

The Results of Radiation Treatment in Carcinoma of the Uterine Cervix

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From July 1979 through March 1985, 112 patients with carcinoma of the uterine cervix were treated by whole pelvis irradiation and intracavitary radiation with Cs-137.

The treatment consisted of 3600rad-5200rad to the whole pelvis by parallel opposing portals, 5 days per week, 180-200rad per day. Parametrial boost with 400-800rad was given in 60 patients. 2 intracavitary Cs-137 radiation using TAO applicator were done with 7-10 days interval. Total treatment times were 40-65 days with average 52 days.

Total dose of radiation to point A varied from 6820 to 10500rad with average 8388rad and to point B from 4850 to 6899rad with average 5898rad.

All patients had follow up from 6 months to 75 months and median follow up of 31 months.

9(8%) had stage Ib, 14(12.5%) had stage IIa, 50(44.6%) had stage IIb, 33(29.5%) had stage III, 6(5.4%) had stage IV. 110 patients had squamous cell carcinoma and 2 patients had adenocarcinoma.

5 year actuarial survival rates were 61.8% for the entire group, 84.6% for stage Ib, 77.8% for stage IIa, 56.7% for stage IIb, 60% for stage III, 33.3% for stage IV. RT dose to medial parametrium (point A) below 8000rad resulted in 7/18 (38.9%) failure (=death) in contrast to 25/94 (26.5%) failure with dose over 8000rad. RT dose to lateral parametrium (point B) below 6000rad yielded 20/63 (34.9%) failure compared to 10/49 (20.4%) failure with dose over 6000rad.

Poor survival group of age were between 40-49 years with failure of 14/41 (34.1%). There was no increased failure rate below age of 40 with failure of 2/11 (13.9%).

The results suggest that survival is as good as other published data, and that higher doses over 8000rad to point A and 6000rad to point B should be delivered.

Key Words: Carcinoma of the uterine cervix, Radiation treatment, TAO applicator, 5 year actuarial survival rate.

INTRODUCTION

Carcinoma of the uterine cervix is the most prevalent cancer among Korean women. Cure rate of the cervix ca is one of the highest in cancer treatment. Radiation Therapy with radium was effectively used in the treatment of cancer in the early 1900s. In the late 1920s and 1930s, external irradiation with high energy x-ray was introduced and was applied

to several types of cancer.

Combination of intracavitary radium and external irradiation were used to cervix cancer, resulting in high radiation dose to pelvic wall and parametrium. In 1950s external radiation therapy sources such as Co-60 and linear accelerator was introduced and recent improvement in dosimetry with computerized

treatment planning resulted in increased survival rate and decreased complication following radiation therapy. Cure rate was improved particularly in stage IIb and stage III.

In stage I and IIa majority of patients were treated by surgery, but it has been well established that radiation therapy also had comparable results.

The aim of this study was to evaluate survival related factors in patients with cervix ca who treated with definitive radiation therapy and to help improving results for the future.

MATERIAL AND METHODS

Between July 1975 and March 1985, total 228 patients were registered for radiation therapy at Hanyang University Hospital. 70 patients received RT postoperatively, 10 for recurrent cervix ca, 28 did not finish recommended dose, 7 for curative external RT only, and 1 had 2 intracavitary radiation without external radiation. This analysis excluded above patients and included standard radiation in terms of combination of intracavitary and external radiation.¹⁾ Total 112 patients were evaluated. As of September 1985, all 112 patients (100%) were followed. Follow up period ranged from 6 month to 6 yr 3 months with median follow up period of 2 yr 7 months. Patients were staged according to FIGO classification. 110 patients were squamous cell ca and 2 patients were adenoca.

There were 9(8%) stage Ib; 14(12.5%) stage IIa; 50(44.6%) stage IIb; 33(29.5%) stage III; and 6(5.4%) stage IV. Table 1 summarized distribution of patients by stages. Early stage of Ib and IIa were 20%, and stage IIb and III were 74.1% of patients.

The reasons of radiation therapy rather than surgery in stage Ib were summarized on Table 2. 3 patients refused to have surgery, and each 2 patients had hypertension, cardiac disease, and obesity. Age distribution at diagnosis was shown in Table 3. Median age of patients was 51 yr 5 month. 9.8% patients were under age 40, and majority of patients (73.2%) ranged in age between the forties and the fifties. 1 case was under age 20 years.

TREATMENT METHOD

As Paterson²⁾ suggested, external radiation followed by 2 intracavitary radiation was delivered. Dosimetry was done by manual isodose curve to the point A and point B. External radiation was given to

whole pelvis with parallel opposing portals, 180-200 rad per day using Co-60 with total 3600-5200 rad. Midline was shielded with 4 cm and additional 600-1,000 rad to the pelvic side walls after whole pelvis dose of 4,000-4,200 rad.

Intracavitary radiation was given with TAO applicator (Kenko Co. Japan).³⁾ 2-3 Cs-137 sources (20mg radium equivalent per source) in tandem and 1 source in each ovoid were loaded. Treatment time was 22-28 hrs as an inpatient. All of the patients ex-

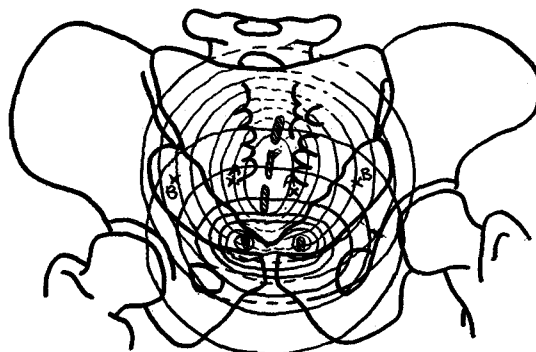


Fig. 1. Isodose curve of TAO applicator with tandem (20mg x 3) and ovoid (20mg each) sources.

Table 1. Carcinoma of Uterine Cervix: Distribution by Stages

Stage	# of patients	%
Ib	9	8.0
IIa	14	12.5
IIb	50	44.6
III	33	29.5
IV	6	5.4
Total	112	100.0

Table 2. Reason of RT rather than Surgery in Stage Ib

Case	Age(yr)	Reason of RT	Survival status
1	59	Obesity	dead, 5 yr 3 mo
2	63	Refuse surgery	dead, 2 yr 4 mo
3	47	Refuse surgery	alive, 5 yr 5 mo
4	47	RBBB of heart	alive, 5 yr 2 mo
5	44	Refuse surgery	alive, 5 yr 2 mo
6	57	Obesity	alive, 3 yr 2 mo
7	42	Hypertension	alive, 2 yr 10 mo
8	48	Hypertension	alive, 1 yr 5 mo
9	70	Myocardial isch	alive, 8 mo

cept 1 case had 2 intracavitary treatment with 7-12 days interval. Standard isodose curves of TAO applicator were used for calculation of point A and point B,⁴⁾ but RT dose to the rectum and bladder were not calculated (Fig. 1).

Total treatment time of external radiation and intracavitary treatment were 56 days (7 wks \pm 1 wk).

Total radiation dose to point A ranged from 6820

rad to 10,500 rad and to point B from 4850 rad to 6899 rad.

RESULTS

Total 32 patients after curative radiation were

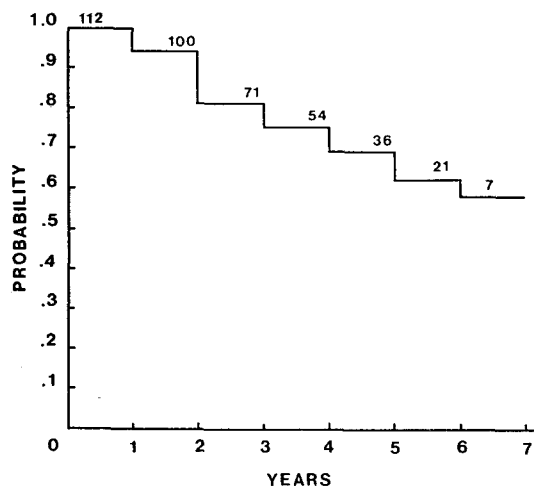


Fig. 2. Actuarial Survival of Total Patients

Table 3. Distribution by Age

Age	# of Pts	%
<20	1	0.9
20-29	0	0
30-39	10	8.9
40-49	41	36.6
50-59	41	36.6
60-69	18	16.0
≥ 70	1	0.9
Total	112	100.0

Table 4. Patient Survival Status According to Stages

	Ib	IIa	IIb	III	IV	Total
#	9	14	50	33	6	112
Alive	7	12	34	25	2	80
Dead	2	2	16	8	4	32

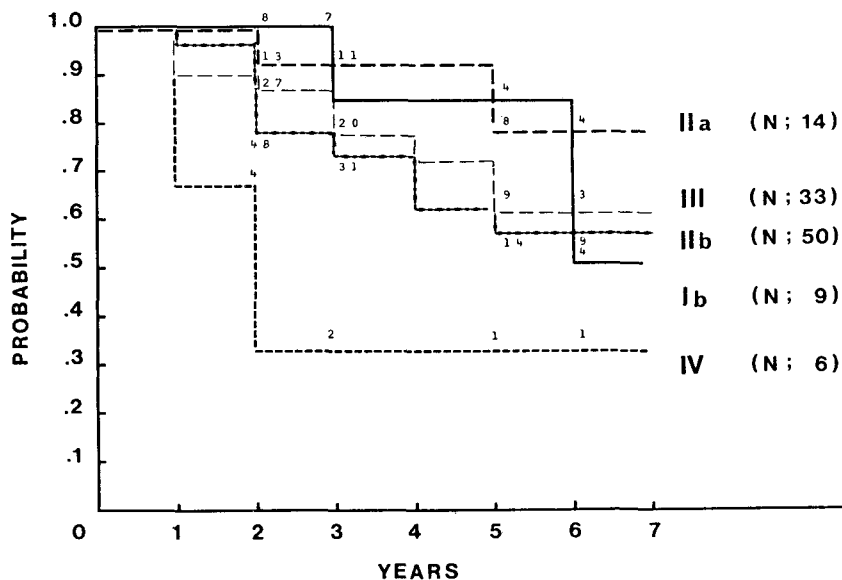


Fig. 3. Actuarial Survival of Each Stage

dead. The patient's death by stages were summarized on Table 4.

The actuarial 5 year survival rate for total patient was 61.8%; for stage Ib, 84.5%; for stage Ila, 77.8%; for stage lib, 56.7%; for stage III, 60.6%; and for stage IV, 33.3% (Table 5, Fig. 2, Fig. 3).

The correlation of radiation dose with failure (= death) rate was analyzed on Table 6 and 7. 25 out of 94 (26.5%) receiving over 8,000 rad to the point A were dead in contrast to 7 out of 18 (38.9%) among those treated under 8,000 rad were dead.

There were 10 death out of 49(20.4%) receiving dose greater than 6,000 rad and 22 death out of 63(34.9%) less than 6,000 rad to the point B. Over

Table 5. 5 Year Actuarial Survival Rates

Stage	# of Pts	%
Ib	9	84.6
Ila	14	77.8
lib	50	56.7
III	33	60.6
IV	6	33.3
Total	112	61.8

Table 6. RT Dose to Point a by Stages

	Dose (rad)			
	≤6999	7000-7999	8000-8999	≥9000
Ib		5(2)	4	
Ila		2	11(1)	1(1)
lib	1(1)	3(1)	38(12)	8(2)
III	2	4(2)	23(4)	4(2)
IV		1(1)	3(2)	2(1)
Total	3(1)	15(6)	79(19)	15(6)
	18(7)		94(25)	

() # of dead patients

Table 7. RT Dose to Point B by Stages

	Dose (rad)		
	≤4999	5000-5999	≥6000
Ib	1(1)	7(1)	1
Ila		10(2)	4
lib		27(10)	23(6)
III		15(5)	18(3)
IV		3(3)	3(1)
Total	1(1)	62(21)	49(10)
	63(22)		

() # of dead patients

6,000 rad, there was 26.1% death in stage lib, 16.7% in stage III, in contrast to 37% in stage lib and 33% in stage III under 6,000 rad. This suggests that patient with higher doses of radiation to point B would yield better survival. with age was analyzed.

Table 8 shows the correlation of death rate with age. Highest failure group was 40-49 years with 33.9%. Under 40 years 18.2% of patients failed.

Cumulative death rate showed 21.9% in 1 year, 59.3% in 2 year, 75.3% in 3 years, 87.5% in 4 years. Majority of patients who failed died within 4 years.

DISCUSSION

Although radical surgery is well known mode of therapy for early cervical cancer in our country, radical radiation has the comparable cure rate. Using high energy x-ray or γ -ray machine and com-

Table 8. Patients Survival Status According to Ages

Age	# of death	% of death	Average
<40	2/11	18.2	
40-49	14/41	34.9	
50-59	12/41	29.3	
≥60	4/19	21.2	
			28.5

Table 9. 5 Yr Survival Rates of Cancer of the Cervix Treated by Radiation Therapy

Author	Stage (%)				Ref #
	I	II	III	IV	
Marchial (1973)	88.0	61	35	19	16
Fletcher (1971)	91.5	A-83.5 B-66.5	40.5	14	10
Perez (1983)	87	A-73 B-68	44	—	9
Masubuchi (1969)	88.2	68.7	43.1	14.8	17
Brand	71.5	57.1	40.1	—	11
Thar (1982)	77	A-73 B-57	A-26	30	12
Hanyang Univ Hosp (1985)	84.6	A-77.8 B-56.7	60.6	33.3	

puterization of dosimetry system have resulted in considerably improves survival rates and lower morbidity. Great controversy has surrounded the selection of therapy with early stage of cervix cancer. Morbidity and complication rate of surgery or radiation are low, therefore either mortality is an acceptable form of treatment.

Curative radiation therapy alone is the established and effective form of treatment for patient with stage Ib, III or IV. When patient with stage Ib, IIa had high risk of surgery such as hypertension, cardiac problem, or patient refused to have a surgery, curative radiation was used.

van Nagell⁵⁾ reported 24% of recurrence following radical hysterectomy in patients with stage Ib with 2-5cm in diameter of tumor as compared to 11% following radiation therapy. Radical surgery is as effective as irradiation only with 2cm less in diameter.

Rutledge⁶⁾ and Mendenhall⁷⁾ reported combined surgery and radiation was more effective than RT alone with lesions greater than 5-6cm in diameter. Gallion⁸⁾ reported combined surgery and radiation was effective treatment in barrel shaped cervix cancer.

This study showed 84.5% of 5 year survival rate in stage Ib, which is similar results of Perez's⁹⁾ data with 87% and slightly lower than Fletcher's¹⁰⁾ 91.5%, and higher results than that of Brand,¹¹⁾ 71.5% and that of Thar,¹²⁾ 77%. But their data had longer median follow up.

In our country 3 year survival rates were reported as 77.8%-100%,^{13,14)} but follow up period and follow up number were not adequate.

In stage IIa, 5 year survival rate was 79.8%. Others reported from 73% to 83.5%.⁹⁻¹²⁾ 3 year survival was reported as 77.4%-78% in our country.^{13,14)}

In stage III, 5 year survival rate was 60.3%, which was a little higher survival rate than stage IIb. Our results were slightly higher than other reported data of 22-24% in Western^{9,10,11,12)} and 39.5-46.3% in our country.^{13,14)} van Nagell¹⁵⁾ reported only 25% of patient had correct staging in stage III due to subjective discrepancy of accuracy of staging.

In stage IV 33.3% of patients had 5 year survival, which was similar results in other reports with 14-33.3%, but patients number were too small to have any evaluation of survival.

Table 9 summarized 5 year survival rate compared with other authors.^{9-12,16,17)} Our results showed average survival rate in stage Ib, IIa and IIb, but higher survival rate in stage III as compared to others.

Correlation of dose and survival to the point A showed lower failure rate with 26.5% over 8,000 rad than with 38.9% under 8,000 rad. Perez reported 17.7% failure rate in stage IIb with dose to point A below 9,000 rad vs 10.2% above 9,000 rad, and in stage III failure rate of 39.5% below 9,000 rad and 22.7% above 9,000 rad. He suggested that above 9,000 rad be recommended dose. Chism et al.¹⁸⁾ indicated that in stage II the recurrence rate was 44% with dose below 6,000 rad, 22% with dose 6,000-7,000 rad, and 15% with dose over 7,000 rad. In stage III the pelvic failure rate was 80% with dose below 6,000 rad, 63% with dose of 6,000-8,000 rad and 50% with higher doses. He suggested that higher doses of radiation would result in increasing tumor control. Our results showed remarkable decrease in death rate in patients with radiation dose over 8,000 rad to point A and are comparable to others.

Jampolis et al.¹⁹⁾ analyzed the results and reported the cause of pelvic failure was due to less than optimal radiation dose of 5,000 rad to point B in over 70% of patient among the failure in stage Ib and IIb, and suboptimal dose with less than 6,000 rad caused 40% of patient among failure in stage III. Our analysis suggested higher dose of radiation was correlated with lower death rate.

Rectal injury by radiation dose was previously reported²⁰⁾ and grade 3 injury which required colostomy was 2.1% and grade 2 which required medical treatment was 17%. Analysis of complication was not done in this paper.

Failure rate by age showed 34% in 40-49 years in contrast to 18.9% below 40 years. Lindell²¹⁾ and Einhorn²²⁾ reported poor prognostic age was below 40 years but our result was not shown any poor prognosis.

SUMMARY

From July 1979 through March 1985, 112 patients with carcinoma of the uterine cervix who were treated by standardized method of radiation consisting of whole pelvis irradiation and 2 intracavitary radiation with Cs 137 sourced were analyzed retrospectively at Hanyang University Hospital.

1. All patient had follow up, 9(8%) had stage Ib, 14(12.5%) stage IIa, 50(44.6%) stage IIb, 33(29.5%) stage III, and 6(5.6%) stage IV.

2. 2 patients were adenocarcinoma and 110 patients were squamous cell carcinoma.

3. 5 year actuarial survival rates were 61.8% for the entire group, 84.6% for stage Ib, 77.8% for stage IIa, 56.7% for stage IIb, 60.6% for stage III, 33.3% for stage IV.

4. RT dose to medial parametrium (point A) below 8000 rad resulted in 7/18(38.9%) failure (=death) in contrast to 25/94 (26.5%) failure with dose over 8,000 rad. RT dose to lateral parameterium (point B) below 6,000 rad yielded 20/63(34.9%) failure compared to 10/49(20.4%) failure with dose over 6,000 rad.

5. Poor survival group of age were between 40-49 years.

6. Cumulative death rate of patients who failed after treatment were 21.9% in 1 year, 59.3% in 2 year, 75% in 3 year, and 87.5% in 4 years.

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국문초록=

자궁경암의 방사선치료 성적

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이 명 자 · 김 정 진

1979년 7월부터 1985년 3월까지 한양대학병원에서 자궁경암의 표준화된 방사선치료기준, 즉 전 골반의 외부방사선조사와 강내조사의 병용요법으로 112명의 환자를 치료하였다. 전원이 추적가능하였고 6~75개월의 추적기간에 평균은 31개월이었다.

2명이 선암이고 110명은 편평상피 세포암이었고 I_b병기 9명(8%), II_a병기 14명(12.5%), II_b병기 50명(44.6%), III병기 33명(29.5%), 그리고 IV병기는 6명(5.4%)이었다.

연령분포는 30대 10명(8.9%), 40대, 50대가 다같이 41명(36.6%)씩으로 73.2%이고 60대 이상이 19명(17%)이며 특수하게 20세미만이 1예 있었다.

방사선치료는 전 골반에 평행대향 조사야로 180~200 rad를 주 5회 4,000~4,200 rad 조사하였고 중앙부 4 cm를 차폐하고 600~1,000 rad를 자궁방결합조직에 추가 조사하였다. 강내조사는 Cs-137 소선원(20 mg 라디움당량)을 자궁강내 2~3개 질강내 2개를 TAO Applicator로 삽입하였고 7~12일 간격으로 2회 시행하였다. 치료기간은 평균 52일간이고 40~65일에 걸쳐서 시행되었다.

A점에 조사한 방사선량은 6,820~10,500 rad로 평균 8,388 rad이고 B점에는 4,850~6,899 rad로 평균 5,898 rad이었다.

생명표 5년 생존율(actuarial 5 year survival rate)은 전체로 61.8%이고, I_b병기에서 84.6%, II_a병기는 77.8%, II_b병기는 56.7%, III병기는 60.6%, 그리고 IV병기는 33.3%이었다.

A점의 방사선량이 8,000 rad 이하일 때는 7/18(38.9%)의 실패율이었고 이에 비해서 8,000 rad 이상일 때는 25/94(26.5%)의 실패율이었다. 또 B점 선량으로 보면 6,000 rad 이하에서 20/63(34.9%)의 실패율에 비하여 6,000 rad 이상일 때는 10/49(20.4%)의 실패율이었다.

연령별로는 40~49세에서 실패율(14/41 24.1%)이 많았다.

본 성적으로 보아서 생존율은 여러 저자들과 큰 차이가 없음을 알 수 있었고 A점 선량은 8,000 rad 이상, B점은 6,000 rad 이상이 조사되어야 적정선량이 됨을 시사해 주고 있다.