Radiation Therapy With or Without Chemotherapy for Cervical Cancer With Periaortic Lymph Node Metastasis

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Abstract: The purpose of this article is to evaluate the efficacy of chemoradiation therapy (CRT) and radiation therapy (RT) alone for cervical cancer with periaortic nodal metastasis (PANM). Twenty-one patients with cervical cancer with PANM were identified. Eleven patients received concomitant CRT with cisplatin-based chemotherapy and 10 received RT alone. The median age was 44 years. Ten, 5, and 6 patients had International Federation of Gynecology and Obstetrics stages IB, IIB, and IIIB disease. The RT doses to point A and the periaortic region were 80 to 85 Gy (low dose rate equivalent) and 45 Gy. The median follow-up was 26 months (range 3 to 141 months). The 1- and 3-year disease-specific survival were 81.8% and 81.8%, and 70% and 30%, respectively, for the CRT and RT groups, ($P = 0.11$). The 1- and 3-year pelvic and periaortic control rates (PPC) were 100% and 100% (CRT), and 56.3% and 42.2% (RT) ($P = 0.03$). The 1- and 3-year free-from-distant metastasis (DM) rates were 81.8% and 81.8% (CRT), and 78.7% and 49.2% (RT) ($P = 0.54$). All patients who developed DM died of their disease. CRT is a feasible treatment option to improve the PPC for these patients. Because of the high rate of distant metastasis despite PPC, more effective systemic therapy should be explored.

Key Words: cervical cancer, periaortic nodal metastasis

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The survival outcome of patients with cervical cancer associated with periaortic lymph node metastasis is poor. Multiple retrospective series demonstrated 5-year survival rates of about 30% with radiation therapy (RT) alone.[1–4] The incidence of periaortic lymph node metastasis correlates with the clinical tumor stage. In the surgical staging study performed by the Gynecologic Oncology Group (GOG), the incidences of positive periaortic lymph nodes were 6%, 16%, and 25% for stage I, II, and III disease, respectively.[5] Periaortic node metastasis has been shown to be an independent prognostic factor for progression-free survival.[6] Some patients with their disease controlled in the pelvis will develop distant metastasis and will die of their disease.

Several randomized trials showed that the addition of cisplatin-based chemotherapy concurrent with RT resulted in improved disease control and survival in patients with cervical cancer without periaortic nodal metastasis.[7–11] In an attempt to improve the treatment outcomes, this approach has been used to treat patients with cervical cancer with positive periaortic nodes. The reported survival rates at 3 to 4 years from 2 national prospective studies were also about 30 to 39%.[12,13]

Here we attempt to review the treatment outcomes for patients with cervical cancer associated with positive periaortic lymph node treated with RT with or without chemotherapy in our institution.

MATERIALS AND METHODS

Patient Characteristics

From the database at Barbara Ann Karmanos Cancer Institute, 249 patients with a diagnosis of cervical cancer treated with curative RT in our department between 1988 and 2000 were identified. Twenty-two among the 249 patients were diagnosed with periaortic lymph node metastasis. One of them had small cell carcinoma and was excluded from the analysis. For the remaining 21 patients, 6 had the diagnosis of periaortic lymph node metastasis made based on computed tomography (CT) and 15 had a pathologic diagnosis. For the 6 patients who had a diagnosis of periaortic nodal metastasis made based on CT, all had unequivocal periaortic adenopathy, measuring 2.1 to 2.5 cm in maximum diameter. For the 15 patients who had a pathologic diagnosis, 7 underwent laparotomy and had radical hysterectomy for their stage IB

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disease abandoned because of the finding of periaortic nodal metastasis, which was not evident on preoperative CT; 8 with periaortic adenopathy suggestive of metastasis (defined as nodal disease 2 cm or smaller) underwent fine-needle aspiration biopsy (n = 6) or lymph node sampling (n = 2).

All the 21 patients were staged according to International Federation of Gynecology and Obstetrics (FIGO) staging system and had pathologic diagnosis of the primary tumor before treatment. Apart from CT of the abdomen and pelvis, work-up also included history and physical examination (including examination with patients under anesthesia), cystoscopy, or rectosigmoidoscopy as indicated, chest radiograph, laboratory tests including blood counts, and liver and renal function tests.

Nine and 12 patients were whites and African Americans, respectively. The median age was 44 years (range 30 to 67 years). Ten, 5, and 6 patients had FIGO stage IB, IIB, and IIIB disease, respectively. Eighteen and 3 patients had squamous cell carcinoma and adenocarcinoma carcinoma, respectively.

Treatment

Eleven patients received concomitant chemoradiation therapy (CRT) with cisplatin-based regimens, and 10 received RT alone. RT consisted of a combination of external beam RT and high dose rate intracavitary brachytherapy. The external beam RT was given utilizing megavoltage beams. Initially, patients received external beam RT to the "pan-handle" field encompassing the pelvis and the periaortic area using 15-MV photons and anterior–posterior parallel opposing pair technique. The superior border was generally the top of the first lumbar vertebra or 1 vertebra above the disease, and the inferior border was at the bottom of the obturator foramen. The lateral borders of the pelvic portion of the field were 1 to 2 cm lateral to the widest margin of the true pelvis; the lateral borders of the para-aortic portion of the field were placed at the transverse processes of the vertebrae. The parametrial and pelvic sidewall doses were supplemented by using anterior–posterior parallel opposing fields and a custom step-wedge block. The details of the step-wedge transmission blocks were described in our previous publication.[14] The daily dose given to this field was 150 to 180 cGy. The median doses delivered to the whole pelvis and the periaortic area were 4500 cGy (range 3420 to 5040 cGy) and 4500 cGy (range 4050 to 5040 cGy), respectively.

The intracavitary therapy was delivered utilizing a Selectron high dose rate (HDR) or a micro-Selectron HDR machine. Brachytherapy was given 3 times a week. The dose per fraction was 3.86 cGy. The rationale behind using this regimen was described in our previous publication.[14] The median number of HDR applications given was 8 (range 2 to 10). Combining the external beam RT and the intracavitary HDR brachytherapy, the total prescribed dose to point A was 80 to 85 Gy (low dose rate equivalent). The dose to point B was in general 55 to 60 Gy.

For the chemotherapy, cisplatin was given together with mitomycin-C every 3 weeks in 4 patients (cisplatin 50 mg/m^2, intravenous, days 1, 22, and 43; mitomycin-C 10 mg/m^2, intravenous, days 1 and 43), given alone weekly for 6 patients (cisplatin 40 mg/m^2, intravenous, weekly) and given together with 5-fluorouracil (5-FU) in 1 patient (cisplatin 75 mg/m^2, intravenous, days 1, 22, and 43; 5-FU 1000 mg/m^2/24 hours for 96 hours, continuous intravenous infusion, beginning on days 1, 22, and 43) during extended-field radiation therapy (EFRT). No maintenance chemotherapy was given.

Follow-up

After treatment, follow-up visits were scheduled at 1, 3, 6, 9, and 12 months, and every 3 to 6 months thereafter. At the start of RT, all patients were instructed to use a vaginal dilator to maintain the patency of the vaginal canal. History taking and physical examination were performed at the time of follow-up. A CT of the abdomen and pelvis was done every 3 months for the first year and every 6 months thereafter or when there was a suspicion of recurrence.

Statistical Methods and Endpoints

Kaplan-Meier analysis was used to determine the overall survival (OS), disease-specific survival (DSS), pelvic control (PC), pelvic and periaortic control (PPC), free-from distant metastasis (FFDM), and free-from recurrence (FFR). Log-rank test was used for the univariate analysis of different prognostic factors. Because of the small number of patients in the series, multivariate analysis was not performed. Crude rates were used to determine the complication rates.

OS was defined as no deaths from any cause. DSS was defined as no deaths as a result of cervical cancer. PC was defined as disease control in the pelvic area. PPC was defined as disease control in the pelvic and periaortic area; recurrence in the pelvic or para-aortic or both areas was coded as a failure; distant metastasis in other sites was not coded as a failure. Distant metastasis was defined as metastatic disease in sites other than the pelvic and para-aortic nodes. FFDM was defined as the absence of distant metastasis. FFR was defined as the absence of any kind of recurrence (pelvic, para-aortic, or distant).

RESULTS

Survival Outcomes

With mean and median follow-up times of 44 and 26 months (range 3 to 141 months), the 1- and 3-year OS and DSS for all patients were 76.2% and 50.5%, and 76.2% and 55.1%, respectively. The comparisons of OS and DSS between the CRT and the RT groups are shown in Table 1. There was no statistically significant difference in OS and

TABLE 1. Comparison of Survival Between the Two Groups

Group	No. of pts.	1-y OS (%)	3-y OS (%)	Med OS (mo)	1-y DSS (%)	3-y DSS (%)	Med DSS (mo)
Chemo-RT	11	81.8	71.6	64	81.8	81.8	90
RT	10	70	30	15	70	30	15
P value			0.41*			0.11*	

OS, overall survival;
Med OS, median overall survival; DSS, disease-specific survival;
Med DSS, median disease-specific survival; RT, radiation therapy.
*Log-rank test.

DSS between the CRT and the RT groups. Figure 1 shows the comparison of DSS between the 2 groups.

Disease Control

The 1- and 3-year PC, PPC, FFDM, and FFR for all patients were 84.6% and 76.1%, 79.3% and 71.3%, 80.4% and 68.8%, and 66.7% and 56.7%, respectively. The comparisons of PC, PPC, FFDM, and FFR between the CRT and the RT groups are shown in Table 2. There was a trend toward better PC for patients who underwent CRT ($P = 0.06$, log-rank test). The CRT group had statistically significantly better PPC than the RT group ($P = 0.03$, log-rank test) (Fig. 2). There was no statistically significant difference in FFDM (Fig. 3) and FFR between the CRT and the RT groups.

Prognostic Factors

On univariate analysis, stage (IB versus IIB/IIIB), use of concurrent chemotherapy (yes versus no), diagnostic method (CT versus pathologic), race (white versus black), and age (≤40 versus >40 years) did not predict DSS (Table 3).

Patterns of Failure

One of 11 patients (9%) who received concomitant chemoradiation and 5 of 10 patients (50%) who received RT alone developed recurrence in the pelvis or the periaortic area. Four of the 11 patients (36%) who received chemoradiation and 4 of 10 patients (40%) who received RT alone developed distant metastasis. All patients who developed distant metastases died of their disease eventually. Table 4 shows the patterns of failure.

Complications

The treatment was well tolerated by all patients. None (0%) of the 11 patients who received chemoradiation developed any grade 3 and 4 complications. Two of the 10 patients (20%) who received RT alone developed serious (grade 3 and

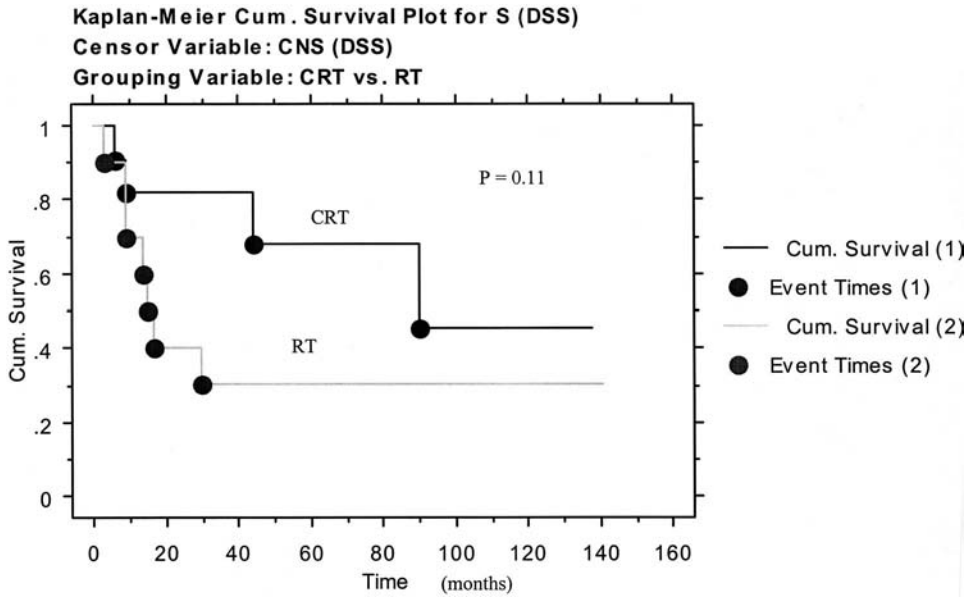

FIGURE 1. Comparison of disease-specific survival for patients who received chemoradiation therapy (CRT) (n = 11) and patients who received radiation therapy (RT) (n = 10). DSS, disease-specific survival.

TABLE 2. Comparison of Disease Control Between the Two Groups

	CRT (%)	RT (%)	*P* value
PC			
1-y	100	67.5	0.062*
3-y	100	50.6	
Median	NR	NR	
PPC			
1-y	100	56.3	0.03*
3-y	100	42.2	
Median	NR	28.5 m	
FFDM			
1-y	81.8	78.7	0.54*
3-y	81.8	49.2	
Median	88 m	23.5 m	
FFR			
1-y	81.8	50	0.10*
3-y	81.8	30	
Median	68 m	9.5 m	

m, months; PC, pelvic control; PPC, pelvic and periaortic control; FFDM, free-from distant metastases; FFR, free-from recurrence; CRT, chemoradiation; RT, radiation therapy; NR, not reached.
*Log-rank test.

4) complications. One patient developed rectal complication 11 months after the completion of the treatment. The other patient developed small bowel obstruction at 4 months after the completion of RT and underwent surgery for the resection of the segment of the small bowels. The same patient also developed ureteric obstruction 6 months later. Both of these patients had prior surgery for attempted radical hysterectomy that was abandoned because of finding pathologic involvement of periaortic lymph nodes.

DISCUSSION

The prognosis of patients with periaortic nodal metastasis from carcinoma of the cervix at initial presentation is poor. There have been several retrospective studies addressing this particular scenario. The survival rates at 5 years were reported to be on the range of 30%.[1–4] Grigsby et al reported a 3- and 5-year OS of 37% (estimated from the survival curve) and 32%, respectively for a cohort of 43 patients with periaortic nodal metastasis from cervical carcinoma treated with EFRT.[1] The median OS was 2.2 years. The cause-specific survivals at 3 and 5 years were 47% (estimated from the survival curve) and 47%. The median cause-specific survival was 2.7 years. There were no statistical differences in survival by clinical stage of disease. Forty percent (n = 17) of the patients developed distant metastasis with or without pelvic failure. There were no differences in the sites of failure by clinical stage of disease. Berman et al reported on a series of 98 patients treated with extended-field irradiation for the treatment of known periaortic nodal metastasis from cervical carcinoma. The median survival was reported to be 15.2 months. The 3-year survival for patients with stage IIB and IIIB disease was 25%.[5] The data suggested that the spread of cervical cancer is often orderly, which renders EFRT a potential curative treatment of patients with periaortic nodal metastasis from cervical cancer. However, the treatment outcome is still poor.

Five separate studies comparing cisplatin-based chemotherapy combined with concurrent RT and RT alone have shown consistent advantage to the use of concurrent chemoradiation therapy for cervical cancer without distant metastasis.[7–11] In 1999, the National Cancer Institute issued a rare clinical alert on this issue. Concurrent chemoradiation therapy is currently regarded as the standard of care for nonmetastatic cervical cancer. Cisplatin mainly acts as a radiosensitizer.

Because of the poor treatment outcome associated with RT alone for patients with periaortic nodal metastasis from cervical cancer, attempts were made to combine cisplatin-based chemotherapy with concurrent RT. Husseinzadeh et al reported the results of a phase 2 trial with 17 patients treated with EFRT combined with either concurrent cisplatin or cisplatin and 5-fluorouracil for periaortic nodal metastasis from cervical cancer.[15] All patients received 4 to 10 cycles of maintenance chemotherapy with cisplatin. Extended-field RT was delivered using megavoltage photons followed by 1 or 2 intracavitary cesium applications. At a median follow-up of 21 months, the median progression-free interval for all patients was 18 months. Patients with microscopic metastasis to periaortic nodes had a median progression-free interval of 26.5 months compared with 14 months in those with macroscopic para-aortic nodal metastasis. Seven of 17 patients (41%) were alive from 17 to 103 months. The median OS for the entire group was 21 months. The median OS for patients with microscopic and macroscopic nodal metastasis was 30 and 21 months, respectively. The 2- and 5-year OS for the entire group was 35 and 12%, respectively. The 2- and 5-year OS with microscopic metastasis to periaortic nodes were 50 and 12%, respectively, compared with survival of 22% at 2 years and 11% at 5 years, respectively, in those with macroscopic nodal metastasis. There was no significant difference between the use of concurrent cisplatin alone or cisplatin and 5-fluorouracil for local disease control. Apparently, maintenance chemotherapy with cisplatin did not significantly improve the 5-year survival. Distant metastases were the predominant sites of failure. The lack of survival benefit could be explained by the fact that single-agent cisplatin might not be an adequate systemic treatment of cervical cancer.

The GOG conducted a multicenter trial of chemoradiation therapy to evaluate the feasibility of extended-field radiation therapy with 5-fluorouracil (5-FU) and cisplatin,

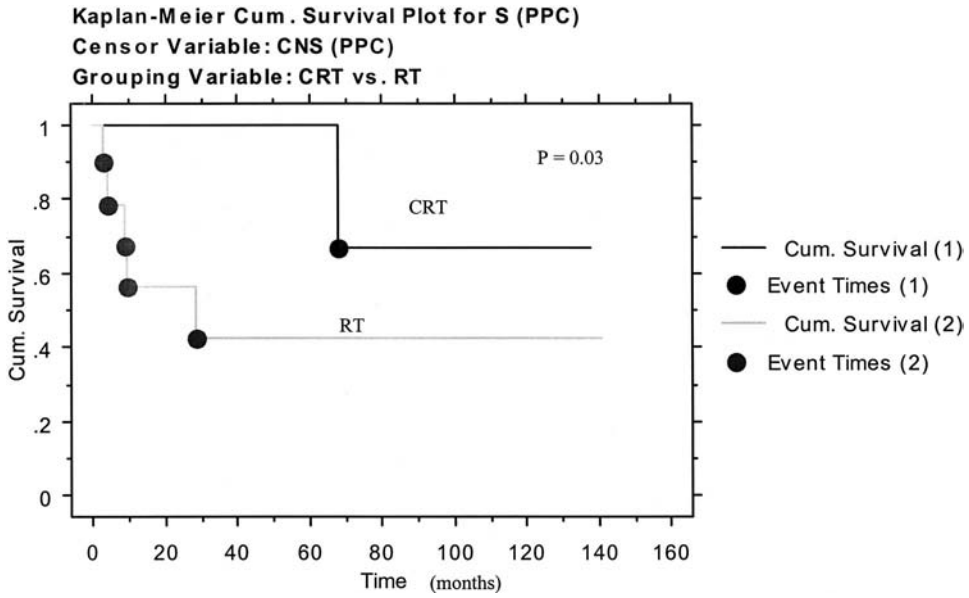

FIGURE 2. Comparison of pelvic and para-aortic control for patients who received chemoradiation therapy (CRT) (n = 11) and patients who received radiation therapy (RT) (n = 10). PPC, periaortic control rates.

and to determine the treatment outcomes in patients with biopsy-confirmed periaortic node metastases from cervical carcinoma.[13] Ninety-five patients with cervical carcinoma and periaortic nodal metastasis were enrolled, of whom 86 were evaluable (14 patients with stage I, 40 with stage II, 27 with stage III, and 5 with stage IVA). External beam RT doses were 4500 cGy to the periaortic area and 3960 to 4860 cGy to the pelvis, depending on the stage of the disease. The intracavitary doses to point A were 4000 cGy for stages IB/IIB disease and 3000 cGy for stages IIIB/IVA disease. The doses to point B doses were raised to 6000 cGy with parametrial boost. Concomitant chemotherapy with 5-FU 1000 mg/m^2/d for 96 hours and cisplatin 50 mg/m^2 was given in weeks 1 and 5. Systemic chemotherapy was not given after the completion of concurrent chemoradiation therapy; 98.9% and 90% of the patients completed RT and both courses of

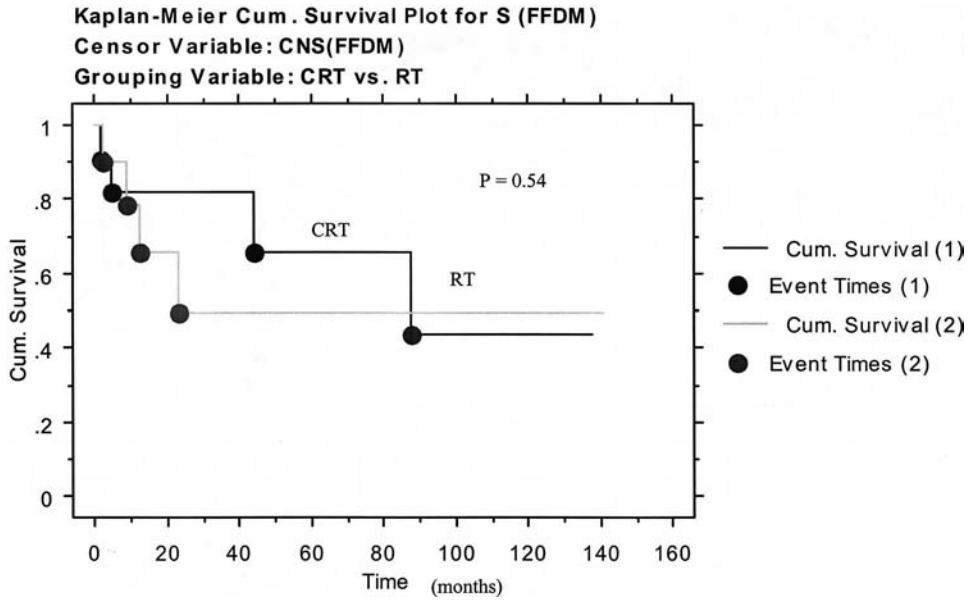

FIGURE 3. Comparison of free-from distant metastasis (FFDM) for patients who received chemoradiation therapy (CRT) (n = 11) and patients who received radiation therapy (RT) (n = 10).

TABLE 3. Univariate Analysis of Different Factors Predicting DSS

Factors	No.	Univariate Analyses 1-y DSS (%)	3-y DSS (%)	*P* Value
FIGO stage				
IB	10	90	67.5	0.43*
IIB/IIIB	11	63.6	43.6	
Chemotherapy				
Yes	11	81.8	81.8	0.11*
No	10	70	30	
Diagnostic method				
CT	6	50	33.3	0.39*
Pathologic	15	86.7	63.2	
Race				
White	9	88.9	47.6	0.52*
Black	12	66.7	58.3	
Age				
≤40 y	12	83.3	63.5	0.36*
>40 y	9	66.7	44.4	

DSS, disease-specific survival; CT, computerized tomography; FIGO, International Federation of Gynecology and Obstetrics.
*Log-rank test.

chemotherapy, respectively. The main grade 3–4 acute toxicities were gastrointestinal (18.6%) and hematologic (15.1%). Overall, 41.9% of the patients developed distant metastasis with or without pelvic failure, and 31.4% of the patients developed pelvic failure with or without distant metastasis. The 3-year OS and progression-free interval were 39% and 34%, respectively, for all 86 patients. The 3-year OS for stages I, II, and III/IVA were 50%, 39%, and 38%, respectively. The authors concluded that EFRT with 5-fluorouracil and cisplatin chemotherapy was feasible in the setting of a multicenter clinical trial and suggested that a proportion of patients could achieve control of advanced pelvic disease and that not all patients with periaortic nodal metastases had systemic disease. This is not surprising because carcinoma of the cervix metastasizes in a predictable pattern, with tumor usually spreading from the primary cervical tumor to the pelvic nodes, para-aortic nodes, and left supraclavicular nodes, and then ultimately to nonnodal distant sites (hematogenous spread).

TABLE 4. Patterns of Failure

	Number of Patients		
	ChemoRT	RT	Total
All patients	11	10	21
NED	7	3	10
All recurrences	4	7	11
Pelvis only	0	2	2
PAN only	0	1	1
Pelvis + DM	0	1	1
Pelvis + PAN + DM	1	1	2
DM only	3	2	5

RT, radiation therapy; NED, no evidence of disease; PAN, periaortic nodes; DM, distant metastases (apart from periaortic nodal metastasis).

The observations of the aforementioned 2 trials were similar to the findings of our study. Distant metastasis remains the major problem apart from the pelvic or pelvic/periaortic control. In our series of patient, there was a trend toward better pelvic control with the use of concurrent cisplatin-based chemotherapy, and the pelvic and periaortic control was significantly improved with the addition of concurrent cisplatin-based chemotherapy to EFRT. However, the distant metastasis rates were not significantly different between the chemoradiation group (36%) and the RT group (40%). One interesting point of note was that the stage of disease, which would predict the survival of patients with cervical cancer without para-aortic node metastasis, did not impact on the disease-specific survival in our series. This may be explained in part by the fact that occult metastasis that could not be detected by conventional diagnostic studies might be present in some patients, thus limiting the impact of improved pelvic and periaortic control on survival. The patterns of failure in our study suggested this hypothesis. For the 11 patients who underwent CRT, 10 (91%) had their pelvic and periaortic disease controlled, whereas 4 (36%) developed distant metastasis, among which 3 (75%) had controlled pelvic and periaortic disease; for the 10 patients who underwent RT alone, 5 (50%) had their pelvic and periaortic disease controlled, whereas 4 (40%) developed distant metastasis, among whom 2 (50%) had controlled pelvic and periaortic disease. All the patients in our series who developed distant metastasis eventually died of their disease. Therefore, to improve the survival of these patients, it is reasonable to consider systemic chemotherapy with more effective agents for the treatment of the occult metastatic disease.

The toxicity of EFRT combined with concurrent chemotherapy has been a concern. The toxicity of EFRT alone was reported to be about 5 to 50%.[1–3,16–19] In the Radiation Therapy and Oncology Group (RTOG) 7920 trial, prophylactic RT to the periaortic area resulted in an overall small bowel toxicity rate of 6%.[16] Patients who had undergone abdominal surgery had a higher rate of severe small bowel complication (11%) compared with those who did not have abdominal surgery (2%). Grigsby et al reported a 5% rate of severe complication.[1] Nori et al reported a 0% severe bowel toxicity rate in 31 patients, all of whom underwent a retro-

peritoneal surgical staging procedure.[2] Crawford et al reported no severe complications in 29 patients who did not undergo laparotomy before EFRT.[17] However, other series reported much higher rates of severe complications (20 to 50%).[3,18,19] When concurrent chemotherapy is added to EFRT, the toxicity will be expected to be higher compared with RT alone. In the GOG multicenter trial (as discussed above), 18.6% and 15.1% of the patients developed GOG grade 3–4 acute gastrointestinal and hematologic toxicities. The 4-year late morbidity actuarial risk was 14%, and most of the complications involved the rectum; 66.3% and 16.3% of the patients underwent retroperitoneal and transperitoneal surgical staging, respectively.[13] In the RTOG 9210 trial, twice-daily radiation doses of 1.2 Gy to the pelvis and para-aortic lymph nodes at 4- to 6-hour intervals, 5 days per week were given to 30 patients with cervical cancer with biopsy-proven positive para-aortic lymph nodes. The total external radiation doses were 24 to 48 Gy to the whole pelvis, 12 to 36 Gy parametrial boost, and 48 Gy to the periaortic region with an additional boost to a total dose of 54 to 58 Gy to the para-aortic nodal metastasis. One or 2 intracavitary implants were performed to deliver a minimum total dose of 85 Gy to point A. Chemotherapy consisted of cisplatin (75 mg/m^2; days 1, 22, and 43) and 5-fluorouracil (1,000 mg/m^2/24 hours × 96 hours, beginning on days 1, 22, and 43) for 2 or 3 cycles. The rates of grades 1, 2, 3, and 4 acute toxicity from chemotherapy were 3%, 17%, 48%, and 28%, respectively. The rates of grades 1, 2, 3, and 4 acute toxicity from RT were 7%, 34%, 21%, and 28%, respectively. The rates of grades 1, 2, 3, and 4 late toxicity were 10%, 17%, 7%, and 17%, respectively. Grade 5 acute toxicity occurred in 1 patient during the course of therapy, but none had a late grade 5 toxicity. The OS rates were 46% at 2 years and 29% at 4 years. The probability of local–regional failure was 40% at 1 year and 50% at 2 and 3 years. The probability of disease failure at any site was 46% at 1 year, 60% at 2 years, and 63% at 3 years.[12] The group concluded that twice-daily external irradiation to the pelvis and lumbar periaortic region with brachytherapy and concurrent chemotherapy resulted in an unacceptably high rate of grade 4 late toxicity without any obvious survival benefit compared with anecdotal data. The number of patients who underwent surgical staging was not mentioned. In our study, none of the 11 patients who received concurrent cisplatin-based chemotherapy combined with EFRT developed grade 3/4 complications compared with 20% (2 of 10 patients) of the patients who received EFRT alone. In the CRT and RT groups, 36.3% (n = 4) and 30% (n = 3) of the patients, respectively, underwent laparotomy and had their radical hysterectomy abandoned because of the finding of the positive periaortic lymph node. Both patients who developed grade 3/4 complications underwent laparotomy, and 1 of them had a severe small bowel complication. We have used daily fractions of 150 to 180 cGy for the EFRT. Apparently, EFRT with concurrent cisplatin-based chemotherapy was no more toxic than EFRT alone with the use of a daily radiation dose of 150 to 180 cGy.

In summary, concurrent chemoradiation therapy with cisplatin-based chemotherapy appears to improve pelvic and periaortic control for patients with cervical carcinoma with periaortic nodal metastasis and should be considered for treatment of these patients, because local and regional disease control is also important to the quality of life of these patients. Because of the same high rate of distant metastasis despite a much better pelvic and periaortic control as seen in patients who received CRT compared with patients who received RT alone in our series, the addition of adjuvant chemotherapy with more effective agents should be explored. The high rate of distant metastasis (DM) is the impedance to better survival, because all patients who develop DM will eventually die.

However, this is a retrospective study with a small number of patients, and the follow-up was relatively short. Furthermore, the chemotherapy given was variable (weekly cisplatin, 3-weekly cisplatin and 5-FU, or 3-weekly cisplatin and mitomycin-C). The question of whether CRT is truly better than RT alone is best answered in a phase III randomized trial comparing CRT with RT alone. Maintenance systemic chemotherapy should be incorporated in the treatment regimen to sterilize any occult metastasis that might be present.

CONCLUSION

Cervical cancer with periaortic metastasis is a potentially curable disease, though the treatment outcome is poor overall. The addition of concurrent cisplatin-based chemotherapy to EFRT for this subset of patients appeared to improve the pelvic and periaortic control but not the rate of distant metastasis and survival. The addition of concomitant chemotherapy to EFRT did not seem to increase the grade 3 and 4 toxicity compared with EFRT alone in our series. Because of the high rate of distant metastasis even when pelvic and periaortic control was achieved, the use of effective maintenance systemic therapy should be explored to improve the survival outcome.

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