

Radical Radiotherapy for Carcinoma of the Prostate

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Purpose : To evaluate effect and tolerance of external beam radiotherapy for carcinoma of the prostate and define the optimal radiotherapeutic regimen.

Materials and Methods : We retrospectively analyzed the records of 60 patients with prostate cancer who were treated with external beam radiotherapy with curative intent in our institution between September, 1987 and March, 2000. Histologic diagnosis was established by transurethral resection or ultrasonography guided biopsy. The major presenting symptoms were a nodule at routine prostatic examination and frequency and urgency of urination, along with dysuria. The median age was 63 years with range of 51 to 87 years. There were 6 patients in Stage A, 20 in Stage B, 26 in Stage C, and 8 in Stage D1. All patients were treated with megavoltage equipment producing 10 MV photons. The 4 field pelvic brick technique was used to a dose of 45 Gy or 50.4 Gy at 1.8 Gy per day in 5 to 6 weeks, after which a small boost field was delivered 2.0 Gy per day to a total dose of 66 to 70 Gy. The follow-up period ranged from 1 to 8 years.

Results : Actuarial 5-year and 7-year survival rates for Stage A, B, C, and D1 were 100% and 84%, 83% and 72%, 67% and 54%, and 40% and 30%, respectively. The corresponding 5-year and 7-year relapse free survival rates were 84% and 84%, 77% and 67%, 48% and 40%, and 33% and 25%, respectively. Relapse free 5-year survival rates for Stage B were 80%, 80%, and 50% for well, moderately, and poorly differentiated tumors, respectively. These were 64%, 44%, and 33% for Stage C, respectively. The local control rates at 5 years were 84%, 85%, 78%, and 60% for Stage A, B, C, and D1, respectively. Mild to moderate complications were observed in 22% of patients. Severe complications requiring surgical procedures were documented in only 3% of patients.

Conclusion : This study confirms that external beam irradiation is an effective and safe treatment for prostatic cancer, providing long-term local control and good survival with acceptable complications.

Key Words : Prostate cancer, Radiation therapy

INTRODUCTION

Prostate cancer is a relatively uncommon malignant tumor in Korea. However, incidence of this tumor has increased over the past 20 years partly due to increase of the aging population. Approximately 50% of patients with prostate cancer will be shown to have metastases to lymph node or distant organ at diagnosis and will be treated with hormonal manipulation, reserving intervention for the onset of symptoms. The management of the remaining 50%, classified as Stage A, B, or C disease, remains controversial. Radical

surgery or radical radiotherapy is strongly favored and patient selection factors continue to cloud the effect of intervention on survival.¹⁻⁵⁾

The advent of megavoltage radiation therapy led several groups to see if the poor results obtained in the kilovoltage era could be improved. Several studies have already shown that external beam radiotherapy is a safe and effective technique in the treatment of carcinoma of the prostate, with survival, local tumor control, and complication results similar to those treated with surgery but with advantage of being more generally applicable.^{1, 2, 6-8)} This retrospective study analyzes our experience with 60 patients treated for cure with external beam radiotherapy and demonstrates that a small institution can produce results similar to those achieved by larger and more specialized institutions.

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MATERIALS AND METHODS

One hundred and fifteen patients with prostate cancer were seen at Department of Therapeutic Radiology in our institution between September, 1987 and March, 2000. Fifty five patients were treated with palliative intent because of demonstrated metastatic cancer. The remaining 60 patients who were treated with curative intent are reported here. Patients were evaluated by history and physical examination and laboratory studies including complete blood count, liver function tests, acid phosphatase, prostate specific antigen, intravenous pyelography, radionuclide bone imaging, and chest radiograph. Histologic diagnosis was established by transurethral resection (TURP) or ultrasonography-guided biopsy. Computed tomography and Magnetic Resonance Imaging of the abdomen and pelvis were added to evaluate lymph node status and locoregional extent of disease. Bipodal lymphangiography and staging pelvic lymphadenectomy were not accomplished. The major presenting signs and symptoms were a nodule felt at routine prostate examination and frequency and urgency of urination, along with dysuria (Table 1). The median age was 63 years with range of 51 to 87 years.

Patients were classified according to the American Urologic System. An elevated acid phosphatase or prostate specific antigen level did not alter the stage of disease. Patients with regionally extensive tumor (ureteral obstruction, extension to pelvic side wall, large pelvic mass, or involvement of rectal wall) were staged as D1. Clinical stage and histologic differentiation are shown in Table 2. There were 6 patients in Stage A, 20 in Stage B, 26 in Stage C, and 8 in Stage D1. The percent distribution for well-differentiated, moderately differentiated, and poorly differentiated was 67, 16, and 16 for Stage A, 45, 45, and 10 for Stage B, and 31, 35, and 35 for Stage C disease. Classification according to the system of Gleason was not uniformly obtained.⁹⁾

Table 1. Presenting Signs and Symptoms

	Number of Patients
Urinary frequency and/or urgency	32
Nodule on rectal examination	24
Dysuria	12
Urinary hesitancy	11
Hematuria	5
Dribbling	3
Perineal pain	2

All patients were treated with megavoltage equipment producing 10 MV photons. Simulator treatment planning was accomplished with occasional opacification of bladder and rectum. Parallel opposed anterior-posterior portals with hip blocks extended 1.5 cm beyond the lateral pelvic walls and from the upper border of the fifth lumbar vertebra to the lower border of the ischial tuberosities; the usual field size was 16 cm×20 cm. The right and left lateral opposed portals usually measured 11 cm×20 cm. The pelvic brick technique was used to a dose of 45 Gy or 50.4 Gy at 1.8 Gy per day in 5 to 6 weeks, after which boost dose was delivered to a small (10 cm×10 cm) field 2.0 Gy per day to a total dose of 66 to 70 Gy.

The follow-up period ranged from 1 to 8 years. Patients were seen at 1 month and 3 months after irradiation, and at 3 month to 4 month intervals thereafter by us or their referring physicians. History and careful examination of the prostate were carried out for evaluation of tumor control. Biochemical studies and bone scanning were accomplished from time to time for asymptomatic patients and whenever clinical signs or symptoms indicated possible recurrence or metastasis. Patients with progressive prostatic enlargement or nodularity on examination, pelvic mass, ureteral obstruction, or reappearance of obstructive symptoms with positive biopsy were considered to have local recurrent disease.

Urinary and rectal late complications were scored clinically using criteria similar to those used by the Joint Center for Radiotherapy investigators (severe complications versus mild to moderate complications).¹⁴⁾ Acute reactions during treatment and those lasting up to 2 months after completion of radiotherapy were not considered as complications.

RESULTS

1. Survival

Actuarial 5-year and 7-year survival rates for Stage A, B,

Table 2. Distribution of Patients according to Stage and Differentiation

Stage	Well	Moderate	Poor	Total
A	4	1	1	6
B	9	9	2	20
C	8	9	9	26
D1	0	2	6	8
Total	21	21	18	60

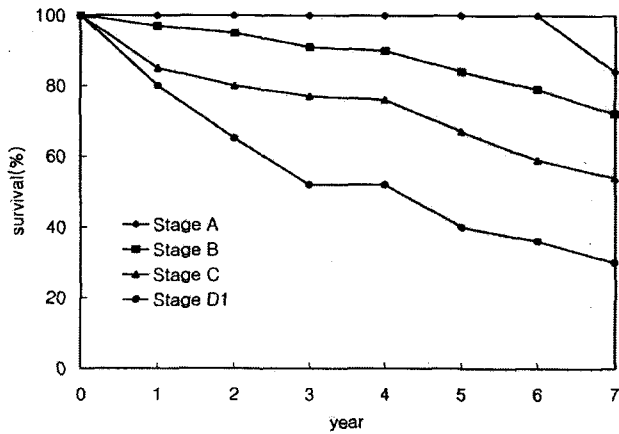


Fig. 1. Actuarial survival rates according to stage.

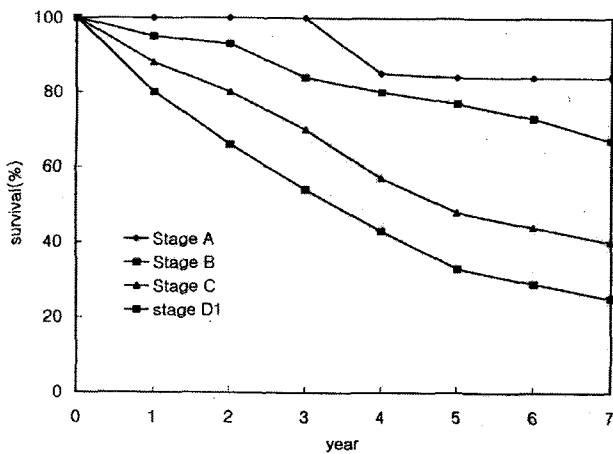


Fig. 2. Relapse free survival rates according to stage.

C, and D1 disease were 100%, 84%, 83% and 72%, 67% and 54%, and 40% and 30%, respectively. The corresponding 5-year and 7-year relapse free survival rates were 84% and 84%, 77% and 67%, 48% and 40%, and 33% and 25%, respectively. Relapse free 5-year survival rates for Stage B disease were 80%, 80%, and 50% for well, moderately, and poorly differentiated tumors, respectively. These were 64%, 44%, and 33% for Stage C disease, respectively. Actuarial and relapse free survival rates according to stage are illustrated in Fig. 1 and Fig. 2, respectively.

2. Failure

The local control rates at 5 years were 84%, 85%, 78%, and 60% for Stage A, B, C, and D1 disease, respectively. The relapse pattern for each stage is shown in Table 3. Among the patients who failed, 57% showed failure with

Table 3. Relapse Pattern

	Number of Patients	Percent
DM	8	57
LF	4	29
DM+LF	2	14
Total	14	100

DM : distant metastasis, LF : local failure

Table 4. Complications

Complications	Number of patients
Severe	
small bowel obstruction	1
colostomy	1
Total	2 (3%)
Mild to Moderate	
asymptomatic rectal bleeding	5
anorectal pain	4
diarrhea	2
colitis	1
hematuria	1
cystitis	1
contracted bladder	1
urethral stricture	1
Total	13 (22%)*

*3 patients developed multiple symptoms.

disseminated disease only, 14% with metastatic foci and local recurrence, and 29% with local recurrence only.

3. Complications

Mild to moderate complications were observed in 22% of patients. Severe complications requiring surgical procedures were documented in only 3% of patients. These include small bowel obstruction and symptoms requiring colostomy. This result is shown in Table 4.

DISCUSSION

Historically, patients with early stage prostate cancer were treated with radical surgery. The 15-year survival rate was 27% for 103 patients in Stage B1 and 18% for 79 patients in Stage B2.³⁾ However, 16% of clinical Stage B1 patients and 50% of clinical Stage B2 patients were noted to have invasion of the seminal vesicles at prostatectomy. For these groups, the 15-year survival rates did fall down to 0% and 5%, respectively.³⁾ In another report from Brady Urological

Institute, Elder et al. reported that 66% of men with clinical Stage B2 disease had tumor extension beyond the prostate and these patients had a 13% 15-year survival rate. This result is in contrast to 50% 15-year survival rate for 33% of clinical Stage B2 patients who remained in Stage B after prostatectomy.⁴⁾ Similarly, Flocks noticed only one apparent success out of 13 patients treated with radical surgery alone when there was extra-prostatic extension.⁵⁾

The management of Stage C disease remains controversial. Although several authors advocate radical surgery, often combined with hormonal therapy, there is no evidence that the survival of these patients is better than what can be obtained with observation and appropriate hormonal therapy. These surgical results are difficult to compare with those after radiation therapy because of major difference in patient selection.¹⁰⁻¹²⁾

The Stanford group first reported that localized carcinoma of the prostate could be treated effectively and safely with external beam radiotherapy.¹⁾ Since 1956, 898 patients with prostate carcinoma were clinically staged and treated with external beam linear accelerator irradiation.

The 5-year, 10-year, and 15-year survival rates were 81%, 60%, and 35%, for disease limited to the prostate, respectively. The corresponding survival rates for patients with extracapsular extension were 61%, 36%, and 18%, respectively. Other large institutions also have reported that external beam radiotherapy can achieve long term local control and disease free survival for patients with carcinoma of the prostate.^{8, 13-16)} The 5-year actuarial survival rates in our studies are comparable with these results with 100%, 83%, 67%, and 40% for Stage A, B, C, and D1 disease, respectively. In addition, 5-year local control rates are similar to those of other studies which showed 96% to 100%, 88% to 95%, 83% to 88%, and 75% to 81% for Stage A, B, C, and D1, respectively.

It is well documented that tumor grade correlates with the probability of lymph node metastasis and survival. Perez et al. showed that patients with well to moderately differentiated tumors had a 5-year survival rate of 70% in contrast to 25% for those with poorly differentiated tumors in Stage C. Histologic differentiation of the tumor had no significant impact on survival in Stage B.²⁾ Also Rosen et al. showed adverse effect of tumor grade on survival.¹⁴⁾ In our study, the histologic grade for Stage C correlated well with 5-year relapse free survival rates. However, 5-year result in Stage B

was 80% for both well and moderately differentiated tumors and this was 50% in poorly differentiated tumors. Overall, we believe that histologic grade is an important prognostic factor for all stages.

Of the patients treated at Stanford, 35% of those who failed did so with local and disseminated disease, 60% with metastatic foci and apparent local control, and 5% with local failure only.¹⁷⁾ Our results showed 57% failing with distant metastases and local control, 13% with local and distant disease, and 29% with only local recurrence. Because approximately 60% of patients who failed radiation therapy did fail with disseminated disease only, efforts should be focused on the control of systemic microscopic metastasis in future studies to improve survival for prostate cancer. Also conformal radiation therapy or advanced brachytherapy technique could be attempted to improve local tumor control without increasing radiation induced morbidity.^{18, 19)}

This report confirms that external beam irradiation is an effective and safe treatment for prostate cancer, providing long-term local control and good survival with acceptable complications.

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국문 초록

전립선암의 근치적 방사선치료

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목적 : 전립선암 환자에서 외부 방사선치료의 효과 및 안전성을 평가하고 최적의 방사선치료 방법을 알아보고자 함이 본 연구의 목적이다.

재료 및 방법 : 1987년 9월부터 2000년 3월까지 본원에서 근치적 목적의 외부 방사선치료를 시행한 60명의 환자를 후향적으로 분석하였다. 요도관통 전립선 절제술 및 초음파를 이용한 조직검사를 시행하여 조직학적 진단을 확인하였다. 진단시의 주된 증상은 직장축진시 전립선의 종괴 촉진, 빈뇨 및 급뇨, 소변시 통증호소 등이었다. 환자 나이의 분포는 51세부터 87세 이었고 중앙값은 63세이었다. A병기 환자는 6명, B병기 환자는 20명, C병기 환자는 26명, D1병기 환자는 8명이었다. 모든 환자는 10 백만볼트 에너지의 선형가속기를 이용하여 치료하였다. 4문대항 골반 상자 치료기법을 사용하여 45~50.4 Gy를 전골반부위에 조사 후 조사야를 축소하여 총조사량 66~70 Gy까지 추가조사를 실시하였다. 추적기간은 1년 내지 8년이었다.

결과 : A병기, B병기, C병기 및 D1병기 환자에서 5년 및 7년 실질 생존율은 각각 100% 및 84%, 83% 및 72%, 67% 및 54%, 40% 및 30%이었다. 각각의 병기에서 5년 및 7년 무병생존율은 84% 및 84%, 77% 및 67%, 48% 및 40%, 33% 및 25%이었다. B병기 환자에서 조직학적 분화에 따른 5년 무병생존율이 80%, 80% 및 50%이었고, C병기 환자에서는 각각 64%, 44% 및 33%이었다. 생존 5년시의 국소 제어율은 A, B, C, D1병기에서 각각 84%, 85%, 78% 및 60%이었다. 경증 및 중등도의 합병증은 22%의 환자에서 관찰되었고, 수술적 처치를 요하는 중증의 합병증은 3%의 환자에서만 발생하였다.

결론 : 본 연구는 전립선암 환자에서 근치적 목적의 외부 방사선치료가 효과적이고 안전한 치료 방법임을 확인하였고 국소제어 및 생존율에서 만족할 만한 결과를 나타내었다.

핵심용어 : 전립선암, 방사선치료