EJGO European Journal of Gynaecological Oncology

Original Research

Positive pelvic lymph node on [18F]-FDG PET is a prognostic factor in early-stage high-risk cervical cancer treated by radical hysterectomy and adjuvant chemoradiotherapy

D. Kim[1], Y. Ki[3], W. Kim[1], D. Park[1], D. Suh[2], K. Kim[2], J. Lee[3], H. Jeon[3], J. Nam[1]

[1]Departments of Radiation Oncology, [2]Departments of Obstetrics and Gynecology, Biomedical Research Institute, Pusan National University Hospital and Pusan National University School of Medicine, Busan

[3]Department of Radiation Oncology, Pusan National University Yangsan Hospital and Pusan National University School of Medicine, Yangsan (Korea)

Summary

Purpose: The prognostic value of [18F]-fluorodeoxyglucose positron emission tomography (FDG PET) in early-stage high-risk cervical cancer patients was evaluated. *Materials and Methods:* A total of 86 Stage IB or IIA cervical cancer patients with high risk factors (positive resection margin (RM), parametrial invasion (PI) or pelvic lymph node (PLN) metastasis) were retrospectively investigated. *Results:* There was a statistically significant decrease in recurrence-free survival (RFS) in patients with bulky tumor ($p = 0.011$), positive RM ($p = 0.001$), and PLN positivity on FDG PET ($p = 0.012$) in multivariate analyses. Independent prognostic factors for overall survival (OS) included non-squamous cell type ($p = 0.005$), bulky tumor ($p = 0.020$), and PLN positivity on FDG PET ($p = 0.007$). Patients with positive PLN on FDG PET had worse five-year RFS (62.0% *vs*. 85.0%, $p = 0.013$) and OS (68.7% *vs*. 89.5%, $p = 0.011$) rates than those with negative PLN uptake. *Conclusion:* PLN metastasis on FDG PET and bulky tumor were found to be statistically significant prognostic factors for both RFS and OS in early-stage high-risk cervical cancer patients.

Key words: Cervical cancer; High risk factors; Adjuvant chemoradiotherapy; FDG PET.

Introduction

Uterine cervical cancer is the fourth most commonly diagnosed malignancy and leading cause of cancer related death worldwide in women [1]. With the implementation of cytologic screening programs, the mortality rates of cervical cancer have declined substantially as more patients are diagnosed at an early stage [2]. In the current guidelines, early-stage cervical cancer [International Federation of Gynecology and Obstetrics (FIGO) stage IA2-IIA] are treated with radical hysterectomy (RH) and pelvic lymph node dissection (PLND) or pelvic external-beam radiation therapy (EBRT) and brachytherapy [3, 4]. Patients with one or more of pathologically high-risk factors for recurrence, such as pelvic lymph node (PLN) metastasis, parametrial involvement (PI), and/or positive resection margin (RM) were advised to receive adjuvant concurrent chemoradiotherapy (CCRT) to reduce the likelihood of recurrence and improve survival [5]. However, despite the significant improvement in treatment outcomes, the survival of this high-risk group remains unsatisfactory.

18F-fluorodeoxyglucose positron emission tomography (FDG PET) has been widely used not only for determining the extent of disease, but also predicting treatment outcome in patients with cervical cancer [6]. Non-squamous cell histologic type, pathologic tumor size ≥ 4 cm, and two or more positive PLN have been identified as prognostic factors for survival in the high-risk group [7]. However, there have been no studies investigating the prognostic value of FDG PET finding that can successfully predict which patients with high-risk factor will recur after receiving adjuvant CCRT. The analysis of risk factors is very important to establish better treatment strategies. Additional treatment options and intensive follow-up schedule can be considered for patients with poor prognostic factors.

The aim of the present study was to identify these prognostic factors and recurrent patterns in high-risk cervical cancer patients who were treated with RH followed by adjuvant CCRT.

Materials and Methods

The authors retrospectively reviewed the medical records of FIGO Stage IB or IIA cervical cancer patients who had been treated with RH followed by adjuvant CCRT in the (hospital name was erased for review) Hospital between 2008 and 2013. All clinical information was investigated after obtaining the approval with exemption of the institutional review board of the hospital (IRB

Published: 15 February 2020

Eur. J. Gynaecol. Oncol. - ISSN: 0392-2936
XLI , n. 1, 2020
doi: 10.31083/j.ejgo.2020.01.4815

approval numbers: H-1707-003-056). Patients who had received neoadjuvant chemotherapy prior to surgery were excluded because it could affect the pathologic findings. Patients with para-aortic LN metastasis determined by preoperative [^{18}F]-FDG PET were also excluded. Adjuvant CCRT was prescribed to patients with the following pathologic high-risk factors: PLN metastasis, PI, and/or positive RM. All patients were clinically staged preoperatively and classified according to the criteria of the FIGO (2009). The pretreatment workup included a complete medical history, physical examination, complete blood count, liver function test, serum squamous cell carcinoma antigen (SCC-Ag), chest X-rays, MRI of the pelvis, and [^{18}F]-FDG PET scan.

The patients were examined using a dedicated PET/CT system after a minimum of four-hour fasting. In addition, 4.0 MBq/kg of FDG was administered intravenously one hour prior to imaging. Whole-body emission PET scan (skull to mid-thigh) was obtained using a 3D acquisition mode with three minutes per bed position. PET images were reconstructed using CT attenuation maps. The standardized uptake value (SUV) was calculated as follows: SUV = [measured activity concentration (MBq/mL)] / (injected activity (MBq) / body weight (g)]. After all hypermetabolic tumor foci were segmented, the software calculated the maximum SUV (SU-Vmax), which was defined as the peak SUV in 1 pixel with the highest counts within the region of interest. The authors refer to SUVmax of the primary tumour as SUV_{cervix} and that of the PLN as SUV_{PLN}. Positive FDG uptake was defined as a focally increased FDG uptake greater than the SUV 3.0. Equivocal or unclear uptakes were interpreted as negative findings.

All patients were treated with RH and bilateral PLND. Para-aortic LN sampling was performed in 21 cases. Patients who had biopsy confirmed para-aortic LN metastasis were excluded from the study.

Adjuvant RT was started within 4–6 weeks after surgery. EBRT was delivered using a 15-MV photon with a four-field box technique. The RT field (entire pelvis) included the tumor bed and the regional lymphatics. The median dose was 50.4 (range, 45.0-50.4) Gy in conventional fractionation. High-dose-rate intravaginal brachytherapy after EBRT was administered in 62 (72.1%) patients using an Ir-192 brachytherapy unit with a total dose of 12-20 Gy in three to five fractions prescribed at 5 mm beyond the vaginal mucosa. All patients received weekly intravenous cisplatin (40 mg/m^2) as a radiosensitizing agent (median 6 cycles, range 3-7). After completion of CCRT, 40 patients underwent consolidation chemotherapy (CCT) every three weeks for a total of three cycles according to the gynecologist's preference. Paclitaxel 135 mg/m^2 diluted in 500 ml of 5% dextrose water was administered over three hours followed by carboplatin 400 mg/m^2 administered over 60 min.

The time to recurrence was calculated in months from the date of surgery to the date of first recurrence. Patients who died without evidence of recurrence or who were lost to follow-up were censored at the date of death or their last follow-up. The following clinical and pathologic variables were included because previous studies have shown they may have some prognostic value: age, FIGO Stage, histologic subtype, differentiation grade, tumor size, depth of stromal invasion, addition of CCT, PLN involvement, number of positive PLN, PI, surgical RM, lymphovascular space invasion (LVSI), and PLN status on FDG PET [5, 8-10].

As for the tumor size, the patients were stratified into two groups: 4 cm or less versus larger than 4 cm. Similarly, the depth of stromal invasion was classified as less than or more than two-thirds of the full thickness of the cervix. Kaplan-Meier method and the log-rank test were used to calculate the survival rates and detect the significance of each survival difference according to prognostic factors. The variables, which were significant in univariate analysis were included in the multivariate model. Multivariate analyses were carried out using the Cox proportional hazards model with a stepwise backward selection procedure. All analyses were based on a two-tailed test for a significance level of 0.05 and were carried out using the SPSS statistical software package, version 18.0.

Results

A total of 86 patients were selected for the statistical analysis. Patient and tumor characteristics are listed in Table 1. The median age at the time of surgery was 49 (range 30–79) years. The histological cell types included 68 squamous cell carcinomas (SCC), 16 adenocarcinomas, and two adenosquamous carcinomas, respectively. The mean (±SD) pathologic diameter of tumors was 4.11±1.87 cm. The median SUV_{cervix} and SUV_{PLN} was 9.4 (range, 3.0-35.3) and 1.0 (range, 0.7-14.2). The difference of mean SUV_{cervix} between disease recurrence and non-disease recurrence group was not statistically significant. With regards to high-risk factors, PLN, PI, and RM were identified positively in 81.4%, 30.2%, and 12.8% of patients, respectively. Nineteen patients had more than two pathologic risk factors and two patients had all three factors. In 70 patients with PLN metastasis, two or more positive PLN were 35 (40.7%). The median number of dissected PLN were 25 (range, 8-47). Median time to CCRT completion was 43 (range, 36–52) days.

Patients were followed regularly up to June 2017. The median duration of follow-up was 48 months (range, 4-118 months) and there were 15 cancer-related deaths. The five-year recurrence-free survival (RFS) and overall survival (OS) rate for the entire population was 74.9% and 79.9%, respectively. Patterns of initial recurrence were seven in the pelvic cavity, 11 hematogenous metastases (six: lung, four: liver, one: skin), and three simultaneous loco-regional/distant failures. When the time to recurrence was examined, 76.2% (16/21) of recurrence had occurred within 18 months of surgery.

The risk factors for prognosis were evaluated by univariate and multivariate analyses. In univariate analysis (Table 2), FIGO Stage IIA, non-squamous histologic type, pathologic tumor size (≥ 4 cm), positive PLN shown by FDG PET, and positive RM were significantly associated with worse RFS and OS. Multivariate Cox proportional analysis revealed that pathologic tumor size (≥ 4cm), RM involvement, and positive PLN on FDG PET were identified as significant prognostic factors for RFS. After multivariate analysis for OS, non-squamous histologic type,

Table 1. — *Clinicopathologic characteristics of patients and tumors.*

	No. of patients (%)
Age (years), median (range)	49 (30-79)
< 50	48 (55.8)
≥ 50	38 (44.2)
FIGO Stage	
IB1	59 (68.6)
IB2	19 (22.1)
IIA1	6 (7.0)
IIA2	2 (2.3)
Histologic type	
Squamous cell	68 (79.1)
Adeno	16 (18.6)
Adenosquamous	2 (2.3)
Differentiation	
Well	13 (15.1)
Moderate	59 (68.6)
Poorly	14 (16.3)
Tumor size (cm)	
≤ 4	49 (57.0)
> 4	37 (43.0)
PLN involvement	
No	16 (18.6)
Yes	70 (81.4)
No. of PLN metastasis	
0-1	51 (59.3)
≥ 2	35 (40.7)
Lymphovascular invasion	
No	31 (36.0)
Yes	55 (64.0)
Depth of invasion	
< 2/3	18 (20.9)
≥ 2/3	68 (79.1)
Resection margin involvement	
No	75 (87.2)
Yes	11 (12.8)
Parametrial invasion	
No	60 (69.8)
Yes	26 (30.2)
PLN status on FDG-PET	
Negative	49 (57.0)
Positive	37 (43.0)
Consolidation chemotherapy	
Yes	40 (46.5)
No	46 (53.5)

FIGO: International Federation of Gynecology and Obstetrics; PLN: pelvic lymph node; FDG-PET: fluorodeoxyglucose positron emission tomography.

pathologic tumor size (≥ 4cm), and PLN metastasis on FDG PET were remained as significant prognostic factors (Table 3). Therefore, patients with positive PLN on FDG PET and bulky tumor size performed poorly in terms of both RFS and OS.

As shown in Figure 1, the RFS and OS rates of the patients with PLN positivity on FDG PET was significantly lower than those without PLN FDG uptake (five-year RFS rate: 62.0% *vs*. 85.0%, $p = 0.013$; five-year OS rate: 68.7% *vs*. 89.5%, $p = 0.011$). Patients with pathologic tumor size (≥ 4cm) had also significantly worse five-year RFS and OS than those without bulky tumor size (five-year RFS rate: 58.4 *vs*. 87.2 %, $p = 0.001$; five-year OS rate: 66.6 *vs*. 89.6%, $p = 0.004$).

Discussion

This study was conducted to evaluate prognostic value of FDG PET finding in early-stage high-risk cervical cancer patients who were primarily treated by RH with adjuvant CCRT. Metastatic PLN was detected in 43% of patients with FDG PET and PLN metastasis was histologically confirmed in 81.4% of patients. Several studies have reported RFS of 70% to 85% in patients with early-stage high-risk cervical cancer who received adjuvant CCRT [11, 12]. The five-year RFS was 74.9% in this study. This is a favorable outcome considering the relatively high PLN metastasis rate in the present study. The recurrence rate was 24.4% and distant metastasis accounted for the majority of treatment failures.

This study demonstrates that among multiple variables, PLN metastasis on FDG PET and bulky tumor were found to be prognostic factors associated with OS and RFS. The pathologic lymph nodes status is generally considered to be the most important prognostic factor in early-stage cervical cancer [5]. However, PLN positivity on FDG PET was more significant than the pathologic findings, such as the number of metastatic PLNs. Pathologically bulky tumor is one of the adverse prognostic factors in intermediate-risk group [8]. In the current investigation, however, tumor size was associated with worse survival, even in the high-risk group.

To investigate the prognostic significance of multiple PLN metastases, the authors classified patients into two groups according to the number of positive PLNs (0-1 or ≥ 2). There was no significant difference in RFS and OS between the two groups. The present findings are consistent with a previous study, which demonstrated that the effect of adding concurrent chemotherapy to pelvic RT was more profound in patients with multiple PLN metastases than in patients with a single PLN metastasis [13]. Therefore, the adverse prognostic impact of multiple PLN metastases was abolished in patients receiving CCRT.

The LN ratio, defined as the ratio of the number of positive LNs to the total number of examined LNs, was emphasized as an important prognostic factor in patients with cervical cancer [14]. Even though the LN ratio may reflect the number of positive LNs and the quality of LN dissection simultaneously, the authors decided not to include the LN ratio in the analysis, due to the wide range of dissected LNs (8~47).

With regards to histologic cell type, there is controversy whether adenocarcinoma was associated with a worse prognosis than SCC [15]. In this study, non-SCC subtype showed significantly worse OS in multivariate analysis.

Table 2. — *Univariate analysis for recurrence-free and overall survival.*

	Five-year recurrence-free survival		Five-year overall survival	
	%	*p*-value[a)]	%	*p*-value[a)]
Age (years)		0.479		0.689
< 50	72.7		79.7	
≥ 50	77.5		78.6	
FIGO Stage		**0.014**		**0.032**
IB	77.4		82.2	
IIA	50.0		53.6	
Histologic type		**0.023**		**0.028**
SCC	80.6		85.7	
Non-SCC	51.1		58.4	
Grade		0.088		0.321
Well	90.9		85.7	
Moderate	75.8		82.0	
Poorly	56.3		67.7	
Tumor size (cm)		**0.001**		**0.004**
< 4	87.2		89.6	
≥ 4	58.4		66.6	
PLN involvement		0.940		0.585
No	73.1		78.1	
Yes	75.1		79.8	
No. of PLN metastasis		0.451		0.289
0-1	77.6		82.6	
≥ 2	71.0		75.5	
Lymphovascular invasion		0.140		0.635
No	67.0		75.8	
Yes	79.3		82.3	
Depth of invasion		0.421		0.392
< 2/3	83.0		88.2	
≥ 2/3	72.6		77.3	
Resection margin involvement		**<0.001**		**0.001**
No	80.8		84.1	
Yes	32.7		50.9	
Parametrial invasion		0.839		0.340
No	76.4		78.7	
Yes	70.9		82.2	
PLN status on FDG PET		**0.013**		**0.011**
Negative	85.0		89.5	
Positive	62.0		68.7	
Consolidation chemotherapy		0.373		0.801
Yes	70.4		76.9	
No	79.8		82.0	

SCC: squamous cell carcinoma. Other abbreviations as in Table 1. [a)]By log-rank test.

Table 3. — *Multivariate analysis of risk factors associated with five-year recurrence-free and overall survivals.*

	Five-year recurrence-free survival		Five-year overall survival	
	HR (95% CI)	*p*-value[a)]	HR (95% CI)	*p*-value[a)]
FIGO Stage (IIA vs. IB)	2.597 (0.840-8.026)	0.097	2.676 (0.694-10.324)	0.153
Histologic type (Non-SCC *vs*. SCC)	2.384 (0.839-6.774)	0.103	4.895 (1.616-14.823)	**0.005**
Tumor size (cm) (≥ 4 *vs*. < 4)	3.473 (1.327-9.088)	**0.011**	3.985 (1.245-12.754)	**0.020**
RM involvement (yes *vs*. no)	4.620 (1.804-11.833)	**0.001**	3.030 (0.848-10.828)	0.088
PLN status on FDG PET (positive *vs*. negative)	3.226 (1.293-8.049)	**0.012**	5.411 (1.603-18.268)	**0.007**

HR: hazard ratio; CI: confidence interval; RM: resection margin. Other abbreviations as in Table 1 and 2. [a)]By backward Cox hazard model.

However, there was no difference in RFS between SCC and non-SCC group.

Previous reports have demonstrated that metabolic parameters of primary tumor and regional LN on ^{18}F-FDG PET may be prognostic biomarkers for the prediction of disease recurrence in patients with locally advanced cervical cancer [16-18]. In early-stage cervical cancer, preoperative SUV_{PLN} ≥2.36 was an independent risk factor for

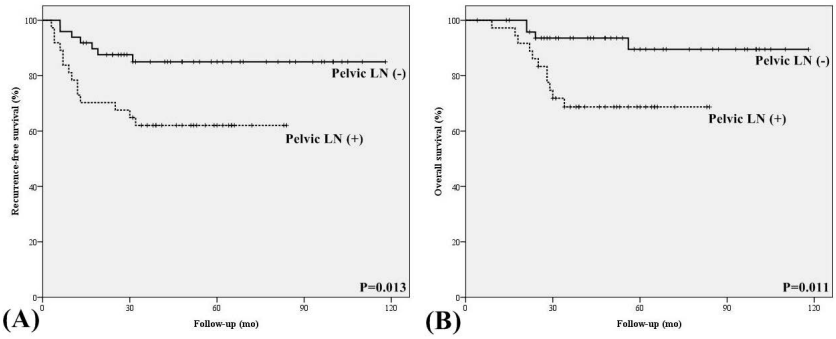

Figure 1. — Kaplan-Meier curve for recurrence-free (A) and overall survivals (B) in patients with and without pelvic lymph node positivity on FDG PET. *p* value was determined by a log-rank test.

recurrence [19]. In the current study, the present authors also demonstrated that PLN positivity on FDG PET is a prognostic biomarker in patients with high-risk cervical cancer. The present presumed that PLN metabolic activity may reflect propensity for metastasis, a major cause of mortality in cervical cancer patients with high-risk factor. To the best of their knowledge, this study is the first to investigate the prognostic value of preoperative ^{18}F-FDG PET in early-stage high-risk cervical cancer. There are several potential limitations to this study that must be acknowledged. It was retrospective and performed at a single institution with a relatively small number of patients. Statistical significance could not be reached in some subgroups because of limited sample size. In addition, the present findings may have difficulty to be generalized because of variability in FDG PET image acquisition and interpretation procedures among institutions.

Although adjuvant CCRT resulted in improved survival outcomes, a significant number of high-risk patients still had recurrences and died of their disease. The major pattern of failure following adjuvant CCRT is distant metastasis rather than local failure [5]. However, not all patients with high-risk factor bear the same risk of distant recurrence. Therefore, it would be valuable to identify the patients at high-risk of recurrence. To further improve the prognosis of this patient group, intensive treatment strategies need to be investigated. One strategy that might improve patient outcomes is the addition of CCT after CCRT. This explanation corresponds to meta-analyses indicating that the addition of systemic chemotherapy has a benefit in reducing the risk of distant failure [8, 20]. CCT did not improve the survival outcomes of the patients in this study population. In consideration of the retrospective nature of this study, selection bias for CCT might have influenced the analysis results. Thus, the clinical benefit of adding CCT after postoperative CCRT in patients who were at high risk for recurrence needs to be investigated in future prospective clinical trials.

Conclusion

The present results suggested that PLN metastasis on FDG PET is an independent prognostic factor for high-risk early-stage cervical cancer after RH and postoperative CCRT. PLN positivity on FDG PET is of potential clinical value because it may help physician offer better patient counseling on clinical outcome and select ideal targets for more aggressive therapy.

Acknowledgements

This work was supported by clinical research grant from Pusan National University Hospital in 2017.

References

[1] Torre L.A., Bray F., Siegel R.L., Ferlay J., Lortet-Tieulent J., Jemal A.: "Global cancer statistics. 2012". *CA. Cancer. J. Clin.*, 2015, *65*, 87.
[2] Mathew A., George P.S.: "Trends in incidence and mortality rates of squamous cell carcinoma and adenocarcinoma of cervix-worldwide". *Asian Pac. J. Cancer Prev.*, 2009, *10*, 645.
[3] Inoue T., Okumura M.: "Prognostic significance of parametrial extension in patients with cervical carcinoma Stages IB, IIA, and IIB. A study of 628 cases treated by radical hysterectomy and lymphadenectomy with or without postoperative irradiation". *Cancer*, 1984, *54*, 1714.
[4] Toita T., Kato S., Niibe Y., Ohno T., Kazumoto T., Kodaira T., *et al.*: "Prospective multi-institutional study of definitive radiotherapy with high-dose-rate intracavitary brachytherapy in patients with nonbulky (<4-cm) stage I and II uterine cervical cancer (JAROG0401/JROSG04-2)". *Int. J. Radiat. Oncol. Biol. Phys.*, 2012, *82*, e49.
[5] Peters W.A., Liu P.Y,. Barrett R.J., Stock R.J., Monk B.J., Berek J.S., *et al.*: "Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix". *J. Clin. Oncol.*, 2000, *18*, 1606.
[6] Kim D.H., Kim W.T., Bae J.S., Ki Y.K., Park D., Suh D.S., *et al.*: "Maximum standardized uptake value of pelvic lymph nodes in ^{18}F-FDG PET is a prognostic factor for para-aortic lymph node recurrence in pelvic node-positive cervical cancer treated with definitive chemoradiotherapy". *Int. J. Gynecol. Cancer,* 2016, *26*, 1274.
[7] Yang K., Park W., Huh S.J., Bae D.S., Kim B.G., Lee J.W.: "Clinical outcomes in patients treated with radiotherapy after surgery for cervical cancer". *Radiat. Oncol. J.,* 2017, *35*, 39.
[8] Sedlis A., Bundy B.N., Rotman M.Z., Lentz S.S., Muderspach L.I., Zaino R.J.: "A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: a

Gynecologic Oncology Group Study". *Gynecol. Oncol.*, 1999, *73*, 177.

[9] Eifel P.J., Burke T.W,. Morris M., Smith T.L.: "Adenocarcinoma as an independent risk factor for disease recurrence in patients with stage IB cervical carcinoma". *Gynecol. Oncol.*, 1995, *59*, 38.

[10] Eifel . Morris M., Wharton J.T., Oswald M.J.: "The influence of tumor size and morphology on the outcome of patients with FIGO stage IB squamous cell carcinoma of the uterine cervix". *Int. J. Radiat. Oncol. Biol. Phys.*, 1994, *29*, 9.

[11] Shibata K., Kajiyama H., Terauchi M., Yamamoto E., Ino K., Nawa A., et al.: "Feasibility and effectiveness of postoperative adjuvant concurrent chemoradiation therapy in Japanese patients with high-risk early-stage cancer of the uterine cervix". *Int. J. Clin. Oncol.*, 2008, *13*, 233.

[12] Ryu H.S., Chun M., Chang K., Chang H., Lee J.: "Postoperative adjuvant concurrent chemoradiotherapy improves survival rates for high-risk, early stage cervical cancer patients". *Gynecol. Oncol.*, 2005, *96*, 490.

[13] Okazawa M., Mabuchi S., Isohashi F., Suzuki O., Ohta Y., Fujita M., *et al.*: "The prognostic significance of multiple pelvic node metastases in cervical cancer patients treated with radical hysterectomy plus adjuvant chemoradiotherapy". *Int. J. Gynecol. Cancer*, 2012, *22*, 490.

[14] Polterauer S., Grimm C., Hofstetter G., Concin N., Natter C., Sturdza A., *et al.*: "Nomogram prediction for overall survival of patients diagnosed with cervical cancer". *Br. J. Cancer*, 2012, *107*, 918.

[15] Niibe Y., Onda T., Matsuo K., Inoue Y., Hayakawa K.: "Phase II Study of Concurrent Chemoradiotheapy Using Nedaplatin for Locally Advanced Uterine Cervical Carcinoma (KGROG0501): Final Results". *Anticancer. Res.*, 2017, *37*, 6983.

[16] Kidd E.A., Siegel B.A., Dehdashti F., Grigsby P.W.: "Pelvic lymph node F-18 fluorodeoxyglucose uptake as a prognostic biomarker in newly diagnosed patients with locally advanced cervical cancer". *Cancer*, 2010, *116*, 1469.

[17] Onal C., Reyhan M., Parlak C., Guler O.C., Oymak E.: "Prognostic value of pretreatment ^{18}F-fluorodeoxyglucose uptake in patients with cervical cancer treated with definitive chemoradiotherapy". *Int. J. Gynecol. Cancer.*, 2013, *23*, 1104.

[18] Onal C., Guler O.C., Reyhan M., Yapar A.F.: "Prognostic value of ^{18}F-fluorodeoxyglucose uptake in pelvic lymph nodes in patients with cervical cancer treated with definitive chemoradiotherapy". *Gynecol. Oncol.*, 2015, *137*, 40.

[19] Chung H.H., Cheon G.J., Kang K.W., Kim J.W., Park N.H., Song Y.S.: "Preoperative PET/CT FDG standardized uptake value of pelvic lymph nodes as a significant prognostic factor in patients with uterine cervical cancer". *Eur. J. Nucl. Med. Mol. Imaging*, 2014, *41*, 674.

[20] Chemoradiotherapy for Cervical Cancer Meta-Analysis Collaboration: "Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: a systematic review and meta-analysis of individual patient data from 18 randomized trials". *J. Clin. Oncol.*, 2008, *26*, 5802.

Corresponding Author:
YONGKAN KI, M.D., PhD
Department of Radiation Oncology
Pusan National University Yangsan Hospital and
Pusan National University School of Medicine
20, Geumo-ro, Mulgeum-eup, Yangsan-si,
Gyeongsangnam-do (Korea)
e-mail: apex7171@hanmail.net