The role of radiotherapy for patients presenting with disseminated cervical cancer at initial diagnosis

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The role of radiotherapy for patients presenting with disseminated cervical cancer at initial diagnosis

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<Abstract>

The role of radiotherapy for patients presenting with disseminated cervical cancer at initial diagnosis

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Purpose: The objective of this study was to clarify the role of radiotherapy (RT) for patients presenting with disseminated cervical cancer at initial diagnosis.

Patients and Methods: We retrospectively analyzed 77 patients diagnosed with disseminated cervical cancer between September 1980 and August 2012. All patients received external beam RT to the pelvis (median dose 45 Gy) and 60 patients (77.9%) treated with high dose rate brachytherapy (median dose 30 Gy). Sixty-four patients

(83.1%) received chemotherapy and 12 patients (15.6%) underwent radical surgery including hysterectomy. We divided into two groups; 58 patients had distant lymph node metastasis only or peritoneal seeding without visceral organ metastasis (group A), 19 patients had visceral organ metastasis (group B).

Results: Median follow-up time was 55 months (range, 15 to 296 months). The 5-year pelvic control rates (PCR), progression free survival (PFS), and overall survival (OS) were 83.7%, 25.1%, and 31.7%, respectively. On univariate analysis, OS rate of the group A were significantly better than that of group B (38.9% vs. 10.5%, P = .001). Multivariate analysis indicated that group B was the only significant independent prognostic factor for PFS and OS. Five-year PCR of group A and B were 82.6% and 89.5%, respectively.

Conclusion: Our data suggests definitive RT be beneficial to disseminated cervical cancer patients without visceral organ metastasis. External beam pelvic RT alone might be considered to palliate symptom and delay pelvic progression in patients with visceral organ metastasis who are expected to have poor prognosis and need systemic chemotherapy.

Keywords : disseminated cervical cancer; visceral organ metastasis; radiotherapy; chemotherapy; survival

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I. INTRODUCTION

International Federation of Gynecology and Obstetrics (FIGO) stage IVB includes either the distant nodal metastases or hematogenous visceral organs metastases. However, this substage has caused confusion to clinician, because the definition of distant node is vague.

Peritoneal seeding is now increasingly being diagnosed as incidental findings due to the development of diagnostic technologies such as the positron

emission tomography-computed tomography (PET-CT), etc. Such disseminated cervical cancer patients tend to show very poor prognosis.[1] But, it is still true that there is no consensus reached regarding the management of the disseminated cervical cancer due to its rarity. The treatment of patients with disseminated cervical cancer varies according to the disease characteristics or the patient's symptoms, or the physician's preference. So far, systemic chemotherapy (CTx) or palliative radiotherapy (RT) for pain, bleeding or discomfort is usually considered for these patients.[2-6] However, little is known about how to combine RT with CTx effectively.

Recently, some reports suggest that concurrent chemoradiotherapy (CCRT) could increase survival in cervical cancer patients with supraclavicular lymph node (SCLN) involvement.[7-9] Other studies found that the use of RT and CTx in patients with stage IVB cervical carcinoma with a curative aim may increase survival.[10-12] The type of metastasis were associated with prolonged survival in patients with disseminated cervical cancer.[13]

The purpose of this study is to retrospectively review the treatment result of the disseminated cervical cancer including FIGO stage IVB including peritoneal seeding and investigate the role of RT in these patient populations.

II. MATERIALS AND METHODS

We retrospectively reviewed the medical records of patients initially diagnosed as disseminated cervical cancers between September, 1980 and August,

2012 at Yonsei Cancer Center, Yonsei University Health System, Seoul, South Korea. The present study includes pathologically proven uterine cervical cancer treated with external beam radiation therapy (EBRT) to the pelvis (radiation dose of ≥ 40 Gy). We defined the disseminated cervical cancer as follows: evidence of distant lymph node (LN) (e.g. supraclavicular, mediastinal, axillary LNs) metastasis, hematogenous metastases to visceral organ, malignant peritoneal cytology, or peritoneal seeding. The diagnosis of disseminated cervical cancer was based on physical examination, diagnostic imaging studies or pathologic findings from biopsy or surgery. Patients who presented with only para-aortic lymph node (PALN) metastasis or recurrent disease were excluded from this study.

The histological classification of uterine cervical cancer was based on the World Health Organization (Geneva, Switzerland) classifications. The clinical staging was grounded on the FIGO stage classifications. The routine procedure for staging included a detailed history, physical examination, laboratory tests, standard chest radiographs, intravenous pyelography, cystoscopy, and sigmoidoscopy. Optional studies (e.g. computed tomography (CT), magnetic resonance imaging (MRI), PET or PET-CT, bone scan) are performed to evaluate the disease extent.

EBRT was delivered to true pelvis, whole pelvis (WP), WP plus lower PALN, or extended-field through the antero-posterior/postero-anterior portals or four-field box technique using megavoltage photon beams using ^{60}Co units or linear accelerators. The superior border of the WP, WP plus lower PALN, and extended-field were usually L4-L5, L2-3, and T11-T12 interfaces, respectively. The daily fraction of EBRT was 1.8 or 2.0 Gy administered once daily for 5 days each week. Selective midline block was done according to treatment response. High–dose rate (HDR) intracavitary

brachytherapy was delivered via a remote afterloading system. From 1979 to 1989, patients were treated with the Ralstron 303 (Shimadzu, Kyoto, Japan), utilizing ^{60}Co source, 3 times per week at 3 Gy per fraction. The GammaMed II (Sauerwein, Haan, Germany) with ^{192}Ir was applied at 5 Gy per fraction to a total dose of 30 Gy since 1989. Applicator insertion was done on an outpatient basis without anesthesia, and each treatment time was required approximately 10 to 15 minutes. Parametrial or pelvic side wall or node boost with central shielding was administered for patients with persistent parametrial disease after planned pelvic RT or between brachytherapy sessions. EBRT to metastatic site was administered concurrently with pelvic RT.

CTx was determined depending on patients' performance and physician's discretion. CTx was combined with RT through various schedules as followings; CCRT with maintenance chemotherapy or CCRT alone, induction CTx followed by RT, induction CTx followed by CCRT, surgery followed by sequencial CTx combined RTx or CCRT, surgery after neoadjuvant CTx followed by sequencial CTx combined RTx. CTx regimens included cisplatin weekly, carboplatin weekly, fluorouracil plus cisplatin or carboplatin at 3-week intervals, paclitaxel plus carboplatin at 3-week intervals, and other regimens.

Laparotomy was done for patients with clinical FIGO stage I to II and then those patients had pathologically confirmed ovarian metastasis, malignant peritoneal cytology or gross peritoneal seeding nodules. Depending on the decision by physician, adjuvant hysterectomy was performed for 2 patients after neoadjuvant treatment.

During RTx, patients were assessed weekly for tumor response. After completion of the therapy, patients were evaluated 1 month after the completion of RT,

every 3 months during the second year, and then every 6 months afterwards.

Recurrences in the cervix, vagina, parametrium, or pelvic LNs were defined as pelvic failure. Systemic progression was defined as new appearance of disease in the visceral organ, distant LNs or peritoneal seeding except original disseminated sites. Overall survival (OS) was calculated from the date of diagnosis to the date of death or date of last visit. An event for progression free survival (PFS) was the first reported occurrence of tumor progression or death. The time to first recurrence event was measured from the date of the diagnosis to the date of the recurrence. The Kaplan-Meier method was used to estimate OS, PFS, and pelvic control rate (PCR). Univariate analysis evaluating the associated risk factors was performed by comparing the survival rates were compared using the log-rank test. Multivariate analyses were evaluated using a Cox proportional hazards model and hazard ratio (HR) and 95% confidence interval (CI) to identify prognostic factors. *P* Values < .05 indicated statistical significance.

III. RESULTS

1. Patient characteristics

Seventy-seven patients were selected for the present study. Patient characteristics are listed in Table 1. The median age was 51 year (range, 22–77). Squamous cell carcinoma was the most common histologic subtype (62 patients,

80.5%). Twenty-four patients (31.2%) had a hemoglobin level less than 10 (g/dL) before treatment and 50 patients (64.9%) had tumors measuring more than 5 cm in diameter. The FIGO stage of primary cervical tumor; 11 patients (14.3%), 38 patients (49.3%), 15 patients (24.7%), and 9 patients (11.7%) corresponded to FIGO I-IIa, IIb, III, IVa, respectively.

Table 1. Patient Characteristics

Characteristic	No. of patients (%)
Age (year)	
Median	51
Range	22-77
ECOG performance status	
0-1	71 (92.2)
2-3	6 (7.8)
Histopathologic type	
Squamous cell carcinoma	62 (80.5)
Adenocarcinoma	7 (9.1)
Small cell carcinoma	5 (6.5)
Adenosquamous cell carcinoma	3 (3.9)
Pre-treatment Hb (g/dL)	
≤ 10	24 (31.2)
> 10	53 (68.8)
Tumor size (cm)	

< 5	27 (35.1)
≥ 5	50 (64.9)
FIGO stage of primary cervical tumor	
I-IIa	11 (14.3)
IIb	38 (49.3)
III	19 (24.7)
IVa	9 (11.7)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; Hb = hemoglobin; International Federation of Gynecology and Obstetrics = FIGO.

Treatment profiles are listed in Table 2. Patients had received CCRT with or without maintenance CTx in 40 (51.9%), induction CTx followed by RT or CCRT in 13 (16.9%), RT alone in 12 (15.6%), laparotomy with preoperative or postoperative RT (with or without CTx) in 12 (15.6%). CTx was done in 64 patients (83.1%), and the most common CTx regimens was weekly cisplatin CTx. EBRT covered the WP in 28 (36.4%), and extended field in 42 patients (54.5%). Median external dose to the pelvis was 45 Gy (range, 41.4 to 54 Gy). Sixty patients (77.9%) were treated with HDR brachytherapy, and median intracavitary irradiation dose was 30 Gy. Total dose delivered to point A ranged from 45 to 91 Gy (median, 69 Gy).

Table 2. Treatment Profile

Characteristic	Median (range)/no. of patients (%)
Treatment type	
CCRT +/- maintenance CTx	40 (51.9)
Induction CTx + RT or CCRT	13 (16.9)
RT alone	12 (15.6)
Laparotomy with preop or postop RT (+/- CTx)	12 (15.6)
CTx	
No	13 (16.9)
Yes	64 (83.1)
CTx regimen	
Weekly cisplatin	22 (28.6)
5-FU/cisplatin	8 (10.4)
Paclitaxel/carboplatin	8 (10.4)
Weekly carboplatin	7 (9.1)
5-FU/carboplatin	7 (9.1)
Others	12 (15.6)
RT field	
True pelvis	1 (1.3)
Whole pelvis	28 (36.4)
Whole pelvis + lower PALN	6 (7.8)
Extended	42 (54.5)

ICR	
No	17 (22.1)
Yes	60 (77.9)
RT dose (Gy)	
External dose	45 (41.4-54.0)
ICR dose	30 (2.5-39.0)
Point A dose	69 (45.0-91.0)

Abbreviations: CCRT = concurrent chemoradiotherapy; CTx = chemotherapy; RT = radiotherapy; Preop = preoperative; Postop = postoperative; 5-FU = 5-fluorouracil; PALN = para-aortic lymph node; ICR = intracavitary radiotherapy.

Distribution of disseminated cervical cancer is shown in Figure 1. Forty-one patients (53.2%) had distant LNs metastasis only, and 19 patients (24.7%) had visceral organ metastasis regardless of metastasis to distant LNs or peritoneal seeding. Peritoneal seeding without visceral organ metastasis was found in 17 patients (22.1%); malignant peritoneal cytology and/or ovary metastasis in 10 patients, and clinically diagnosed peritoneal seeding nodules with PET-CT in 7 patients. Localized seeding nodules in the pelvic cavity or within one quadrant of the abdomen was identified by PET-CT in 6 of 7 patients.

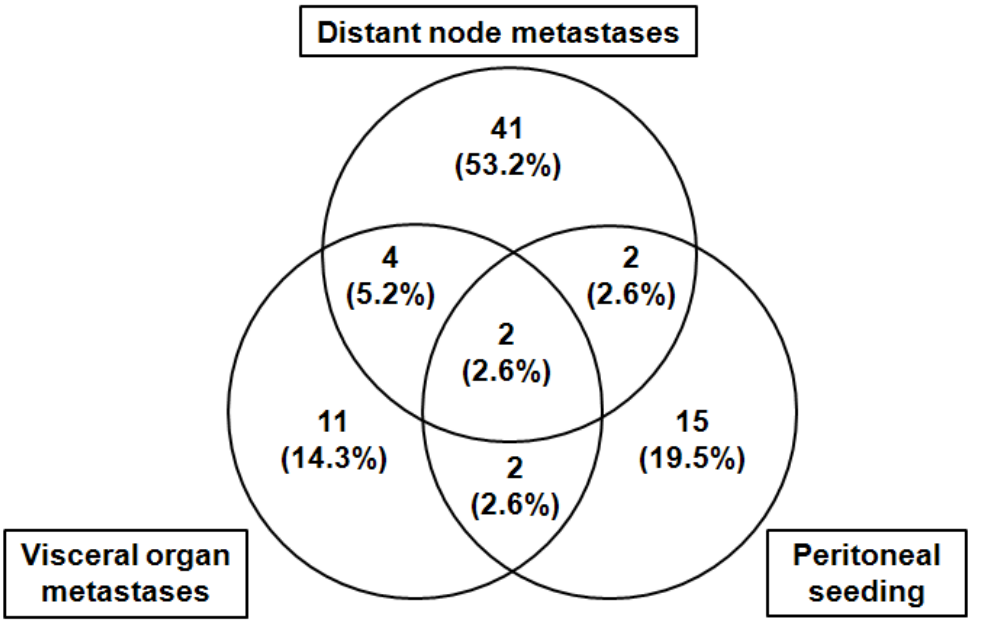

Fig. 1. Venn diagram showing the distribution of disseminated cervical cancer.

2. Patterns of failure

The median follow-up time of the surviving patients was 55 months (range, 15 to 296 months). The site of first recurrence was evaluated in all patients over the entire follow-up period. There were a total of 55 failures in 77 patients (71.4%), and systemic progression was the dominant type of failure. Pelvic recurrences were the first event in 11 patients (14.3%), and systemic progression occurred first in 51 patients (66.2%). Seven patients had both locoregional relapse and systemic progression.

3. Survival and prognostic factors

Twenty-six of 77 patients (33.8%) survived at least until the end of the follow-up period. The median PFS and OS time was 9 and 22 months respectively (Figure. 2). The 5-year PCR, PFS, and OS were 83.7%, 25.1%, and 31.7%, respectively.

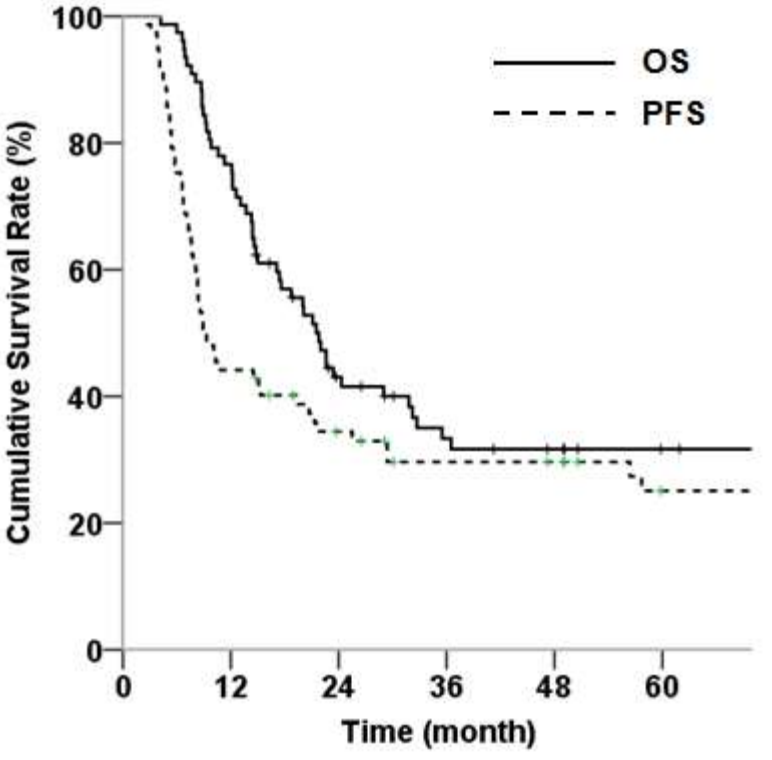

Fig. 2. Progression free survival and overall survival rates for all 77 patients.

Univariate analysis was performed to identify the significant prognostic factors of PCR, PFS, and OS (Table 3). The univariate analysis showed that tumor size more than 5 cm and visceral organ metastasis were independent prognostic factors for PFS and OS ($P < .05$). FIGO stage of primary cervical tumor was the significant prognostic factor for PCR and OS ($P < .05$). Pre-treatment Hb level of at least 10 (g/dL) was the significant prognostic factor for PFS ($P < .05$).

Table 3. Univariate Analysis of Prognostic Factors

Prognostic factor	Group	No. of patients	*P*		
			PCR	PFS	OS
Age (y)	≤ 50	38	NS	NS	NS
	> 50	39			
Performance status	0-1	71	NS	NS	NS
	2-3	6			
Pathology	SCCa	62	NS	NS	NS
	non-SCCa	15			
Pre-treatment Hb (g/dL)	≤ 10	24	NS	.028	NS
	> 10	53			
FIGO stage of primary cervical tumor	I-II	49	.016	NS	.010
	III-IVA	28			
Tumor size (cm)	< 5	27	NS	.005	.005
	≥ 5	50			
Point A dose (Gy)	≤ 66	37	NS	NS	NS

	> 66	40			
Visceral organ metastasis	No	58	NS	.001	.001
	Yes	19			
Peritoneal seeding	No	56	NS	NS	NS
	Yes	21			
Distant LN metastasis only	No	36	NS	NS	NS
	Yes	41			

Abbreviations: PCR = pelvic control rate; PFS = progression free survival; OS = overall survival; NS = not significant; SCCa = squamous cell carcinoma; Hb = hemoglobin; LN = lymph node; International Federation of Gynecology and Obstetrics = FIGO.

The results of the multivariate analysis of PCR, PFS, OS and are shown in Table 4. Visceral organ metastasis ($P < .05$) was the only significant prognostic factor for PFS and OS on multivariate analysis. FIGO stage of primary cervical tumor was the significant prognostic factor for PCR ($P < .05$) in the multivariate analysis.

Table 4. Multivariate Analysis of Prognostic Factors

		PCR		PFS		OS	
Variables	Risk group	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Pre-treatment Hb (g/dL)	> 10 vs. ≤ 10			0.595 (0.334-1.059)	NS	0.716 (0.396-1.294)	NS
FIGO stage of primary cervical tumor	III-IVA vs. I-II	4.065 (1.182-13.982)	.026			1.521 (0.836-2.766)	NS
Tumor size (cm)	≥ 5 vs. < 5			1.703 (0.910-3.185)	NS	1.661 (0.821-3.359)	NS
Visceral organ metastasis	Yes vs. no			2.288 (1.242-4.215)	.008	1.916 (1.024-3.585)	.042

Abbreviations: PCR = pelvic control rate; PFS = progression free survival; OS = overall survival; HR = hazard ratio; NS = not significant; Hb = hemoglobin; International Federation of Gynecology and Obstetrics = FIGO.

4. Subgroup analysis according to the presence of visceral organ metastasis

Whole patients were divided into two groups according to visceral organ metastasis. Group A (n=58) included patients with distant LN metastasis only or peritoneal seeding without visceral organ metastasis. Group B (n=19) included patients with visceral organ metastasis. The 5-year PFS and OS rate of the group A were significantly better than that of group B (29.8% vs. 10.5%, P = .001; 38.9% vs. 10.5%, P = .001) (Figure. 3). The median PFS and OS in group B were 7 and 12 months, respectively. The patients with group A and B had similar 5-year PCR (82.6% and 89.5%, respectively) (Figure. 3).

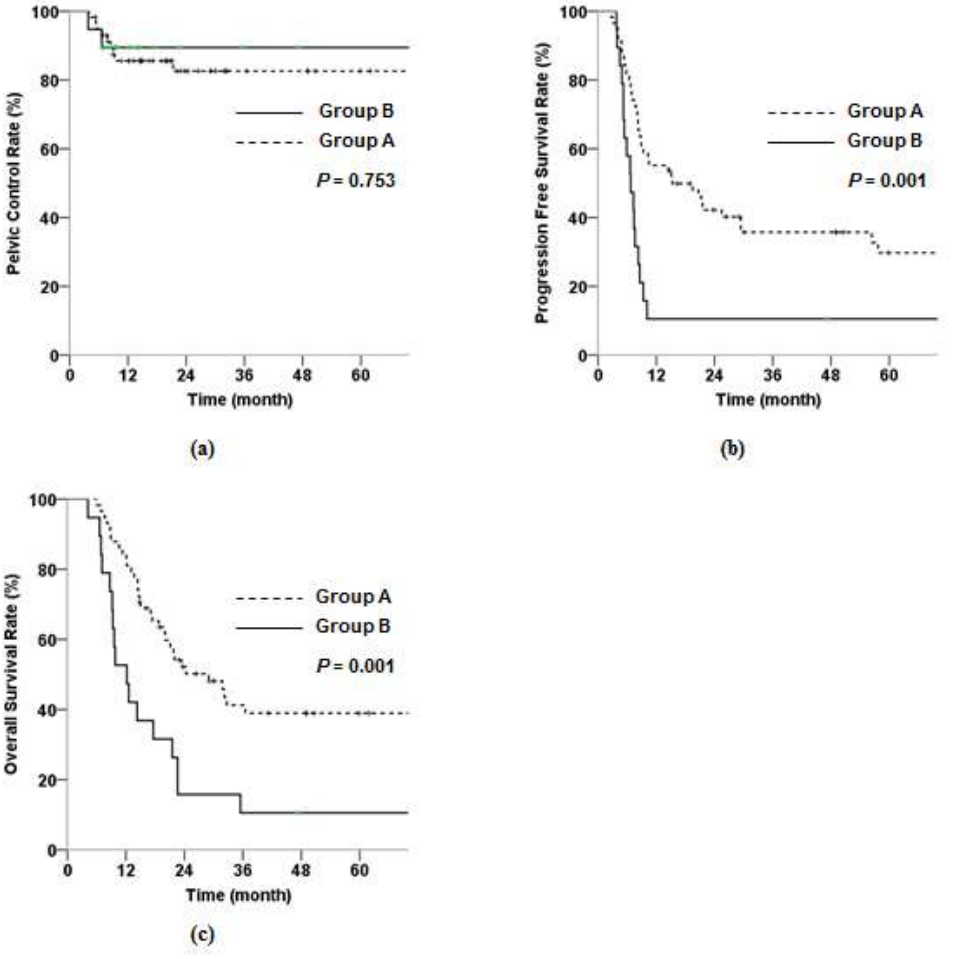

Fig. 3. Pelvic control rate (a), progression free survival rate (b), and overall survival rate (c) in group A and B.

IV. DISCUSSION

Due to the recent progress in the imaging technology, the frequency of identifying disseminated cases is increasing in management of cervical cancer patients. However, the classification of the FIGO stages is not clear yet and there is no consensus drawn in terms of the treatment direction. National Comprehensive Cancer Network Guideline offers no description on the FIGO Stage IVB, while there is a recommendation only for the distant metastasis.[14] Even though two flows are suggested according to amenableness of local treatment, no detail description was provided with regard to what is amenable to local treatment. Therefore, it is important to determine who receive local treatment. As most disseminated cases present locally advanced disease, it would have a significant influence on prognosis to decide what patients RT can be applied to rather than surgery.

Disseminated diseases show heterogeneous prognosis depending on the distribution of the dissemination or bulkiness of tumors.[12, 13] Some recent studies showed that aggressive treatment using CCRT was safe and effective with patients with limited LN metastasis, such as SCLN metastasis.[7-9, 15, 16] Kim et al. reported that 3-year OS rate in patients with PALN and SCLN metastases with curative CCRT was 49%.[7] They suggested that CCRT may be more effective than systemic CTx for improving survival for stage IVB cervical cancer patients with distant lymphatic metastasis.[9]

In this study, the results corresponded with those from the previous studies. The patients without visceral organ metastasis treated with RT showed relatively more

favorable results even though they belonged to FIGO stage IVB. However, the patients with the visceral organ metastasis showed poor prognoses due to systemic progression. Therefore, personalized approach of RT should be considered depending on the visceral organ metastasis. In case of patients who have lymphatic metastasis without visceral organ metastasis, definitive aimed RT with CTx might be recommended to achieve maximal local control and survival benefit. However, because patients with visceral organ metastasis are expected to have a short survival, it would be more important to try systemic CTx to delay systemic progression. The role of RT would be limited to palliative aims to relieve vaginal bleeding or pelvic pain or prevent vesicovaginal or rectovaginal fistula caused by local progression.

The result of this study showed that the patients with the visceral organ metastasis had higher PCR compared to the patients without the visceral organ metastasis (89.5% and 82.6%, respectively). The major patterns of failure of the participants were systemic progressions (66.2%), while the median PFS and OS of the patients with the visceral organ metastasis were 7 months and 12 months, respectively. The patients with the visceral organ metastasis seem to have systemic progressions before the pelvic recurrences occurred. We believe that the systemic progression happened ahead of the pelvic failures and because the cause of death for these patients, which also contributed to a relatively higher PCR.

Recently, the efficacies of CTx are gradually getting important. New cytotoxic CTx or molecular targeted agents are being investigated in recurrent or metastatic settings. Paclitaxel-based CTx has been shown to have a radiosensitizing effect. Objective response rates were from 33% to 67.9% for carboplatin/paclitaxel studies and from 29.1% to 67% for cisplatin/paclitaxel studies.[17] Cisplatin/paclitaxel

CTx was the best combination in the treatment of advanced or recurrent cervical cancer.[3] The overall response rate of combination of docetaxel, carboplatin and 5-fluorouracil in patients with metastatic cervical carcinoma was 56%.[18]

Recently we often saw some patients responded well to upfront systemic CTx before RT. Despite not enough supporting evidences, upfront systemic CTx seems to be worthy being tried to patients with visceral metastasis. If the response is favorable, RT might be extended to a consolidation aim to control microscopic or minimal residual disease after CTx. Otherwise, palliative RT seems to be reasonable for bulky disease.

V. CONCLUSIONS

Our data suggests definitive RT including be external beam pelvic RT with ICR be beneficial to disseminated cervical cancer patients that have limited disease to distant LN metastasis only or peritoneal seeding without visceral organ metastasis. However, in case of patients with visceral organ metastasis who are expected to have short term survival and need systemic CTx, external beam pelvic RT alone may be considered to relieve symptoms, such as vaginal bleeding or pelvic pain, and delaying pelvic progression.

REFERENCES

1. Quinn MA, Benedet JL, Odicino F, Maisonneuve P, Beller U, Creasman WT, et al. Carcinoma of the cervix uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet 2006;95 Suppl 1:S43-103.

2. Moore DH, Blessing JA, McQuellon RP, Thaler HT, Cella D, Benda J, et al. Phase III study of cisplatin with or without paclitaxel in stage IVB, recurrent, or persistent squamous cell carcinoma of the cervix: a gynecologic oncology group study. J Clin Oncol 2004;22:3113-9.

3. Monk BJ, Sill MW, McMeekin DS, Cohn DE, Ramondetta LM, Boardman CH, et al. Phase III trial of four cisplatin-containing doublet combinations in stage IVB, recurrent, or persistent cervical carcinoma: a Gynecologic Oncology Group study. J Clin Oncol 2009;27:4649-55.

4. van Lonkhuijzen L, Thomas G. Palliative radiotherapy for cervical carcinoma, a systematic review. Radiother Oncol 2011;98:287-91.

5. Kim DH, Lee JH, Ki YK, Nam JH, Kim WT, Jeon HS, et al. Short-course palliative radiotherapy for uterine cervical cancer. Radiat Oncol J 2013;31:216-21.

6. Horowitz NS, Tamimi HK, Goff BA, Koh WJ, Schmidt RA, Greer BE, et al. Pretreatment scalene node biopsy in gynecologic malignancy: prudent or passe? Gynecol Oncol 1999;75:238-41.

7. Kim JY, Kim JY, Kim JH, Yoon MS, Kim J, Kim YS. Curative

chemoradiotherapy in patients with stage IVB cervical cancer presenting with paraortic and left supraclavicular lymph node metastases. Int J Radiat Oncol Biol Phys 2012;84:741-7.

8. Lee SH, Lee SH, Lee KC, Lee KB, Shin JW, Park CY, et al. Radiation therapy with chemotherapy for patients with cervical cancer and supraclavicular lymph node involvement. J Gynecol Oncol 2012;23:159-67.

9. Kim JY, Yoo EJ, Jang JW, Kwon JH, Kim KJ, Kay CS. Hypofractionated radiotheapy using helical tomotherapy for advanced hepatocellular carcinoma with portal vein tumor thrombosis. Radiat Oncol 2013;8:15.

10. Waggoner SE. Cervical cancer. Lancet 2003;361:2217-25.

11. Zighelboim I, Taylor NP, Powell MA, Gibb RK, Rader JS, Mutch DG, et al. Outcomes in 24 selected patients with stage IVB cervical cancer and excellent performance status treated with radiotherapy and chemotherapy. Radiat Med 2006;24:625-30.

12. Hwang JH, Lim MC, Seo SS, Kang S, Park SY, Kim JY. Outcomes and toxicities for the treatment of stage IVB cervical cancer. Arch Gynecol Obstet 2012;285:1685-93.

13. Kim K, Cho SY, Kim BJ, Kim MH, Choi SC, Ryu SY. The type of metastasis is a prognostic factor in disseminated cervical cancer. J Gynecol Oncol 2010;21:186-90.

14. National Comprehensive Cancer Network. Cervical cancer clinical practice

guidelines in oncology (Version.I.2014). Fort Washington: National Comprehensive Cancer Network. Available from URL: http://www.nccn.org. [accessed April 5, 2014].

15. Qiu JT, Ho KC, Lai CH, Yen TC, Huang YT, Chao A, et al. Supraclavicular lymph node metastases in cervical cancer. Eur J Gynaecol Oncol 2007;28:33-8.

16. Chao A, Ho KC, Wang CC, Cheng HH, Lin G, Yen TC, et al. Positron emission tomography in evaluating the feasibility of curative intent in cervical cancer patients with limited distant lymph node metastases. Gynecol Oncol 2008;110:172-8.

17. Lorusso D, Petrelli F, Coinu A, Raspagliesi F, Barni S. A systematic review comparing cisplatin and carboplatin plus paclitaxel-based chemotherapy for recurrent or metastatic cervical cancer. Gynecol Oncol 2014;133:117-23.

18. Lin JT, Shih SC, Chang TH, Chang CS. Docetaxel, carboplatin and 5-fluorouracil (TCF) chemotherapy in patients with unresectable metastatic carcinoma of cervix. Gynecol Oncol 2010;117:65-9.

ABSTRACT(IN KOREAN)

진단 시 원격전이된 자궁경부암 환자에서 방사선치료의 역할

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임 정 호

목적: 본 연구의 목적은 진단 시 원격전이된 자궁경부암 환자에서 방사선치료의 역할을 규명하는 것이다.

대상 및 방법: 1980년 9월부터 2012년 8월까지 원격전이된 자궁경부암으로 진단된 77명의 환자에 대해 후향적으로 분석하였다. 모든 환자들은 골반에 외부방사선치료 (중위수 45 Gy)를 시행받았고 60명 (77.9%)은 고선량률 근접치료 (중위수 30 Gy)를 시행받았다. 64명 (83.1%)의 환자들은 항암화학치료를 받았고 12명 (15.6%) 의 환자는 자궁적출술을 포함한 근치적 수술이 시행되었다. 두 그룹으로 구분하여 분석하였다. 첫 번째 그룹 (그룹 A, 58명)은 원격림프절에만 전이가 있거나 원격장기에 전이가 없는 복막전이

환자로 정의하였다. 두 번째 그룹 (그룹 B, 19명)은 원격장기에 전이가 있는 환자로 정의하였다.

결과: 대상환자의 중앙추적조사기간은 55개월 (15~296개월)이었다. 5년 골반국소제어율, 무병생존율, 생존율은 각각 83.7%, 25.1%, 31.7%이었다. 단변량분석 결과 그룹 A가 그룹 B보다 통계학적으로 유의하게 5년 생존율이 높았다. (38.9% vs. 10.5%, p = .001). 무병생존율과 생존율에 대한 다변량분석 결과 그룹 B가 유일한 의미 있는 예후 인자였다. 그룹 A와 그룹 B의 5년 골반국소제어율은 각각 82.6%, 89.5%였다.

결론: 원격장기 전이가 없는 원격전이된 자궁경부암 환자에 대해서는 근치적 방사선치료가 도움이 될 것으로 생각된다. 또한 예후가 불량하고 전신항암화학치료가 필요할 것으로 생각되는 원격장기 전이가 있는 자궁경부암 환자에 대해서는 증상 완화 및 골반국소제어를 위해 외부방사선단독치료가 고려되어야 할 것이다.

핵심되는 말 : 원격전이된 자궁경부암, 원격 장기 전이, 방사선치료, 항암화학치료, 생존율