventy-four patients with cervical carcinoma, stages IIA-IVA, treated with primary radiotherapy at SUNY-Health Science Center at Brooklyn and Kings County Hospital between 1985 and 1996 comprised the study group. Pertinent information was abstracted from the patient's medical record, the tumor registry and the tumor board notes. The patients were then divided into three groups, those undergoing pretreatment laparotomy (group 1), those undergoing clinical staging only (group 2), and those undergoing CT guided fine needle aspiration (FNA) of suspicious paraaortic lymph nodes (group 3). Data regarding patients in group 3 were included in the calculations of the incidence of paraaortic node metastases but were not included in survival analyses. The incidence of paraaortic lymph node metastases as well as incidence of extrapelvic spread was determined. The pretreatment laparotomy included an extraperitoneal paraaortic lymph node sampling from the mid-common iliac artery to the level of the inferior mesenteric artery and intraperitoneal exploration with pelvic washings for cytology similar to the method described by Berman *et al.* [3]. Pelvic nodes were biopsied only if adenopathy was detected by palpation. A standard pelvic radiation technique was used, combining external beam and intracavitary radiotherapy. The borders of the standard pelvic portal for external beam radiotherapy were the L4-L5 interspace, a 2 cm margin lateral to the medial aspect of the bony pelvis, and the lower border of the obturator foramen. In cases of extended field radiation the superior border of the pelvic portal was extended to the L1-L2 interspace with a width of approximately 10 cm.

Received November 18, 1998
revised manuscript accepted for publication December 15, 1998

The incidence of intraoperative and postoperative complications associated with pretreatment staging laparotomy was determined. The median survival of all patients in groups 1 and group 2 were calculated using the method of Kaplan-Meier [6] and compared using the log-rank test. Statistical significance was set at .05 for all tests.

Results

Eighty-nine patients (32.5%) underwent pretreatment staging laparotomies (group 1). One hundred and seventy-two patients (62.8%) began radiotherapy without surgical staging (group 2). Thirteen patients (4.7%) underwent FNA of paraaortic adenopathy (group 3). The mean ages of patients in group 1 and group 2 were 51 and 57 years, respectively (p=.001). The ethnic distribution within the two groups did not differ significantly with 68.5% of group 1 being Black, compared to 75.4% of patients in group 2 (p=.23). Table 1 contains the stage distribution within the two groups. The distribution of histologic types of cervical cancer within the two groups was similar and is shown in Table 2. Of 89 patients undergoing pretreatment laparotomy, 11 (12.3%) were found to have paraaortic metastases. Including the paraaortic lymph node biopsy results from patients in group 3, the incidence of paraaortic lymph node metastases was determined to be 13.3% for stage IIB, 32% for stage IIIB, and 50% for stage IVA. The incidence of extracervical spread found at the time of staging laparotomy was low and is outlined in Table 3. Five patients were incidentally found to have a second primary tumor.

Nine of the 11 patients with paraaortic metastases received extended field radiotherapy, while 6 of the 11 received systemic chemotherapy. Two patients with documented negative paraaortic nodes received prophylactic extended field radiation and 2 patients in group 2 received prophylactic paraaortic radiation. Systemic chemotherapy was given to 2 of the 4 patients with extrapelvic disease documented at laparotomy. One patient with positive peritoneal cytology only received no systemic chemotherapy and 1 patient with small bowel serosal involvement had chemotherapy held secondary to intercurrent medical conditions.

The doses of external beam radiation delivered to point A did not differ significantly between group 1 and group 2. Group 1 received a mean dose of 4707 cGy, compared to 4340 cGy for group 2 (p=.095). Patients in group 2 received a lower mean dose of brachytherapy (1,126 cGy) compared to group 1 (1,934 cGy).

Intraoperative complications associated with the pretreatment staging laparotomy were rare. Only one case of intraoperative hemorrhage was noted (estimated blood loss 800cc). Major postoperative complications occurred at an overall rate of 8.9%. Five patients (5.6%) had fascial dehiscence, 2 patients (2.2%) had pulmonary embolus, and 1 patient (1.1%) suffered evisceration and subsequent death. There were 3 superficial wound separations giving a minor complication rate of 3.4%.

Table 4 outlines the recurrence patterns for patients in groups 1 and 2. Patients in group 1 were more prone to distant recurrences than pelvic (18.4% vs 3.9%), while pelvic and distant recurrences were equal in group 2 (8.6%). A higher percentage of patients in group 2 had persistent disease which was defined as failing to achieve local control or having a disease-free interval of less than 6 months.

Figure 1 shows the Kaplan-Meier survival curve of patients who underwent surgical staging with negative versus positive paraaortic nodes. Paraaortic lymph node metastases clearly worsened the prognosis. The median survivals were 37 months and 14 months, respectively (p=.006). The median survival of patients in groups 1 and 2 were then compared (Figure 2). The median survivals were 29 and 19 months, respectively. Patients undergoing pretreatment laparotomy had a significantly longer median survival compared to patients who did not undergo surgical staging (p=.01). In order to address the differences in stage distribution and age between group 1 and group 2, a multivariate analysis was performed using the Cox Regression and controlling for both stage and age. Pretreatment staging laparotomy remained a significant predictor of survival (p=.03). Patients in group 2 had a relative risk of death equal to 1.44, compared to

Table 1. — *Stage distribution of groups 1 and 2. Pearson chi-square test p=.02.*

	STAGE		
	II	III	IV
Group 1	44	42	3
	49.4 %	47.2%	3.4%
Group 2	60	93	19
	34.9%	54.1%	11.0%

Table 2. — *Distribution of histologic types in groups 1 and 2. Pearson chi-square test p=.83. SCCA = squamous cell carcinoma.*

	STAGE			
	SCCA	Adenocarcinoma	Other	Total
Group 1	80	5	4	89
	89.9%	5.6%	4.5%	100%
Group 2	150	13	8	171
	87.7%	7.6%	4.7%	100%

Table 3. — *Incidence of extracervical spread in group 1.*

	Frequency	Percent
None	73	82
Abdominal	4	4.5
Pelvic	7	7.9
2nd primary	5	5.6
Total	89	100

Table 4. — *Recurrence patterns in groups 1 and 2.*

	None	Pelvic	Distant	Persistent Disease	Total
Group 1	33	3	14	26	76
	43.4%	3.9%	18.4%	34.2%	100%
Group 2	38	13	13	87	151
	25.2%	8.6%	8.6%	57.6%	100%
Total	71	16	27	113	227
	31.3%	7%	11.9%	49.8%	100%

patients in group 1. When the median survival of the 11 patients in group 1 with documented paraaortic metastases was compared to the median survival of group 2, no statistical difference was found (14 months vs 19 months, p=.24).

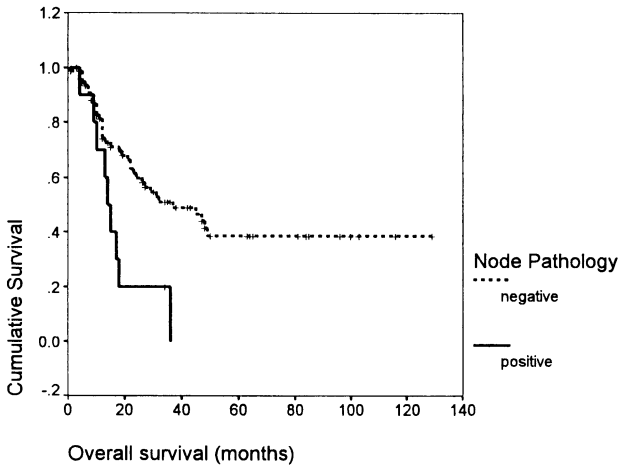

Figure 1.

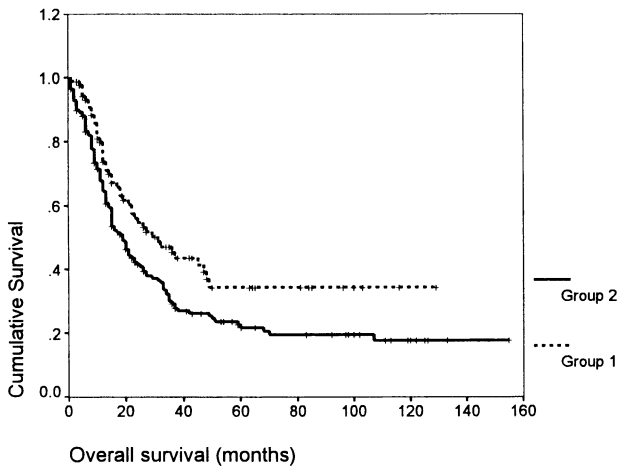

Figure 2.

Discussion

The role of pretreatment laparotomy and surgical staging in locally advanced cervical cancer is controversial. Clearly, those patients who stand to benefit from the procedure are also the patients who have the lowest chance for prolonged disease-free survival (ie. positive paraaortic nodes or extrapelvic metastases). The critical question to answer is whether treatment alterations caused by the findings of the procedure are able to effect a clinically significant improvement in survival. Previous studies by LaPolla [4], Podczaski [5], and Jazy *et al.* [7] defined benefit from the pretreatment laparotomy only in terms of prolonged disease-free survival. A comparison of median survival between patients who had undergone pretreatment laparotomy and those who had clinical staging only was not performed. The present study sought to determine if an improvement in median survival could be demonstrated in patients undergoing surgical staging.

The distribution of paraaortic metastases by stage in the present series is similar to previous reports [5, 8, 9]. The 50% rate of paraaortic metastases for stage IVA disease is higher than previously reported but probably more accurately represents the true incidence as the number of patients at this stage in the present series is higher than in the previous studies. Similar to the Gynecologic Oncology Group experience [9], intraoperative complications associated with extraperitoneal lymph node biopsy were rare. The postoperative complication rate is also comparable except for the higher rate of fascial dehiscence seen in our patients. This may be attributed to the use of a paramedian incision at the lateral border of the rectus muscle in many cases which may represent an area of relative weakness compared to a more medial or midline incision.

It has been the policy at our institution to routinely offer pretreatment laparotomy to all patients with locally advanced cervical carcinoma. It is possible that selection bias played a role in determining which patients received surgical staging, however, patient preference was the major determinant of whether or not the procedure was performed. It is also possible that the survival difference is explained by a lower mean of brachytherapy dose seen in group 2. In some cases, patients who refused pretreatment laparotomy were also noncompliant with scheduled radiation treatments.

Any improvement in survival attributed to surgical staging of cervical cancer must result from treatment alterations caused by positive findings at the time of laparotomy. In the present series, 12.3% of the patients undergoing surgical staging received some additional treatment in the form of extended field radiation and/or systemic chemotherapy for positive paraaortic nodes and 5% received systemic chemotherapy for intraabdominal metastases. When the median survival of patients with documented paraaortic metastases and those undergoing clinical staging only was compared, no statistically significant difference was seen. Our data indicate that at least 12% of the patients in group 2 had undetected paraaortic metastases and the lack of treatment to this metastatic site may account for the equivalent survival when compared to a population with 100% incidence of paraaortic metastases who received treatment. Although prolonged disease-free survival for patients with paraaortic metastases or intrabdominal spread was rare (only 2 of the 11 patients with paraaortic metastases survived greater than 30 months), patients undergoing pretreatment laparotomy had a significantly longer median survival compared to patients who underwent clinical staging only. This observation is consistent with the findings of Rotman, *et al.* [10] who noted an improved overall survival in patients with locally advanced cervical cancer who received prophylactic paraaortic radiation compared to those receiving pelvic radiation alone. It is probable that the addition of paraaortic radiation for patients with micro-

scopic paraaortic metastases accounts for this improvement in survival. A more recent study by Cosin *et al.* [11], which found similar survival in patients with macroscopic nodal metastases which were removed at the time of pretreatment laparotomy compared to patients with microscopic nodal metastases, offers another potential benefit of surgical staging.

Conclusion

Our data suggest that pretreatment staging laparotomy may be beneficial in patients with locally advanced cervical carcinoma. The observed improved survival in patients undergoing the procedure may result from the treatment of otherwise undetected extrapelvic metastases. A randomized prospective study is necessary to further clarify the role of surgical staging in cervical carcinoma.

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