

Residual, Unresectable and Recurrent Rectal Cancer: Role of External Radiation Therapy in 46 Patients

Hack Joon Gil, M.D., Yoon Kyeong Oh, M.D., Sei Chul Yoon, M.D.
Kyung Sub Shinn, M.D. and Yong Whee Bahk, M.D.

*Division of Therapeutic Radiology, Department of Radiology,
Catholic University Medical College, Seoul, Korea*

Fifty patients with residual, unresectable or recurrent rectal cancer were treated with external irradiation using a 6-MV linear accelerator at the Division of Therapeutic Radiology, Department of Radiology, Kangnam St. Mary's Hospital, Catholic University Medical College during the period of April 1983 to December 1987.

This paper describes the results of a retrospective analysis of the results of external irradiation for the residual, unresectable and recurrent rectal cancer in 46 patients. Four patients were lost to follow-up. Of the 46 patients, 18 (39%) presented with unresectable primary lesions and 28 (61%) with residual or recurrent rectal cancer.

In 93%, the pathologic diagnosis was adenocarcinoma. Response to irradiation was observed in 22 (73%) out of 30 patients who were treated for pain, 12 (86%) out of 14 patients who were treated for mass, and 17 (77%) out of 22 patients who were treated for bloody discharge. The actuarial postoperative 2-year and 3-year survival rates in recurrent and unresectable patients were 43% and 22%, respectively. However, the post-RT 2-year survival rate was 13% (6/46).

Key Words: Residual, Unresectable and Recurrent Rectal cancer, External radiotherapy

INTRODUCTION

Since the classic work of Miles in 1908, the advent of radical surgery including the abdominoperineal resection and anterior resection has been able to cure 30% of patients with colorectal cancer¹. However, the cure rate for patients with extensive local disease or with spread to regional lymph nodes has not been that high.

Recent studies have demonstrated local recurrence rates to be 30~50% in those who undergo curative resection for colorectal carcinoma and distant metastases appear in approximately 40% of patients¹⁻⁵. Survival rates have improved slightly over the past 25~30 years, mainly as a result of improved surgical management. Five year disease-free survival rates have been approximately 50% in patients with stage B disease and about 30% in patients with stage C disease^{2,3}.

A serious problem is pelvic recurrence, which is usually unresectable and 50~60% will die as a result of the local recurrence⁴. The probability of curing patients with pelvic recurrent disease is dismal, less than 5%, and radiation alone or with

chemotherapy can achieve only limited palliation in 75~80% of cases⁶. Local recurrence may develop from subclinical deposits of cancer cells left in the surgical bed, and postoperatively, this subclinical disease can be controlled in a high percentage of cases by moderate doses of radiation (45~50 Gy)⁷. In many patients, the local failure site is the major symptom-producing area after surgical resection¹.

The purpose of this paper is to analyze the results of radiation therapy for residual, unresectable and recurrent rectal cancer, and establish the role of radiation therapy.

METHODS AND MATERIALS

1. Patients Characteristics

From April 1983 to December 1987, 50 patients with residual, unresectable and recurrent rectal cancer were treated at the Division of Therapeutic Radiology, Kangnam St. Mary's Hospital, Catholic University Medical College. Four patients were lost to follow-up. The remaining 46 patients, who were irradiated on the pelvis by a 6-MV linear accelerator, were analyzed for this study.

The patients consisted of 25 males and 21 females. The age ranged from 22~79 years, with

*This paper was supported by 1988 CUMC Clinical Medical Research Fund.

Table 1. Patient Characteristics

Characteristics		Number of patients (46)	Percentage
Sex	Male	25	54
	Female	21	46
Age range		22 – 79 (median 54 years)	
Previous resection			
Curative		28	61
Abdominoperineal resection		21	46
Low anterior resection		5	11
Hemicolectomy		1	2
Subtotal colectomy		1	2
Palliative		18	39
Colostomy only		16	35
Partial resection		1	2
Electrofulguration		1	2
Pathology			
Adenocarcinoma		43	93
Grade I		15	33
Grade II		7	15
Grade III		6	13
Ungraded		14	30
Mucinous type		1	2
Leiomyosarcoma		1	2
Not available		2	4
Stage	residual, or recurrent	unresectable total	
B1	2	— 2	4
B2	5	— 5	11
C1	1	1 2	4
C2	20	10 30	65
D	—	7 7	15

the median being 54 years. Of the 46 patients, a curative and palliative surgery was performed in 28 (61%) and 18 (39%) patients, respectively, as shown in Table 1. The pathologic diagnosis was adenocarcinoma in 93%. According to Astler-Coller's modification of Duke's classification, 30 (65%), 7(15%), 5(1%) and 2(4%) each were in C2, D, B2, and B1 & C1 stage.

2. Radiation Therapy Techniques & Follow-up

The radiation fields used were AP and PA whole pelvis including perineum with field size of (15 ~20) × (15~16) cm and shrinking- or boost-field techniques using 3 portals or Box techniques after a dose of 4500~5000 cGy. A bolus was applied at the perineal scar and/or recurrent masses on alternative day.

The minimum follow-up was 7 months and the maximum 55 months.

RESULTS

1. Analyzing the relation between stages and the time intervals from surgery to RT, 20(71%) out of 28 patients were in C2 stage, and 12 showed recurrences within postoperative 12 months (Table 2). Two (7%) of 28 patients, B1 stage, showed no recurrence within 24 months. The ratio between residual or recurrent and unresectable rectal cancer were 28(61%) to 18(39%).

2. Of 46 patients, 33(72%) received over 5000 cGy/5~7 weeks (Table 3).

3. Of 46 patients, 30(65%), 22(48%) and 14(30%) had pain, bloody discharge and mass. Twenty-two (73%) out of 30 patients with pain, 12 (86%) out of 14 patients with mass, and 17(77%) out of 22 patients with bloody discharge showed radiosensitivity (Table 4).

Table 2. Relation between Stages and the Time Intervals from Surgery to RT (Number and (%))

Duration	Below 12 mos	12–18 mos	19–24 mos	25–36 mos	Above 3 years	Total
Stage						
B1	—	—	—	1	1	2 (7)
B2	2	3	—	—	—	5 (18)
C1	1	—	—	—	—	1 (4)
C2	12	2	2	2	2	20 (71)
Total	15 (53)	5 (18)	2 (7)	3 (11)	3 (11)	28 (100)

Mos :Months

4. Of 46 patients, 4 with extrapelvic metastases and 1 with low-dose 2000-cGy irradiation were excluded. Of the remaining 41 patients, 18(58%) showed good palliative response for 1~3 months. The higher the dose were given, the better the palliative response were observed (Table 5).

Table 3. Relation between Radiation dose and Disease Status (Number and (%))

Disease extent RT dose (cGy)	Residual or recurrent	Unre- sectable	Total
Below 2,000	—	1	1 (2)
2,000 — 2,999	1	3	4 (9)
3,000 — 3,999	3	1	4 (9)
4,000 — 4,999	3	1	4 (9)
5,000 — 5,999	16	11	27 (59)
Above 6,000	5	1	6 (13)
Total	28 (61)	18 (39)	46 (100)

RT : Radiation therapy

5. The complications observed during and after RT were dry or wet desquamation in 28(61%), erythematous pigmentation in 16(35%), urinary problems in 8(17%) (Table 6).

6. The actuarial postoperative 2-year and 3-year survival rates in recurrent and unresectable patients were 43% (20/46) and 22% (10/46), respectively, and the actuarial post-RT 2-year survival rate was 13% (6/46) (Fig. 1 & 2).

DISCUSSION

The management of rectal adenocarcinoma by radiotherapy was first reported by Symonds in 1914⁸⁾. In the mid-1950s, a report from London on primary treatment by high voltage X-rays increased the role of radiation therapy in the treatment of rectal adenocarcinoma. And the surgical extirpation of the circumferential spread is often difficult to achieve when the disease involves the fibro-fatty tissues, the sacrum and sacral nerves, and pelvic organs. The mean survival, after proof of unresectability or metastasis has been estimated, was 9.

Table 4. Relations between Disappearance of Clinical Symptoms and Radiation Dose (Number and (%))

Symptom Response Dose (cGy)	Pain (N=30)		Mass (N=14)		Bloody discharge (N=22)	
	With	Without	With	Without	With	Without
Below 2,000	8	0	0	0	6	0
2,000 — 2,999	8	0	1	0	4	0
3,000 — 3,999	3	0	2	0	2	1
4,000 — 4,999	1	1	0	1	1	1
Above 5,000	2	7	9	1	4	3
Total	22 (73)	8 (27)	12 (86)	2 (14)	17 (77)	5 (33)

N = total number

Table 5. Duration of Palliative Response by RT Dose (Number and (%))

Duration Dose (cGy)	1—3 mos.	4—6 mos.	7—12 mos.	Above 1 year	Total
2,000 — 2,999	2	—	—	—	2
3,000 — 3,999	2	—	—	—	2
4,000 — 4,999	3	2	—	1	6
Above 5,000	11	3	1	6	21
Total	18 (58)	5 (16)	1 (3)	7 (23)	41 (100)

Mos. : Months, RT : Radiation therapy

5 months⁹). So the residual, unresectable, and recurrent rectal carcinoma are major problems to the oncologist.

The incidence of local failure after surgery alone is strongly dependent on pathologic staging¹⁰). With stages B2, B3, and C1 disease, the risk of pelvic failure with resection with or without RT was: B2-23% vs 9%, B3-53% vs 0% and C1-50% vs 20%. Differences in 5-year NED survival were B2-47% vs 76%, B3-27% vs 69%, and C1-25% vs 69%²⁵). So the radiation therapy is the treatment of choice of

Table 6. Complications during & after RT (Number and (%))

Complications	Number of complications
Dry or wet desquamation	28 (61)
Erythema & pigmentation	16 (35)
Dysuria & cystitis	8 (17)
Delayed wound healing	2 (4)
Leukopenia	2 (4)
Edema of perineum	2 (4)
Adhesive ileus	2 (4)*
Intestinal perforation	11 (2)
Hydronephrosis	1 (2)

* Two patients had surgical intervention

recurrent rectal cancer. While local failure was lower in irradiated C2 patients (47% vs 21%), the difference 5-year NED survival was minimal (27% vs 34%). With C3 disease, improvements in either local control or survival were minimal. Tepper et al. noted that the lack of overall improvement in C2 and C3 patients was caused by an increase in metastatic spread²⁵). In an earlier analysis by Hoskins *et al.*, the risk of distant failure in C2 and C3 patients was nearly twice that in B2, B3 and C1 patients, and all peritoneal failures were in the C2 and C3 stages⁴).

In patients with recurrent tumor, good palliation has been achieved with 5000 cGy or less and palliation of 6 months or more was increased as the radiation dose increased⁹). In our hospital, the response of the tumor mass was slightly higher than that of pain and bloody discharge, whereas the response of the tumor mass was lower than that of the pain and bloody discharge by Wang *et al.*¹¹) And we observed that bloody discharge through colostomy or rectum were controlled with relatively lesser doses of radiation as shown by Wang *et al.*

In residual disease, the incidence of local recurrence after external irradiation was 54% for gross residual and 26% for microscopic residual. In microscopic residual disease, approximately 10% local-failure risk was shown when the boost dose was over 600 cGy in contrast to 33% risk when the

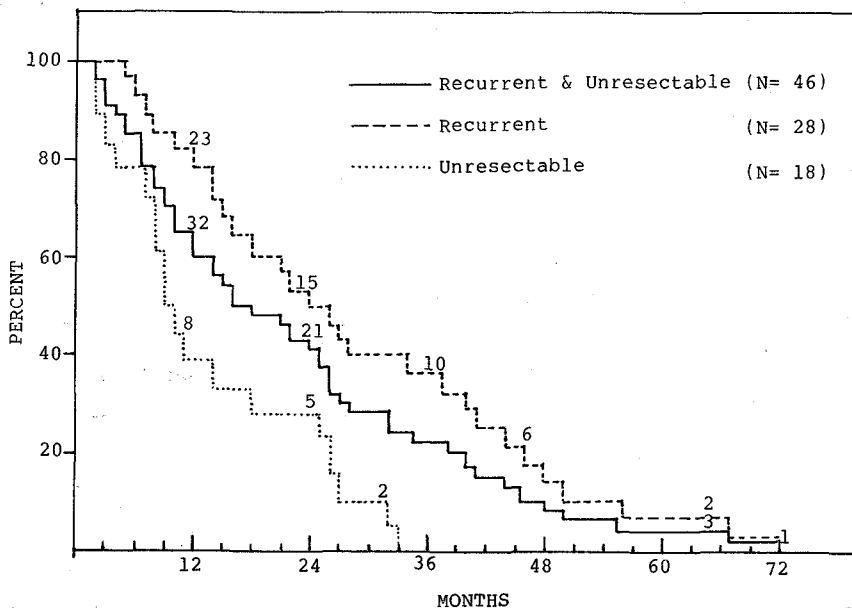


Fig. 1. Actuarial postoperative survival (by K-M method).

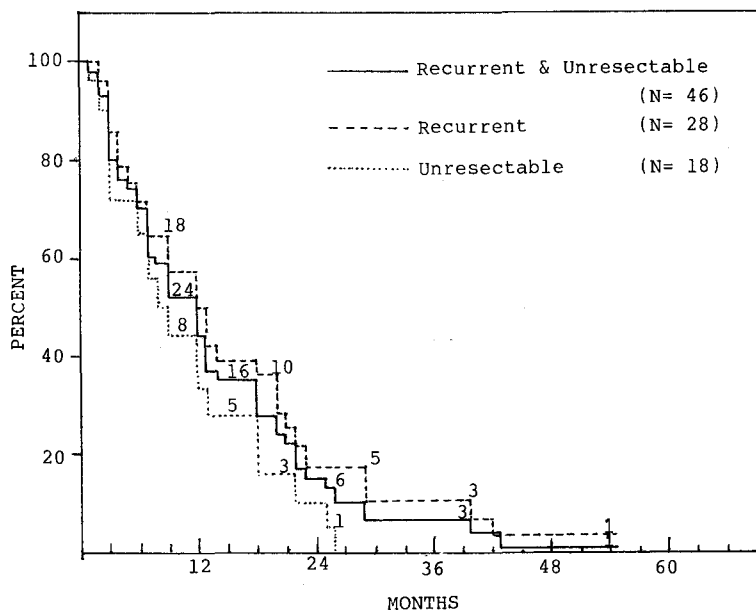


Fig. 2. Actuarial post-RT survival (by K-M method).

dose was below 5500 cGy¹²⁾. But, in patients with gross residual disease, the radiation response was not correlated with dose.

Local recurrence is a significant problem in residual disease even when high-dose external radiation therapy is used. Our results of 43% of 2-year survival was comparable to 50±7% of the Massachusetts General Hospital¹³⁾.

For the patients with residual and recurrent lesion, the major difference in treatment plan is the necessity of including the sacral canal as target volume for the initial 4500 to 5000 cGy^{14,15)}. This is indicated because of the increased risk of tumor spread along the nerve roots. Failure to do so may result in a marginal recurrence in the sacral area. Perineum is a well recognized site of recurrence followed by a painful outcome¹⁶⁾.

Pre-operative radiation therapy is of benefit in rectal cancer, especially in those with a low rectal lesion or those with regional lymph node involvement¹⁷⁻²²⁾. The resectability rate after pre-operative doses of 4500~5000 cGy has varied from 50 to 75%. But, in spite of their resectability, the local recurrence is still as high as 36~45%. Survival in patients receiving combined pre-operative and postoperative irradiation was 78%²³⁾.

Routine intraoperative boosts seem to decrease the incidence of local failure and to improve survival^{13,24)}. However, in C3 lesions, because of the

high risk of systemic failure the routine use of intraoperative boosts may not yield any survival gain until better systemic tools are developed²⁵⁾. One series of 16 patients with unresectable primary lesions, the addition of intraoperative radiotherapy has resulted in a total absence of local recurrence at the end of 20 months follow-up and survival rate went up compared with the previous group treated with only external RT and surgical resection¹²⁾.

The combination of external irradiation and chemotherapy can achieve useful palliation in 75~80% of patients and even an occasional cure^{18,26)}. CEA radioimmunoassay has been directed to postoperative follow-up in the patients who underwent a potentially curative surgery to detect recurrence and to monitoring patients with known recurrence undergoing chemotherapy²⁷⁾.

In view of the prognostic factors, in addition to stage, tumor resection margin and location, histologic grade, involvement of lymph nodes, blood vessel invasion, and age affect adversely^{28,29)}. Because all of our cases were referred for RT from affiliated hospitals of CUMC with various kinds of surgical techniques and postoperative management, we could not determine those factors.

The incidence of moderate or severe soft-tissue complications has increased as the result of a combination of aggressive treatment. Most of the acute reactions during radiation therapy were mild

or moderate and easily controlled with conservative treatment. In our cases, radiation induced complications were generally subtle and tolerable, but two patients with adhesive ileus needed surgical intervention.

CONCLUSION

Forty-six patients with residual, unresectable and recurrent rectal cancer, were treated by radiation therapy after curative or palliative surgery during the period of April 1983 to December 1987, at the Division of Therapeutic Radiology, Kangnam St. Mary's Hospital.

Retrospective analysis was done. Twenty-two (73%) of 30 patients irradiated for pain, 12 (86%) of 14 patients irradiated for mass, and 17 (77%) of 22 patients irradiated for bloody discharge showed positive response. And 18 (58%) of 41 patients showed good palliative response for 1~3 months.

The complications we noted were dry and wet desquamation in 28 (61%), erythematous pigmentation in 16 (35%), urinary problems in 8 (17%), etc. The actuarial postoperative 2-year and 3-year survival rates were 43% (20/46) and 22% (10/46), respectively, and the actuarial post-RT 2-year survival rate was 13% (6/46).

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—국문초록—

국소 재발성 또는 진행된 직장암의 방사선 치료

—46예의 치료 성적 분석—

가톨릭 의과대학 치료방사선과학교실

길학준 · 오윤경 · 윤세철 · 신경섭 · 박용휘

가톨릭 의과대학 강남성모병원 방사선치료실에서는 1983년 4월부터 1987년 12월까지 4년 8개월 동안에 국소 재발성 또는 진행된 직장암환자 46예의 외부 방사선 치료를 실시하였다. 방사선 치료는 6MV선형가속기를 사용하였으며 전후 2대문조사 및 4문조사를 혼합 사용하였고, 매일 160~180 cGy씩 주 5회 분할조사하여 총 4,500~6,000 rad/5~7주를 시도하였다. 필요시는 수술창 및 회음부에 격일로 Bolus를 사용하여 다음과 같은 결과를 얻었기에 보고하는 바이다.

1. 총 46명중 남자 25명, 여자는 21명이었고, 연령 분포는 22세부터 79세까지였다(중앙연령; 54세).
2. 수술후 재발된 직장암이 28예였고, 수술 불가능한 경우가 18예였다.
3. 재발된 예 28명에서 Astler-Coller's Modification of Duke's Method 분류상 C2가 20명이었는데 그중 12명이 수술후 12개월내에 재발하였다. B1 병기에서는 24개월내 재발한 예는 전혀 없었다.
4. 방사선 치료에 대한 반응으로 통증완을 주소로 했던 30명중 22명(73%)에서, 종괴완을 주소로 한 14명중 12명(86%)에서, 출혈완을 주소로 한 22명 중 17명(77%)에서 각각 반응을 보였다.
5. 합병증은 건성 췌는 습성 피부탈락과 홍반성 색소침착, 요도—방광염이 61%, 35%, 17%에서 각각 관찰되었고, 2예에서는 수술을 요하는 장유착이 있었다.
6. 수술후 2년과 3년 생존율은 각각 43%, 22%였고, 방사선 치료 후 2년 생존율은 13%였다.