

The Results of Curative Radiation Therapy for 49 Patients of the Uterine Cervical Carcinomas*

Mi Ryeong Ryu, M.D., Yeon Sil Kim, M.D., Byung Ock Choi, M.D.
Sei Chul Yoon, M.D., Kyung Sub Shinn, M.D.
Sung Eun Namkoong, M.D.** and Seung Jo Kim, M.D.**

*Department of Therapeutic Radiology, Obstetrics and Gynecology**
Catholic University Medical College, Kangnam St. Mary's Hospital, Seoul, Korea*

Fifty patients with carcinoma of the uterine cervix received curative radiotherapy by external irradiation of the whole pelvis and intracavitary radiation at the Department of Therapeutic Radiology, Kangnam St. Mary's Hospital from September, 1983 to October, 1986.

External beam whole pelvic irradiation was done first up to 4500-5940 cGy in 5 weeks to 6.5 weeks, followed by an intracavitary radiation. Total dose of radiation to point A varied from 6500 cGy to 11344 cGy (average 6764 cGy).

Of the 50 patients, one patient was lost to follow up and follow up period of the remaining 49 patients ranged from 3 months to 93 months (median 32 months). According to FIGO classification, 6 (12.2%) were in stage Ib, 6 (12.2%) in stage IIa, 25 (51%) in stage IIb, 7 (14%) in stage III, and 5 (10.2%) in stage IV. Age of the patients ranged from 33 to 76 years (median 60 years). Pathologically, forty six (94%) patients had squamous cell carcinoma, 2 (4%) had adenocarcinoma, and 1 (2%) had adenosquamous cell carcinoma.

Overall response rate was 84%. 5-year survival rate was 49% for entire group (75% for stage Ib, 83% for Stage IIa, 42.5% for stage IIb, 25% for stage III, 40% for stage IV).

Complications were observed in 11 (22.4%) patients, who revealed rectal complications with most common frequency. Others were self limiting trifle ones such as wet desquamation, fatigue, mild leukopenia, etc.

The correlation of the survival rate with various factors (age, dose, Hb level, pelvic lymph node status, performance status, local recurrence) was evaluated but showed no statistical significance except the age and local recurrence in this series; survival of patients less than 50 years of age was worse than that of the older, and the presence of local recurrence had worse prognosis ($p < 0.05$).

Key Words: Carcinoma of the uterine cervix, Curative radiotherapy, Intracavitary radiation, 5-year survival rate, Complications

INTRODUCTION

Carcinoma of the uterine cervix is one of the most common cancer in Korean women and is highly curative than any other plague cancer.

High curability of the uterine cervical cancer was reported already in early 1900s¹⁾. Cervical carcinoma spreads slowly via predictable pathway from cervix, through surrounding lymphatics, to the pelvic lymph nodes.

It tends to confine itself to the pelvis for a considerable period of time, thus making it amenable to the locoregional therapy of irradiation.

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Radiation therapy has firmly established its role in the treatment of carcinoma of the uterine cervix either alone for any clinical stage tumor or combined with surgery for selected patients with stage I and IIa tumor.

Currently the two main modalities of irradiation are external photon beam and intracavitary irradiation. Especially by intracavitary radiation, adjacent normal organs such as bladder, rectum, and small bowel are able to be escaped from the radiation damage even with considerably high dose irradiation.

The aim of this paper is to investigate the clinical results after treatment, factors influencing on survival rate and treatment related complications in patients who had cervical cancer, followed by

external radiotherapy (ERT) and intracavitary radiation (ICR).

MATERIALS AND METHODS

From September 1983 to October 1986, fifty patients with previously untreated carcinoma of the uterine cervix were treated by combination of external radiotherapy (ERT) and intracavitary radiation (ICR) at the Department of Therapeutic Radiology, Kangnam St. Mary's Hospital.

The distribution of patients according to FIGO stage, age, performance status, pelvic LN status, and Hb level are shown in Table 1. Pathologically, 46 (94%) patients had squamous cell carcinoma, 2 (4%) patients had adenocarcinoma, and 1 (2%) had adenosquamous cell carcinoma.

Follow up was done in 49 patients and follow up period was 3 to 93 months (median; 32 months).

The treatment consisted of 4500 cGy-5940 cGy in 5 to 6.5 weeks to the whole pelvis using 6 MV X-ray by parallel two opposing or 4 oblique box portals with daily 180-200 cGy, 5 times per week, and then, an intracavitary Cs-137 irradiation using Fletcher-Suit applicator was performed with 2 to 12.9 week intervals after ERT.

The field of external radiation therapy included all primary lesions including contiguous pelvic lymph nodes (LNs), and radiation dose was determined by the stage of the disease and performance

Table 1. Patient Characteristics

	No. of patients (%)
FIGO stage	
Ib	6 (12.2)
IIa	6 (12.2)
IIb	25 (51)
III	7 (14)
IV	5 (10.2)
Age	
31-40	4 (8)
41-50	6 (12.2)
51-60	17 (34.7)
61-70	20 (40.8)
71-	2 (4)
Karnofsky Performance status	
PS < 70	4 (8.2)
70 ≤ PS < 80	33 (67.3)
80 ≤ PS < 90	11 (22.4)
90 ≤ PS	1 (2)
Hemoglobin Level	
< 10	4 (8.2)
10.1-11	5 (10.2)
11.1-12	20 (40.8)
12.1-13	16 (32.7)
13.1-	4 (8.2)
Status of pelvic lymph node	
positive	17 (34.7)
negative	32 (65.3)
Total 49 (100)	

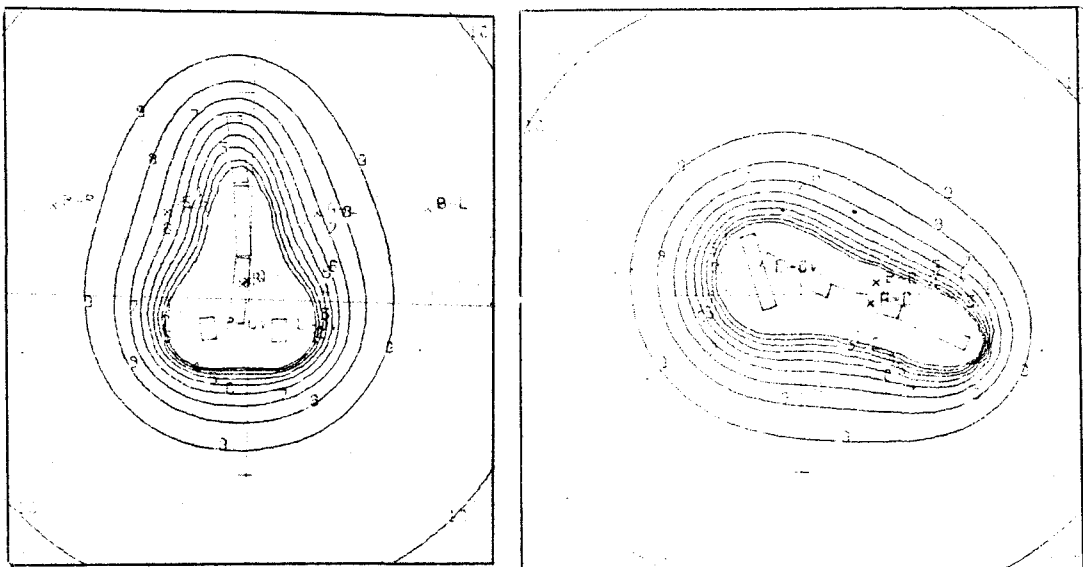


Fig. 1. Isodose distribution of intracavitary radiation.

status of patients.

The reference point of intracavitary radiation dose are point A & B, maximum bladder and rectal dose. Average dose to point A was 3408 cGy and average dose rate was 73.5 cGy/hr. Mean bladder and rectal dose were 1620 cGy and 1734 cGy, respectively. Therac 2000 (NEC) was utilized as a planning computer. The example of computer-generated isodose curve for intracavitary irradiation is shown in Fig. 1.

RESULTS

1. Survival Rates

5-year survival rate (5YSR) was obtained in 49 patients by Kaplan-Meier method. Overall 5YSR and 5-year disease free survival rate were 49% and 45%, respectively (Fig. 2). 5YSR was 75% in stage Ib, 83% in stage IIa, 42.5% in stage IIb, 25% in stage III, 40% in stage IV (Fig. 3).

The correlation of survival rate with various factors such as age, radiation dose, Hb level, pelvic LN status, performance status, and local recurrence are shown in Fig. 4~9. Among above factors, age and local recurrence were the only significant factors influencing on survival ($p < 0.05$); survival of the patients less than 50 years old was worse than that of the older, and the presence of local recurrence had worse prognosis.

2. Pattern of Failure

Overall response rate was 84%. Table 2 indicates the response rate by the stage. The overall disease control rate was 80%; five (10.2%) patients had locoregional failure and five (10.2%) patients developed distant metastasis.

The mean duration of local recurrence was 14.5 months.

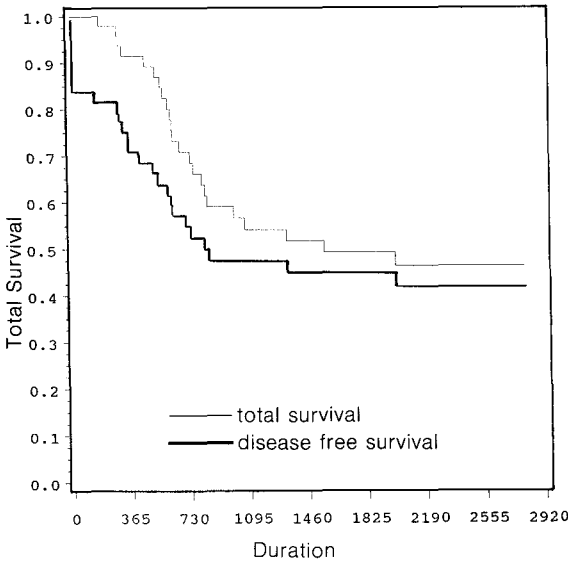


Fig. 2. Total survival and disease free survival.

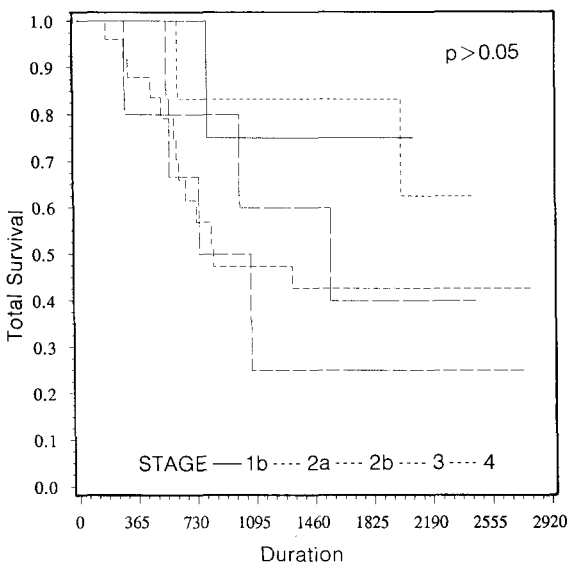


Fig. 3. Total survival by FIGO staging.

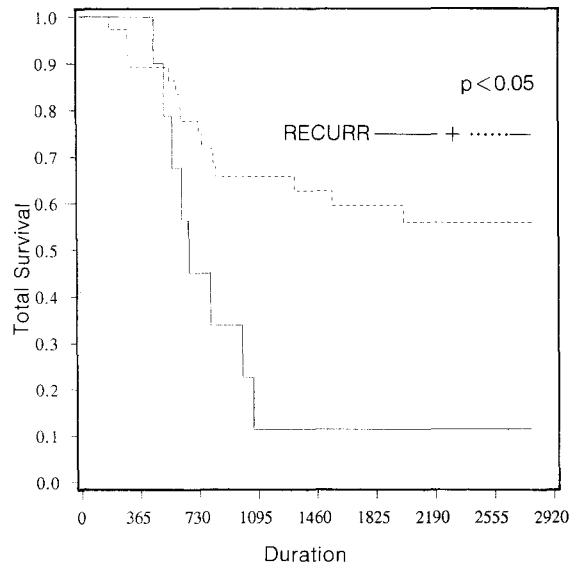


Fig. 4. Total survival by presence or absence of recurrence.

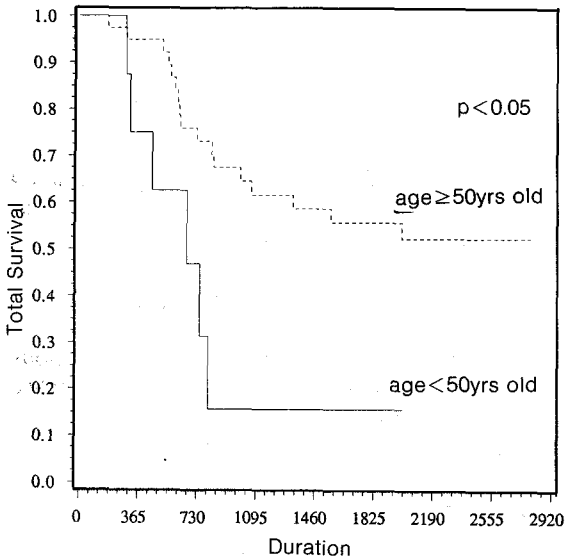


Fig. 5. Total survival by age.

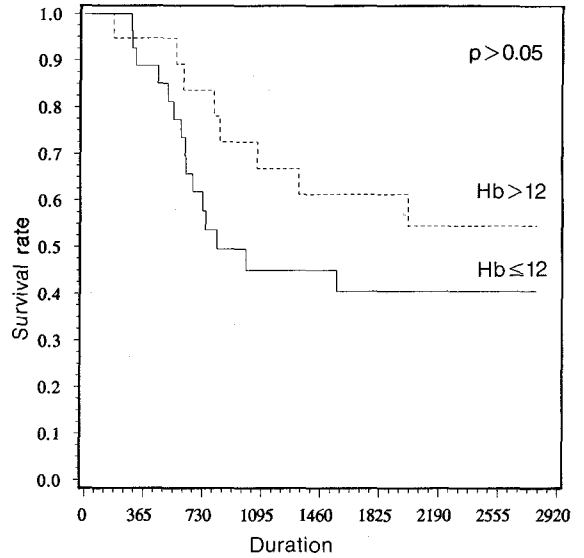


Fig. 7. Total survival by Hb level.

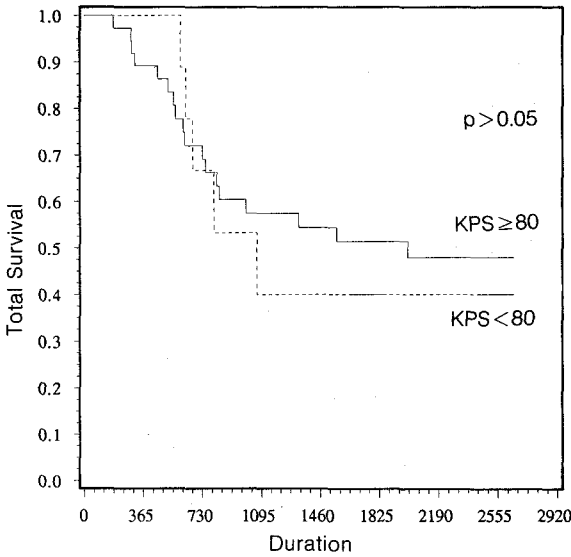


Fig. 6. Total survival by performance status.

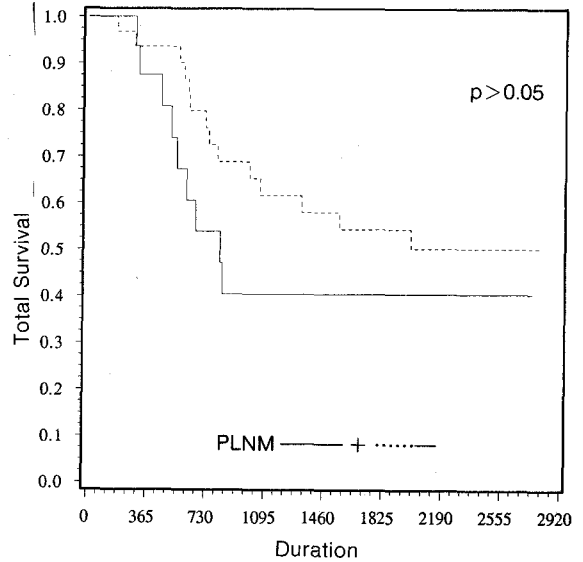


Fig. 8. Total survival by pelvic LN status.

Table 2. The Response Rate by FIGO Classification (%)

Stage	response (+)
Ib	6/6 (100)
Ila	6/6 (100)
Iib	22/25 (88)
III	4/7 (57)
IV	3/5 (60)
Total	41/49 (84)

The locoregional failure by stage is shown in Table 3.

Two patients had distant metastasis in paraaortic node and three in supraclavicular lymph node.

Table 4 shows the comparison of survival between recurrence or metastasis and age.

3. Complication

Radiation induced complications were obser-

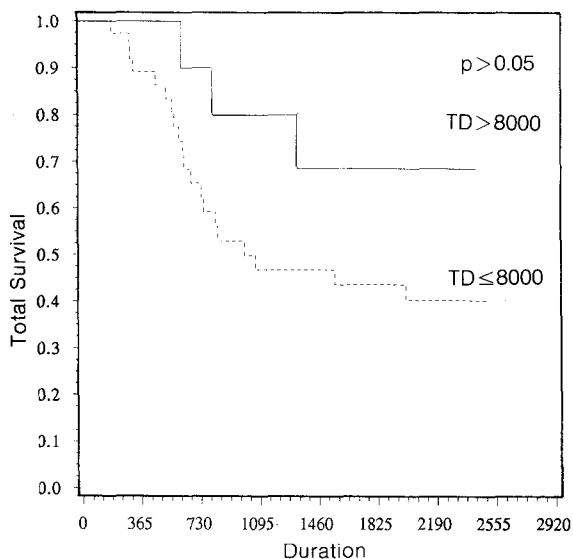


Fig. 9. Total survival by total RT dose.

Table 3. Locoregional Failure by FIGO Classification (%)

Stage	Locoregional failure	Distant metastasis
Ib	0/6 (0)	2/6 (33.3)
Ila	0/6 (0)	0/6 (0)
Iib	3/25 (12)	2/12 (16.7)
III	1/7 (14.3)	1/7 (14.3)
IV	1/5 (20)	0/5 (0)
Total	5/49 (10.2)	5/49 (10.2)

Table 4. The Comparison of Survival between Recurrence or Metastasis and Age (%)

Age	<50	≥50
5YSR	15.6%	55.7%
Locoregional recur	3/10 (30)	2/39 (5)
Distant metastasis	2/10 (20)	3/39 (7.7)

YSR: year survival rate

ved in 11 patients (22.4%); cystitis in 3 patients, proctitis in 6 patients, lymphedema in 1 patient, and adhesive ileus in 1 patient.

We analyzed the relationship between total treated dose and rectal complication (Table 5). Two out of 30 (6.7%) patients who received less than 7000 cGy to the rectum, and 4 out of 19 (21.1%) patients who received above than 7000 cGy showed rectal complication.

So there was a close relationship between rectal dose and rectal complication even though there was no statistical significance in this series ($p > 0.05$).

DISCUSSION

Radiation therapy is the effective treatment in the uterine cervical cancer, especially in more than stage Ib and is consisted of external radiation therapy with high energy X-ray or gamma-ray and intracavitary radiation using Cesium or Radium.

Since intracavitary radiation had been introduced in early 1900s, now a days, improved skill and mechanics to treat the uterine cervical cancer resulted in increased number of cure of the disease.

Paterson and Russel³⁾ demonstrated that an initial attempt of external radiation therapy to the pelvis followed by successive secondary intracavitary irradiation indicates better results to

Table 5. The Relationship between Total Treated Rectal Dose and Complication (%)

Total rectal dose	complication (+)
<7000	2/30 (6.7)
≥7000	4/19 (21.1)
Total	6/49 (12.2)

Table 6. 5Yrs of Cancer of the Cervix Treated by Radiation Therapy

Author	Stage (%)				Ref.
	I	II	III	IV	
Marcial (1973)	88.0	61	35	19	4
Fletcher (1971)	91.5	83.5 (A) 66.5 (B)	40.5	14	5
Perez (1983)	87	73 (A) 68 (B)	44	-	6
Hanyang Univ Hos (1985)	84.6	77.8 (A) 56.7 (B)	60.6	33.3	7
Akine (1990)	85 (B)	65 (A) 57 (B)	41 (B)	41 (B)	4 (A) 11 (B)
SNUH (1992)	81.8 (B)	72.1 (A) 67.0 (B)	66.7 (A) 51 (B)	33.3 (A)	8, 9
Kangnam St. Mary's Hosp	75 (B)	83 (A) 42.5 (B)	25	40	

*SUNH; Seoul National University Hospital

control the disease, because the external pelvic irradiation can improve the geometry of the intracavitary application into the case with bulky cervical lesions.

In Table 6, we summarized 5-year survival rate of our series compared with other authors^{2,4-9}). Our series showed 49% of 5-year survival rate in all stages and it seemed to be somewhat lower than that of other reports.

Between ERT and ICR there should be an interval of 1 to 2 weeks during which radiation-induced reactions to normal tissue should subside¹⁰). Interval longer than three weeks allows tumor regrowth and is associated with poor outcome¹¹). The mean interval between ERT and ICR was 5.9 weeks in our series.

The prognostic factors associated with improved outcome such as age, radiation dose, Hb level, pelvic LN status, performance status, and local recurrence were also evaluated. Among them, age and local recurrence were the only significant prognostic factors ($p < 0.05$) and the others had little statistical significance ($p > 0.05$).

Though many papers argued on whether the age of the patient had influenced upon the survival rate or not, in our series, we found the younger, the poorer prognosis; especially so were the younger who had higher incidence of local and distant failure resulted from poor histologic grade¹²⁻¹⁴).

In general, higher dose of irradiation yield increasing tumor control. Perez⁹) reported that higher doses of radiation yielded higher local control rates in all stages except Ib. They also observed higher survival rates in patients with higher parametrial doses in stage IIb and III.

We could not analyze any obvious relationship between the amount of radiation dose and local control rate or survival rate, due to uneven distribution regard to comparable points and small numbers of total patients in this study, which was not prospectively controlled.

Kottmeier and Gray¹⁵) demonstrated a relationship between major complication and the dose treated to the rectum and the bladder. Similar results were shown in Perez¹⁶); when less than 8000 cGy was given, the complications were observed in less than 5% of patients. Our data showed that the rectal complication seemed to be more related closely with total amount of irradiation dose than that of bladder, even though the statistical insignificance ($p > 0.05$).

The goal of therapy of patients with cancer is to obtain the highest possible tumor control and long

term survivals with lowest incidence of major complication and minimal interference with anatomical and functional integrity.

From this study, we admit some problems in retrospective analysis in which various factors to affect prognosis were not taken into consideration in a general analysis.

To evaluate the relationship between outcome and related various factors¹⁷), more randomized prospective trial of large numbers is required and to improve the results, careful choice of treatment schedule is also needed in the future.

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== 국문초록 ==

자궁 경부암의 근치적 방사선 치료 효과

— 49 예의 분석 —

가톨릭대학교 의과대학 강남성모 병원 치료방사선과, 산부인과학교실*

유미령 · 김연실 · 최병옥 · 윤세철
신경섭 · 남궁성은* · 김승조*

1983년 9월 부터 1986년 10월 까지 37개월 동안에 강남성모병원 치료방사선과에서 50명의 자궁경부암 환자가 완치목적으로 골반부위에 외부방사선치료 및 자궁강내 방사선치료를 받았다. 외부방사선치료는 4500 cGy/5주에서 5940 cGy/6.5주를 골반부위에 먼저 시행하였고 강내방사선치료를 이어서 시행하였으며, A 점에 도달한 총 치료 선량은 6500 cGy 에서 11344 cGy로 평균 6764 cGy 였다.

50명의 환자중 1명이 추적조사에서 제외되었으며, 나머지 49명의 환자를 대상으로 3개월에서 93개월 까지 추적조사하였는데, 중간 추적조사 기간은 32개월 이었다. FIGO 분류에 따라 병기별로 보면, 1기가 6명(12.2%), 2a기가 6명(12.2%), 2b기가 25명(51%), 3기가 7명(14%), 그리고 4기가 5(10.2%)명 이었다. 환자의 나이는 33세에서 76세까지의 분포를 보였으며(중앙 연령, 60세), 병리조직학적 분류로는 편평상피암이 46명(94%), 선암이 2명(4%), 그리고 편평상피선암이 1명(2%)이었다.

전반적인 반응율은 84%였고, 5년 생존율은 49%였다. (병기별 5년생존율은 1b기가 75%, 2a기가 83%, 2b기가 42.5%, 3기가 25%, 4기가 40%였다.) 합병증은 11명(22.4%)에서 발생하였고, 직장내 합병증이 가장 흔한 합병증이었으며, 나머지는 사소한 일과성의 자연치유되는 질환들이었다.

생존율과 여러 인자들(나이, 방사선 치료선량, 헤모글로빈치, 골반임과절 전이상태, 전신상태, 그리고 국소 재발 유무)과의 관련성에 대해 분석한 바, 나이와 국소재발유무를 제외하고는 모두 통계학적으로 유의하지 않게 나왔으며, 50세 미만의 생존율이 50세이상의 생존율보다 더 나빴고($p < 0.05$), 국소재발 존재시 생존율이 더 나빴다($p < 0.05$).