

Adjuvant Radiotherapy Following Radical Hysterectomy and Bilateral Pelvic Lymph Node Dissection for the Uterine Cervical Cancer : Prognostic Factors and Failure Patterns

Doo Ho Choi, M.D.

Department of Radiation Oncology, Soonchunhyang University Hospital, Seoul Korea

Purpose : To identify variable prognostic factors and analyse failure patterns in the uterine cervix cancer after radical operation and adjuvant radiotherapy, a retrospective analysis was undertaken.

Materials and Methods : I analysed one hundred and twenty four patients with uterine cervix cancer, FIGO stage IB, IIA and IIB, treated with radical hysterectomy and pelvic lymph node dissection followed by adjuvant radiotherapy between May 1985 and May 1994. Minimum follow up period was 24 months. All of them were treated with full dose external radiotherapy with linear accelerator and/or high dose rate intracavitary radiation.

Results : Overall 5 year survival rate and relapse free survival rate were 75.4%, 73.5%, respectively. Significant prognostic factors by relapse free survival were wall involvement thickness, lymph node location and number, parametrium involvement, tumor size, stage, uterine body involvement, vaginal resection margin involvement. By multivariate analysis, lymph node metastasis, tumor size and vaginal resection margin involvement were significant prognostic factors.

Treatment related failure were 33 cases. Locoregional failure were more likely in the stage IIB, lymph node positive or vaginal resection margin positive patients whereas distant failures were relatively more frequent in stage IB, IIA and lymph node, vaginal resection negative patients. In stage IIB, 5 year relapse free survival rate was only 56% and nine of twenty two patients recurred.

Conclusion : Postoperative radiotherapy results are good for patients with relatively low risk factor. But the results are poor for patients with multiple, high risk factors or stage IIB. To control recurrence for patients with high risk factors, postoperative adjuvant radiotherapy is not sufficient treatment method. To raise control rate, adding other methods such as radiosensitizing agent or chemotherapy is necessary and prospectively randomized study is needed for evaluation of postoperative radiotherapy efficacy and /or other

이 논문은 1997년 7월 9일 접수하여 1997년 9월 24일 채택되었음.

Correspondence to: Doo Ho Choi, M.D., Department of Radiation Oncology, Soonchunhyang University Hospital, 657-58, Hannam-dong Yongsan-ku, Seoul, Korea

methods. And it is reasonable to treat primary radical radiotherapy for patients with stage IIB cervical cancer instead of radical operation and adjuvant radiotherapy and/or chemotherapy regimen.

Key Words : Cervical Cancer, Radical Hysterectomy, Radiotherapy, Prognostic Factors

INTRODUCTION

Radical hysterectomy and bilateral pelvic lymph node dissection is a well established mode of therapy for relatively early stage uterine cervical cancer. The results have been recognized as equally efficacious as external pelvic radiotherapy and intracavitary radiation with respect to local control and survival^{1,2}. There is a tendency to choose operation for the young patients, but radiotherapy is preferred to surgery for patients with old age, refusing and medical contraindication for surgery. Advantages of primary surgical approach are preservation of ovarian and sexual function and avoidance of late radiation complication. Another advantage of surgical approach is to provide additional information in determining further therapy.

Investigators evaluated retrospectively many factors which influence prognosis such as lymph node metastasis³⁻¹³, lymphovascular space tumor emboli¹³⁻¹⁵, stage, tumor size, depth of stromal invasion or parametrium^{3, 4, 6-11} and tumor grade^{13, 16}. Adjuvant postoperative radiotherapy was recommended in treating these high risk patients with variable result. I reviewed the clinical outcome of 124 patients with risk factors who were treated with radical hysterectomy and postoperative radiotherapy and/or chemotherapy. Other pathologic variables and substrata of prognostic factors were examined retrospectively to determine their prognostic significance.

MATERIALS AND METHODS

Patients with clinical stage IB-IIB cancer of the uterine cervix treated by radical hysterectomy, bila-

teral pelvic lymphadenectomy were eligible for this retrospective analysis if they had one or more of the following risk factors: 1) pelvic lymph node metastasis, 2) deeply invasive lesions 50% or greater stromal invasion, 3) microinvasion of parametrium or positive margin of vaginal resection, 4) large primary tumor greater than or equal to 3cm in diameter, 5) nonsquamous histology, 6) neoplastic involvement of adjacent uterine body and/or 7) microinvasion of paracervical lymphovascular channels.

Age of the patients at diagnosis ranged from 26 to 71 years (median 50 years). One hundred and ten patients (88.7%) has squamous cell carcinoma, 14 (11.3%) adenocarcinoma. Sixty three patients underwent operation at the Soonchunhyang University Hospital, sixty one patients referred from other hospitals for radiotherapy. All the patients included in the analysis underwent bilateral pelvic lymphadenectomy, even if some nodes were grossly replaced by metastatic tumor. Selected patients also underwent a paraaortic lymphadenectomy. Bilateral salpingo-oophorectomies were performed on all postmenopausal women and ovarian transposition was performed in some premenopausal women desiring ovarian conservation. A mean numbers of 22 lymph nodes per patient were resected (range 5-71).

Thirteen patients (mainly stage IIB) received 2 cycles of cisplatin based preoperative chemotherapy, twelve patients with high risk factors received 2 cycles of postoperative chemotherapy. One hundred patients initiated radiotherapy within 6 weeks of the date of radical hysterectomy, twelve patients delayed due to surgical complication or delayed referral, twelve patients due to postoperative chemotherapy.

Postoperative radiotherapy consisted of megavo-

litage irradiation employing 4 MV linear accelerator delivering 5040cGy to the whole pelvis using a four field box technique. Five patients were treated with dose less than 5040cGy. All the stage IIB patients except one received boost dose 540–900cGy to the tumor bed areas. Therapy was given over 6 to 7 weeks in 180cGy fractions to all 124 patients. Three patients with metastatic disease in the paraaortic lymph nodes received extended field radiation to the level of the tenth thoracic vertebrae with 4500cGy over 5 week period. High dose rate remote afterloading intracavitary radiotherapy with Co-60 also was administered to 12 patients with positive vaginal resection margin employing colpostats delivering an additional 2100–3000cGy/6–8 fractions to the paravaginal tissue at 0.5cm depth.

Surveillance for recurrent disease consisted of physical examinations and Pap smears every 2 months for the first year, every 3 months for the second year and every 4–6 months thereafter. All recurrences of central region were confirmed pathologically but diagnosed radiologically in side wall and distant metastasis. The clinical and surgical data were abstracted from patient medical records. Follow up information was obtained by medical record, correspondence, telephone, review of death certificates or information from referring physicians.

Major complications were defined as those requiring hospital admission and/or surgical correction. The median follow up of 124 patients included in this analysis was 54 months (mean 59, range 11–121 months). All survivors have at least 24 months of follow up and none were lost to follow up (all patients of follow up loss or radiation dose less than 4000cGy were excluded in this analysis).

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS).

Kaplan–Meier estimates were used for survival analysis and log–rank test was used to identify important prognostic factors. Cox proportional hazard model were performed to compare the survival distribution for each prognostic group.

RESULTS

The overall and disease free survival at 5 year were 75.4%, 73.5%, respectively. At 5 years, the relapse free survival rates for FIGO stage IB, IIA and IIB were 81.2%, 67.6% and 56.3%, respectively (Fig. 1). Factors relating to the pathologic specimen, FIGO stage, preoperative tumor size and age were examined by univariate analysis to determine their effect on disease free survival. All the factors except age, tumor histology and vessel involvement showed a statistically significant effect

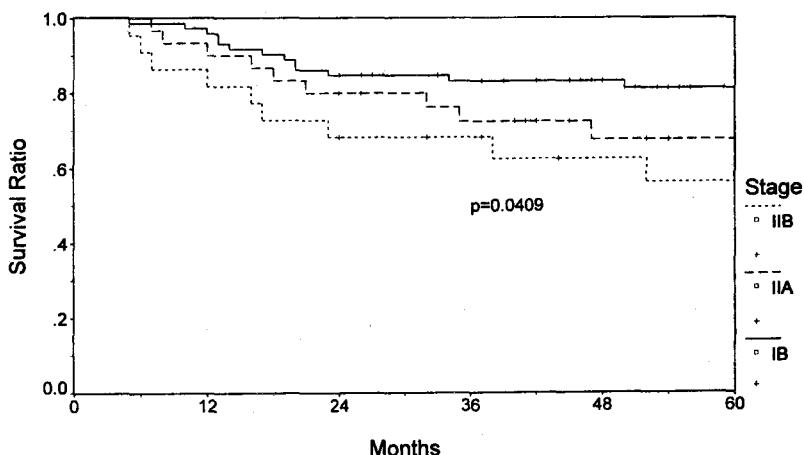


Fig. 1. Disease free survival rate according to FIGO Stage.

Table 1. Survival Rates and Prognostic Factors Relating to the Pathology and Patients Characteristics

Factors	No. of patients	No. of recurrence	5YDFSR*(%)	P-value
Age				
<40	31	7	76.2	
≥40	93	26	72.5	0.6278
FIGO Stage				
IB	72	13	81.2	
IIA	30	11	67.6	
IIB	22	9	56.3	0.0409
Tumor Size				
<3cm	83	14	81.8	
≥3cm	41	19	56.8	0.0002
Histology				
squamous cell ca	110	29	72.9	
adenocarcinoma	14	4	77.9	0.9388
LN location				
no meta	73	10	86.6	
one pelvic side	27	9	63.8	
both pelvic sides	16	8	46.9	
common iliac node	8	6	37.5	0.0000
LN number				
no meta	73	10	86.6	
1-3	38	14	61.3	
4 or more	13	9	36.9	0.0000
Cervix wall invasion				
<1/2	44	8	83.5	
≥1/2	8	1	87.5	
≥2/3	41	10	75.2	
near full thickness	31	14	45.2	0.0111
Parametrium involvement				
no	98	20	80.1	
one side	18	8	53.3	
both sides	8	5	37.5	0.0007
Corpus involvement				
no	101	23	77.6	
yes	23	10	55.8	0.0125
Vaginal resection involvement				
no	115	28	76.2	
yes	9	5	40.0	0.0143
Lymphovascular vessel				
no	94	21	75.3	
yes	30	12	66.4	0.0580

*5YDFSR : 5 year disease free survival rate

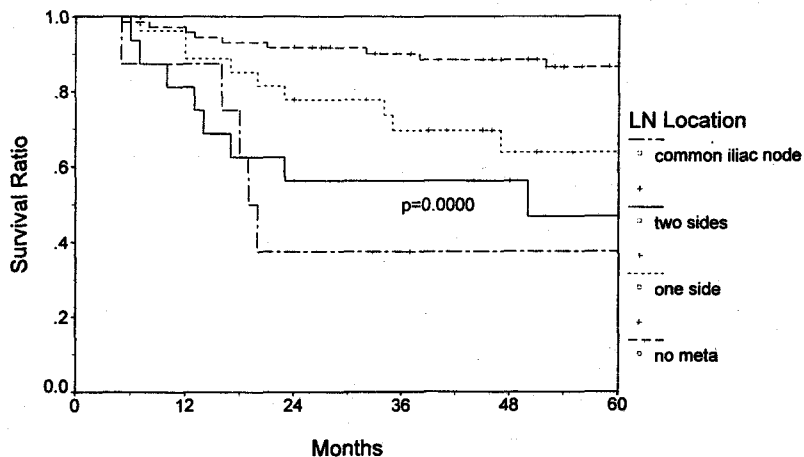


Fig. 2. Disease free survival rate according to LN location status.

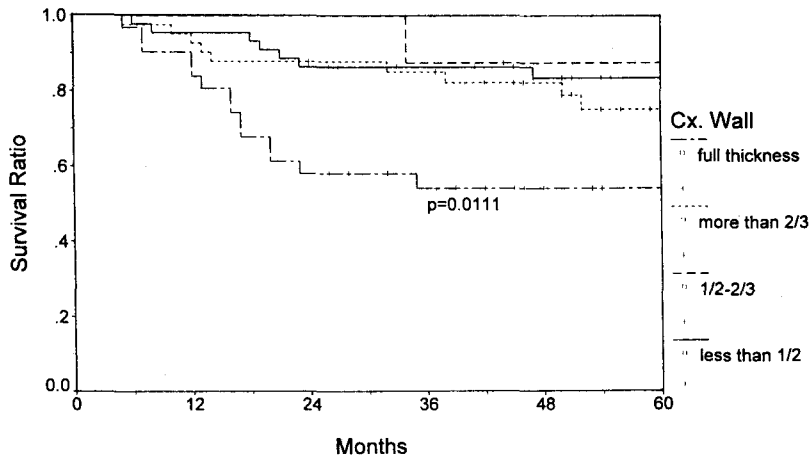


Fig. 3. Disease free survival according to cervix wall extension.

Table 2. Cox Multivariate Analysis in All 124 Patients for Disease Free Survival

Variables	Exp(β)	95% Confidence bounds	Significance
Age	1.0366	0.4345-2.4730	0.9354
Wall invasion	1.1242	0.8113-1.5577	0.4818
Lymph node meta	2.6167	1.5939-4.2961	0.0001
Histology	1.2156	0.3590-4.1166	0.7357
Parametrium extension	1.6265	0.9228-2.8670	0.0926
Tumor size	3.2990	1.5010-7.2507	0.0030
FIGO Stage	1.2468	0.7825-1.9868	0.3534
Uterine body invasion	1.1693	0.4507-3.0334	0.7478
Vaginal margin	3.2192	1.0621-9.7573	0.0388
Vessel involvement	1.2044	0.6706-2.1633	0.5336

on survival (Table 1). The most important prognostic parameter was lymph nodal status, both of extent and number of lymph node involvement ($P=0.0000$). Fig. 2 and Fig. 3 show disease free survival according to extent of lymph node involvement and extent of cervical wall involvement, respectively.

By multivariate analysis, lymph node metastasis, tumor size and involvement of vaginal resection margin were found to be independent predictors of disease free survival (Table 2) (To avoid analysis error, numbers and locations of involved lymph node considered as a single prognostic factor, because the correction coefficient of the two variables approximate to unity).

Treatment related factors were also examined by univariate analysis to determine their effect on disease survival. Chemotherapy, intracavitary radiation (ICR), and radiation dose showed a signifi-

cants effect on survival (Table 3). After a median follow up of 54 months, 33 patients recurred with a 26.6% overall incidence. Site of recurrence related to stage, lymph node status and vaginal resection margin are shown in Table 4.

A relationship between lymph node involvement and type of recurrence was suggested. The sixteen patients (70%) who recurred locoregionally (and/or distant metastasis) were node positive, while only four of the ten patients (40%) who recurred locoregionally (and/or distant metastasis) had node negative pathology. Significant relationship was also observed between vaginal involvement and risk of recurrence; the incidence of recurrence was 56% (5/9) for patients with vaginal involvement whereas 24% (28/115) for those with negative patients. In particular, four of the five patients with vaginal involvement who recurred present locoregional relapse (including one case of

Table 3. Treatment Related Prognostic Factors by Univariate Analysis

Factors	No. of patients	No. of recurrence	5-YDFSR*(%)	P-value
Chemotherapy				
no	99	24	75.7	
preoperative	13	7	51.3	
postoperative	12	2	81.5	0.0431
Intracavitary radiation				
no	112	27	76.4	
yes	12	6	44.4	0.0152
Op-RT** interval				
< 6weeks	100	27	73.9	
≥ 6weeks	24	6	70.4	0.9913
External RT dose				
≤ 50.4Gy	103	24	77.0	
> 50.4Gy	21	9	55.7	0.0408

*YDFSR: year disease free survival rate, **RT: radiotherapy

Table 4. Failure Patterns According to Stage, Lymph Node Metastasis and Vaginal Resection Margin Involvement

Variables	No. of patients	L-R failure()	DM	L-R+DM()	Total failure	Intercurrent death
FIGO Stage						
IB	72	4(2)	6	3(1)	13	2
IIA	30	4(2)	5	2(0)	11	0
IIB	22	5(3)	2	2(1)	9	0
LN metastasis						
no	73	2(1)	6	2(0)	10	2
yes	51	11(5)	7	5(2)	23	0
Vaginal resection						
no	115	12(3)	12	6(2)	28	2
yes	9	3(3)	1	1(1)	5	0

L-R: loco-regional DM: distant metastasis (): No. of central failure

coincidental distant metastasis), all the four patients present central pelvic relapse without pelvic side wall relapse. Regarding to stage, patients with stage IIB had nine recurrences of the twenty two, and 5 year relapse free survival rate was only 56%.

The median time of recurrence was 17 months (range 6–55 months), 25 (75.8%) of the 33 recurrences were diagnosed within 24 months of surgery. Twenty eight of the 33 patients died of the disease. The median survival time of the died patients following recurrence was 11 months. Five patients were still alive up to the completion of follow up, three of them has been suffered from the progressive disease. But 2 patients still alive up to now without disease evidence 48, 52 months after retreatment. Both patients, single pelvic bone metastasis and left supraclavicular node metastasis, received radiotherapy with 50Gy and

more than 3 cycles of chemotherapy. The frequent sites of distant metastasis (including coincidental locoregional recurrence) were the paraaortic nodes (5), supraclavicular nodes (5), lung (3), and bone (3). Two patients died of intercurrent disease, one of them had second primary lung cancer.

Complications requiring operative intervention occurred in 7 patients (5.6%) of which 2 were combined with tumor recurrence. Of the remaining 5 patients, two developed ureter stricture, two developed bowel obstruction and one vesicovaginal fistula.

DISCUSSION

Radical hysterectomy and bilateral pelvic lymph node dissection for early stage cervical cancer produces high cure rates. But many patients with poor prognostic features have been associated

with increased local failure and decreased survival. The role of postoperative adjuvant radiation therapy is to improve local control of disease by sterilizing remaining microscopic and gross residual disease. The clinicopathologic factors which predict a poor prognosis for patients with an early carcinoma of the cervix have been well established.

This report presents 9-year experience with combined therapy of surgery and radiotherapy.

This series has yielded an overall 5 year survival of 75.4% among patients with completely resectable stage IB, IIA, and IIB cervical cancer who had some bad prognostic factors. When compared to historical control, these favorable results suggest that combining radiation and surgery may improve long-term pelvic control and cure rate despite high risk factors. But we could not make any definitive conclusion because of small number of patients and selection bias. Patients with more advanced cervical lesion and lymph node involvement tend to be referred for postoperative pelvic irradiation¹⁷.

Although one study, Stock et al.¹⁰, demonstrated that pelvic irradiation had shown a significant positive prognostic effect on disease free survival with a 5 year survival of 65% versus 41% for patients not receiving radiotherapy, and Monk et al.¹⁸ suggested favorable results compared to historical control, a controlled prospective clinical trial comparing surgery alone versus surgery and postoperative radiotherapy will definitively determine the advantage and disadvantage of these two therapeutic modalities.

To identify prognostic factors, various clinicopathologic variables were analyzed in this report. By univariate analysis, lymph node status, parametrial extension, tumor size, stromal involvement thickness, uterine body involvement, vaginal resection margin involvement and FIGO stage were found to be a significant prognostic factors in disease free survival ($P < 0.05$). By multivariate analysis, only lymph node metastasis, vaginal resection involvement and tumor size were significant.

Among the prognostic factors, Lymph node metastasis was the poorest prognostic factor

($P = 0.0000$). Moreover, there was a trend toward increased frequency of recurrences among patients with four or more nodal metastasis compared to those with one to three positive node (Table 1). This is consistent with the findings of the other investigators^{4, 19}. Bilateral pelvic node and/or common iliac spread as well as numbers of nodal metastasis were also predictive of poor outcome (Table 1). Similar results reported by Martimbeau et al.²⁰. They reported that only 2 out of 32 patients with metastasis in the common iliac nodes survived 5 years compared with 52 out of 88 (59%) with metastasis to the external iliac and obturator lymph nodes.

The observation that nonsquamous carcinomas and poorly differentiated tumors were associated with a worse prognosis demonstrated by other investigators^{5, 13, 17, 21}. Depth of stromal invasion had also influenced on survival. Especially in patients with nearly full thickness involvement, 5 year disease free survival was only 54.2% in this series.

The poor prognosis for patients with both parametrial extension, a 5 year survival 37.5% in the current report, has been previously described by others²². Influence of parametrial extension to treatment related failure also demonstrated in the inappropriate hysterectomy result reported previously by author²³ and Roman et al.²⁴. They reported that 5 year survival rate were about 30% when parametrium was grossly extended. Many patients with parametrial extension and/or deep stromal invasion have been treated with a higher external radiation dose, this may have a role in the multivariate analysis that these factors were not found to be a significant factor.

However, patients with involvement of vaginal resection margin presented poor disease free survival with statistical significance by multivariate analysis ($P = 0.0388$), in spite of treating external radiotherapy and intracavitary radiation. These results signify that microscopic disease can be controlled by an adequate radiation dose with some acceptable complication rate, but it is difficult to control recurrences for patients with a distinct

residual tumor by radiotherapy alone. Accordingly, the addition of chemotherapy as a radiosensitizer deserves continued study in the subset of high risk patients.

Lymphovascular space involvement, uterine corpus involvement, previously reported as a prognostic factors by van Nagell et al.²⁵⁾, and Boicy et al.²⁶⁾, also appeared to be a prognostic factors in the current study (marginally significant in vessel involvement, $P=0.0580$), although these were found non-significant after a multifactorial analysis.

Tumor size influenced on poor prognosis for the second next to lymph node metastasis in the univariate and multivariate analysis ($P=0.0030$). The size criteria which separates large from small tumors is not consistent among studies. Numerous investigators have reported that tumor size is an important prognostic indicator^{1-11, 14, 17-20)}. The poor surviving patients with a large tumor³⁾ reflects in part the greater frequency of nodal metastasis, the effect of size on prognosis can be also confounded by a number of other prognostic factors including occult parametrial extension, extrapelvic disease, and tumor histology. So, Bross et al.⁷⁾ suggested that tumor volume alone might not be an adverse prognostic factor when favorable histology, good surgical margins, and the absence of nodal metastasis were found.

In the analysis of treatment related factors, intracavitary treatment, radiation dose and chemotherapy were adverse prognostic factors. This means higher radiation dose including intracavitary radiation and chemotherapy for patients with higher risk factors dose not influences sufficiently to control disease in this series. As has been reviewed by others²⁷⁾, intracavitary treatment was given for cases in which the vaginal margin is positive or where there was a short cancer-free space from the resection margin in the extirpated vagina or sometimes in patients with lymphatic permeation, deep stromal, parametrial invasion and lymph node metastasis. But whether additional vaginal cuff irradiation should be given is not so well defined.

Analyzing the patterns of recurrences, authors

observed a relationship between nodal involvement and recurrence. Recurrence sites seem to be dependent on the presence or absence of positive nodal involvement, a higher incidence of pelvic side wall and distant recurrences in patient with positive nodes was observed in accordance with Fuller²¹⁾, and Garzetti¹²⁾. Similarly, patients with vaginal resection involvement experienced central recurrences except one patient with distant failure only.

As suggested and supported by other reports^{12, 21, 28-29)}, cervical carcinoma which recur centrally may be biologically different from those which recur distantly or at pelvic sidewall. Central recurrence risk seems to be related to the direct neoplastic extension as observed higher central recurrence in stage IIB or vaginal resection involvement in the current report. The risk of pelvic sidewall and distant recurrences seems to be related to primary nodal involvement, a higher biologically aggressiveness and a precocious lymphatic dissemination, which led to increase distant failures. Garzetti et al.¹²⁾ observed a relationship between 72-kDa metalloproteinase staining— which specifically cleaves type IV collagen and seems to play a critical role in tumor invasion and metastatic dissemination— and nodal involvement ($P < 0.0001$), both factors influence in increasing risk of pelvic side wall and distant recurrence. This fact—higher relapse on the pelvic side wall or distant metastasis in patients with node positive— may have an important effect on good radiotherapy result after surgery related central failure with lymph node negative patients^{21, 29)}. Good salvage results by radiotherapy in patients with node negative and central failure also may be higher radiation dose including intracavitary radiation, which can be delivered in the vaginal cuff area and avoiding high dose to rectum and bladder.

In principle, treatment of choice in stage IIB cervical carcinoma is radical radiotherapy including intracavitary radiation. We observed higher relapse and poor survival in the stage IIB patients in spite of radical resection. The 5 year relapse free survival rate result, 56%, in these patients after ra-

dical surgery and postoperative radiotherapy is inferior to primary radical radiotherapy result, 62%, data from the 169 patients with stage IIB in this hospital. This result implies that primary surgery and other adjuvant therapy (neoadjuvant chemotherapy, postoperative radiotherapy) may be not an alternative method in treating stage IIB patients.

In conclusion, lymph node metastasis, tumor size and vaginal resection margin involvement were significant prognostic factors in multivariate analysis. The 5 year survival rate about 75% is favorable as a whole. To control higher recurrences for patients with multiple, poor prognostic factors, postoperative radiotherapy is not sufficient. More effective or aggressive treatment method is needed and prospectively randomized large scale study is necessary for identifying precise role of adjuvant radiotherapy. Lastly, primary radiotherapy is more reasonable than radical surgery and adjuvant therapy in treating patients with stage IIB cervical carcinoma.

REFERENCES

1. DiSaia PJ, Creasman WT. Invasive cervical cancer. In: Clinical Gynecologic Oncology, 4th ed., St. Louis: Mosby, 1993: 58-125
2. Goodman HM, Bowling MC, Nelson JH. Cervical malignancies. In: Knapp RC Bercowitz, eds. Gynecologic Oncology, Newyork: Macmillan, 1986: 225-274
3. Piver MS, Chung WS. Prognostic significance of cervical lesion size and pelvic node metastasis in cervical carcinoma. *Obstet Gynecol* 1975; 46:507-510
4. Pilleron JP, Durand JC, Hamelin JP. Prognostic value of node metastasis in cancer of the uterine cervix. *Am J Obstet Gynecol* 1974; 119:458-462
5. Berman ML, Bergen S, Salazar H. Influence of histologic features and treatment on the prognosis of patients with cervical cancer metastatic to pelvic lymph nodes. *Gynecol Oncol* 1990; 39:127-131
6. Fuller AF, Elliott N, Kosloff C et al. Lymph node metastasis from carcinoma of the cervix, stage IB and IIA: Implications for prognosis and treatment. *Gynecol Oncol* 1982; 13:165-174
7. Bloss JD, Berman ML, Mukhererjee J et al. Bulky stage IB cervical carcinoma managed by primary radical hysterectomy followed by tailored radiotherapy. *Gynecol Oncol* 1992; 47:21-27
8. Kim RY, Slater MM, Shingleton HM. Adjuvant postoperative therapy following radical hysterectomy in stage IB cancer of the cervix—Analysis of treatment failure. *Int J Radiat Oncol Biol Phys* 1988; 14:445-449
9. Bradley JM, Cha DS, Walker JL, Burger RA et al. Extent of disease as an indication for pelvic radiation following radical hysterectomy and bilateral pelvic lymph node dissection in the treatment of stage IB and IIA cervical carcinoma. *Gynecol Oncol* 1996; 54:4-9
10. Stock RG, Chen AS, Flickinger JC et al. Node-positive cervical cancer: impact of pelvic irradiation and patterns of failure. *Int J Radiat Oncol Biol Phys* 1995; 31:31-36
11. Gulyuz Atkovar, Omer Uzel, Mahmut Ozsahin et al. Postoperative radiotherapy in carcinoma of the cervix: treatment results and prognostic factors. *Radiother Oncol* 1995; 35:198-205
12. Garzetti GG, Ciavattini A, Lucarini G et al. Recurrence patterns in locally advanced cervical carcinoma: role of nodal status and 72-kDa Methyloproteinase index. *Gynecol Oncol* 1996; 61:83-89
13. Hopkins MP, Morley G. Stage IB squamous cell cancer of the cervix: clinicopathologic features related to survival. *Am J Obstet Gynecol* 1991; 164: 1520-1529
14. Burghardt E, Baltzer J, Harjanto TA et al. Results of surgical treatment of 1028 cervical cancers studied with volumetry. *Cancer* 1992; 70:648-655
15. Boice JG, Fruchter RG, Nicastrì AD et al. Vascular invasion in stage I carcinoma of the cervix. *Cancer* 1984; 53:1175-1180
16. Himmelmann A, Willen R, losif S et al. Prospective histologic malignancy grading to indicate the degree of postoperative treatment in early cervical carcinoma. *Gynecol Oncol* 1992; 46:37-41
17. Soisson AP, Soper JT, Clarke-Person DL et al. Adjuvant radiotherapy following hysterectomy for patients with stage IB and IIA cervical cancer. *Gynecol Oncol* 1990; 37:390-395
18. Monk BJ, Cha DS, Walker JL et al. Extent of disease as an indication for pelvic radiation following radical hysterectomy and bilateral pelvic lymph node dissection in the treatment of stage IB and IIA cervical carcinoma. *Gynecol Oncol* 1994; 54:4-9
19. Hsu CT, Cheng YS, Su SC. Prognosis of uterine cervical cancer with extensive lymph node metastasis: special emphasis on the value of pelvic

- lymphadenectomy in the surgical treatment of uterine cervical cancer. *Am J Obstet Gynecol* 1972; 114:954-962
20. **Martimbeau PW, Kjorstad KE, Iverson S.** Stage IB cervical carcinoma of the cervix, the Norwegian Radium Hospital. II. results when pelvic nodes are involved. *Obstet Gynecol* 1982; 60:215-218
 21. **Fuller AF, Elliot N, Kosloff C et al.** Determinants of increased risk for recurrence in patients undergoing hysterectomy for stage IB and IIA carcinoma of the cervix. *Gynecol Oncol* 1989; 33:34-39
 22. **Burghaddt E, Pickel H, Haas J et al.** Prognostic factors and operative treatment of stages IB to IIB cervical cancer. *Am J Obstet Gynecol* 1987; 156: 988-996
 23. **Choi DH, Huh SJ, Nam KH.** Radiation therapy results for patients undergoing inappropriate surgery in the presence of invasive cervical carcinoma. *Gynecol Oncol* 1997; 65:506-511
 24. **Roman LD, Morris M, Mitchell MF et al.** Prognostic factors for patients undergoing simple hysterectomy in the presence of invasive cancer of the cervix. *Gynecol Oncol* 1993; 50:179-184
 25. **van Nagell JR, Donaldson ES, Wood EG.** The significance of vascular invasion and lymphocytic infiltration of invasive cervical cancer. *Cancer* 1978; 41:228-234
 26. **Boice JC, Fruchter RG, Nicastrri AD.** Prognostic factors in stage I carcinoma of the cervix. *Gynecol Oncol* 1981; 12:154-165
 27. **Ampil F, Datta R, Datta S.** Elective postoperative external radiotherapy after hysterectomy in early-stage carcinoma of the cervix. is additional vaginal cuff irradiation necessary? *Cancer* 1987; 60:280-288
 28. **Burke TW, Hoskins WJ, Heller PB et al.** Clinical patterns of tumor recurrence after radical hysterectomy in stage IB cervical carcinoma. *Obstet Gynecol* 1987; 69:382-385
 29. **Thomas GM, Dembo AJ, Myhr T et al.** Long term results of concurrent radiation and chemotherapy for carcinoma of the cervix recurrent after surgery. *Int J Gynecol Cancer* 1993; 3:193-198

= 국문 초록 =

근치적 절제술과 수술 후 방사선치료를 시행한 자궁경부암 환자의 치료성적, 예후인자와 실패양상

순천향대학교 의과대학 방사선종양학교실

최 두 호

목적 : 근치적 절제술과 골반림프절 절제술을 시행한 자궁경부암 환자 중에서 치료실패의 위험인자가 있어서 수술 후 방사선치료를 시행한 환자를 대상으로 치료성적, 예후인자, 실패양상을 알아보기 위하여 후향적 분석을 시행하였다.

대상 및 방법 : FIGO 병기 IB, IIA와 IIB 환자 중에서 근치적 수술과 방사선치료를 시행하고 추적조사가 가능하였던 124명을 대상으로 하였다. 환자들은 1985년 3월부터 1994년 3월까지 수술 후 방사선치료를 시행하였으며 최소 추적기간은 24개월이었다. 모든 환자는 4-MV 선형가속기를 이용한 외부방사선치료를 전골반에 50-60Gy를 조사하였고 일부 환자는 코발트를 이용한 고선량을 강내치료를 추가하였다.

결과 : 전체 환자의 5년 생존율과 5년 무병 생존율은 각각 75.4%, 73.5%였고, 단변수 분석상 5년 무병 생존율에 영향을 미치는 인자는 림프절 전이 유무, 개수와 위치, 종양의 크기, 자궁체부 침윤, 자궁주위조직 침윤, 병기, 자궁경부벽 침윤정도, 질 절제면 양성, 그리고 치료 관계 인자로 방사선량, 강내치료, 항암제 등이 통계상 유의하였으며, 다변량 분석상 림프절 전이와 종양의 크기, 질 절제면 양성 이 유의하였다.

치료 실패는 33명이었고 2명은 다른 원인으로 사망하였고 부위별로는 국소재발이 13명, 원격 전이 13명 국소-원격 동시 실패가 7명이었고 추적 종료시점까지 5명이 생존하였다. 국소재발은 병기 IIB, 림프절 전이 양성 또는 질 절제면 양성 환자에서 많이 발생하였으며 림프절 전이 음성 환자에서는 빈도는 낮았으나 원격전이가 상대적으로 더 많았다. 그리고 병기 IIB에서 5년 생존율은 56% 였고 22명 중에서 9명이 재발하였다.

결론 : 수술 후 방사선치료는 비교적 효과적인 방법이지만 다수의 재발 위험인자들을 가진 환자에게 수술 후 방사선치료만으로는 재발을 막기가 충분하지 않으므로 방사선감작제의 추가나 동시 방사선-항암치료 등의 보다 효과적인 방법이 필요할 것으로 생각되며, 수술 후 방사선치료의 효율을 정하기 위하여 무작위 표본 추출에 의한 전향적 연구가 필요하다. 그리고 병기 IIB는 항암치료와 수술 후 방사선치료를 시행해도 치료 성적이 나쁘므로 일차적으로 근치적 방사선치료를 시행해야 한다.