International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Clinical Investigation: Gynecologic Cancer

Curative Chemoradiotherapy in Patients With Stage IVB Cervical Cancer Presenting With Paraortic and Left Supraclavicular Lymph Node Metastases

Ji-Yoon Kim, MD,[*] Joo-Young Kim, MD, PhD,[†] Jin Hee Kim, MD, PhD,[‡] Mee Sun Yoon, MD,[§] Juree Kim, MD, PhD,[‖] and Young Seok Kim, MD[¶]

[*]Department of Radiation Oncology, The Catholic University of Korea, College of Medicine, Seoul, Republic of Korea; [†]Research Institute and Hospital, National Cancer Center, Goyang, Republic of Korea; [‡]Department of Radiation Oncology, Dongsan Medical Center, Keimyung University School of Medicine, Daegu, Republic of Korea; [§]Department of Radiation Oncology, Chonnam National University Hwasun Hospital, Chonnam National University Medical School, Jeollanam-do, Republic of Korea; [‖]Department of Radiation Oncology, Cheil General Hospital and Women's Healthcare Center, Kwandong University, College of Medicine, Seoul, Republic of Korea; and [¶]Department of Radiation Oncology, Asan Medical Center, University of Ulsan, College of Medicine, Seoul, Republic of Korea

Received Sep 21, 2011, and in revised form Jan 13, 2012. Accepted for publication Jan 22, 2012

Summary

To evaluate the efficacy and toxicity of concurrent chemoradiotherapy, the authors reviewed the clinical data of 25 patients with cervical cancer initially presenting with paraortic and left supraclavicular lymph node metastases. Acute grade 3-4 hematologic toxicity was observed in 16 women. Complete response was observed in 13 patients and 3-year overall survival rate was 49%. These findings indicate that concomitant chemoradiotherapy is feasible in patients with

Purpose: To evaluate the efficacy and toxicity of concurrent chemoradiotherapy (CCRT) with curative intent in patients with stage IVB cervical cancer initially presenting with paraortic and left supraclavicular lymph node metastases.

Methods and Materials: The medical records of 25 patients with both paraortic and left supraclavicular lymph nodal metastases (group I) were reviewed and compared with those of 101 women with paraortic lymph node metastases alone (group II). Group I received a mean 59.4 Gy to the paraortic and left supraclavicular areas and 50.4 Gy to the pelvis, followed by 30 Gy of high-dose-rate brachytherapy in 6 fractions. Group II received the same dose to the paraortic area and pelvis followed by intracavitary brachytherapy. All patients received platinum-based chemotherapy simultaneously.

Results: Of the 25 patients in group I, 16 (64%) experienced acute grade 3-4 hematologic toxicities, and 1 had a late grade 3 genitourinary toxicity. Complete responses, including the primary mass and pelvic, paraortic, and left supraclavicular lymph nodes, were observed in 13 patients (52%). At a median follow-up of 32 months for surviving patients, 3 experienced in-field failure, 6 showed distant failure, and 9 showed both. The 3-year overall and disease-free survival rates were 49% and 33%, respectively. In comparison, of the 101 patients in group II, 16 showed in-field failure, 14 experienced distant failure, and 11 showed both. The 3-year overall and disease-free survival rates were 69% and 57%, respectively.

Conclusions: Curative CCRT is feasible in patients with stage IVB cervical cancer presenting with paraortic and left supraclavicular lymph nodal metastases, with acceptable late toxicity and high response rates, despite high rates of acute hematologic toxicity.

Reprint requests to: Young Seok Kim, MD, Department of Radiation Oncology, Asan Medical Center, University of Ulsan, College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul, Republic of Korea. Tel: +82 2 3010 5614; Fax: +82 2 3010 6950 E-mail: ysk@amc.seoul.kr

Acknowledgment—This work is supported by grant no. 1110540 and NCC 1010100-3 from National Cancer Center, Goyang, Republic of Korea.

Int J Radiation Oncol Biol Phys, Vol. 84, No. 3, pp. 741–747, 2012
0360-3016/$ - see front matter
doi:10.1016/j.ijrobp.2012.01.070

distant lymph node metastases, even in left supraclavicular nodes.

Keywords: Uterine cervical cancer, Radiotherapy, Chemotherapy, Lymph node metastasis, Prognosis

Introduction

The staging system of the International Federation of Gynecology and Obstetrics (FIGO) for uterine cervical cancer has classified patients with distant lymph node (LN) involvement, including the paraortic LN (PALN) and left supraclavicular LN (SCLN), as stage IVB. Patients with stage IVB cervical cancer have a 5-year survival rate of only 9% (1) and are usually considered candidates for systemic chemotherapy or are treated with palliative radiotherapy for specific symptom control. A recent phase III trial of cisplatin-based doublet combination chemotherapy in patients with stage IVB, recurrent, or persistent cervical cancer yielded disappointing results, with a response rate of 22%-36% and a median survival time of 9.7-12.8 months (2, 3). Patients initially diagnosed with FIGO stage IVB cervical cancer include those with distant nodal metastases or metastases to other hematogenous visceral organs. Although considered beyond the indications for curative radiation therapy, patients with limited distant nodal metastases, such as those to the PALN and/or left SCLN, may be candidates for radiotherapy with curative intent by extending the radiation field.

Because of advances in radiotherapy techniques, curative doses of extended-field radiotherapy (EFRT) and concurrent chemotherapy can be safely delivered to patients with FIGO IVB cervical cancer presenting with only PALN metastasis, using 3-dimensional conformal radiotherapy (3D CRT) or intensity-modulated radiotherapy (IMRT). Increasing the radiation dose to the involved paraortic area to 55-60 Gy, plus concurrent chemotherapy, resulted in acute grade 3-4 gastrointestinal toxicity rates of 9%-11% (4-6). Of these patients, 85%-100% completed their planned treatment, and the 5-year overall survival (OS) rate was 47%-77% (4-6). In contrast to the established role of the extended-field concurrent chemoradiotherapy (CCRT) in patients with cervical cancer involving PALN metastases, its role in patients with both PALN and SCLN metastases remains undefined. We therefore performed this retrospective analysis (*1*) to evaluate the efficacy and toxicity of CCRT in patients presenting with cervical cancer and pelvic, PALN and SCLN metastases and (*2*) to compare these findings with those in patients with PALN without SCLN metastases who received extended-field CCRT.

Methods and Materials

Patients

The records of patients with carcinoma of the cervix treated at four institutions in Korea from 1998-2010 were retrospectively evaluated. Patients were included if they had biopsy-proven carcinoma of the cervix with evidence of PALN and left SCLN metastases on imaging or surgical sampling at initial diagnosis and received CCRT with curative intent. Patients were excluded from this analysis if they had histologic evidence of small cell or clear cell carcinoma, distant metastases other than PALN or left SCLN, had received radiotherapy alone, or had received sequential chemoradiation treatment. To compare the efficacy and toxicity of chemoradiotherapy in patients with PALN and SCLN metastases (group I, $n = 25$), we also collected the records of women with PALN but without SCLN metastases (group II, $n = 101$).

All patients underwent physical and pelvic examinations, routine laboratory testing, chest radiography, intravenous pyelography, cystoscopy, sigmoidoscopy, and magnetic resonance imaging (MRI) or positron emission tomography-computed tomography (PET-CT). Any PALN or SCLN showing discrepancies on MRI and PET-CT was investigated surgically.

Treatment

Before radiation treatment, all patients underwent CT simulation using intravenous contrast agents. The abdomino-pelvic field encompasses a volume that included the primary mass, the entire uterus, the paracervical, parametrial, and uterosacral regions; and the external iliac, hypogastric, obturator, and paraortic LNs. The superior border of the abdomino-pelvic field was usually the T12-L1 interface, but was adjusted based on the position of the positive PALNs. The left supraclavicular field encompassed the positive SCLNs and supraclavicular lymphatics. The median daily fraction of EBRT was 1.8 Gy (range, 1.5-2.0 Gy), administered once daily, 5 times per week using 3D CRT ($n = 25$ in group I, $n = 94$ in group II) or IMRT with a linear accelerator or a helical tomotherapy machine. Proton therapy was included as a boost for 1 patient in group II. All patients received median doses of 59.4 Gy to the PALN and 50.4 Gy to the entire pelvis, and patients in group I also received a median dose of 59.4 Gy to the left SCLN region simultaneously. At the end of external beam radiation therapy (EBRT), high-dose-rate intracavitary brachytherapy was administered with Fletcher-Suit after-loading applicators. Six to seven fractions of 4-5 Gy were delivered to point A, twice or three times per week, with no EBRT treatment on the same day of brachytherapy. Parametrial boosts were integrated between brachytherapy sessions.

All patients were prescribed platinum-based chemotherapy, as determined by each physician, concurrently with EBRT. Chemotherapy regimens included cisplatin weekly ($n = 11$ in group I, $n = 76$ in group II); fluorouracil plus cisplatin monthly ($n = 8$ in group I, $n = 14$ in group II); paclitaxel plus cisplatin at 3-week intervals ($n = 6$ in group I, $n = 9$ in group II); and paclitaxel plus carboplatin at 3-week intervals ($n = 2$ in group II).

Follow-up and statistical analysis

During treatment, patients were evaluated weekly for toxicity and tumor response. After completion of therapy, patients were evaluated 1 month after the completion of chemoradiotherapy, every 3 months for the next 2 years, every 6 months for 3 years, and yearly thereafter. History taking and pelvic examination were