

The Role of Postoperative Adjuvant Radiation Therapy in the Management of Adenocarcinoma of the Colon

—A Review of 21 Patients—

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From March 1970 to December 1984, 21 patients treated initially with curative surgery for adenocarcinoma of the colon, referred to the Department of Radiation Oncology, College of Medicine, Yonsei University, were analyzed retrospectively.

Thirteen of 21 patients who were considered to be a high risk group (i.e, mainly stage B2 or above), received adjuvant postoperative radiation therapy.

However, 2 of 13 patients did not complete their courses of radiotherapy as planned because of poor tolerance to radiotherapy or patient's refusal and were excluded from this study. Remaining 8 of 21 patients who did not receive postoperative radiotherapy, presented with recurrence at the time of referral and treated with palliative radiotherapy.

In 11 patients with postoperative radiotherapy, overall local failure rate was 9%(1/11) and the 5 year acturial survival rate was 55%.

Local failure rates by stage were 0(0/4), 14%(1/7) for stage B2+B3, C1+C2+C3 respectively and 0(0/2), 17%(1/6), 0(0/3) for stage C1, B2+C2, B3+C3 respectively.

Key Words: Adenocarcinoma, Colon, Adjuvant postoperative radiotherapy, Local failure, Survival

INTRODUCTION

Surgical removal has been the mainstay of the curative treatment for adenocarcinoma of the large bowel proximal to the pelvic-peritoneal reflection(i.e, colon).

Although histologically indistinguishable from rectal tumors, these tumors may behave quite differently because of its anatomical characteristics determine patterns of disease dissemination.

Whereas multiple published series¹⁻⁴⁾ have demonstrated a clear benefit to postoperative radiotherapy in adenocarcinoma of the rectum, the role of adjuvant irradiation in the curative management of adenocarcinoma of the colon has not been defined completely.

Increasing data are being accumulated from autopsies⁵⁾, clinical⁶⁻¹¹⁾ and reoperative series¹²⁾ that indicate that local tumor recurrence is a significant problem after resection for tumors of the colon including rectal lesions. The data suggest that the addition of postoperative adjuvant radiation therapy may decrease local recurrence¹³⁻¹⁶⁾ and improve survival^{13,14,17-19)} in selected patients with colon cancer.

The purpose of this study is to evaluate the role of postoperative radiotherapy for patients with adenocarcinoma of the colon proximal to the pelvic-peritoneal reflection, in terms of local failure and survival rate.

Patient's characteristics, patterns of failure, initial site of tumor, radiotherapy treatment technique as well as its morbidity are discussed in this study.

MATERIALS AND METHODS

From March 1970 to December 1984, the charts of 21 patients with adenocarcinoma of the colon, referred to the Department of Radiation Oncology, College of Medicine, Yonsei University, were retrospectively reviewed.

Patients with tumors at or below the peritoneal reflection were not included. All 21 patients treated initially with curative surgery(right hemicolectomy; 9, left hemicolectomy; 4, anterior resection; 1, segmental resection; 5, sigmoidectomy; 2). Thirteen of 21 patients who were considered to be a high risk group, received adjuvant postoperative irradiation. However, 2 of 13 patients did not complete their courses of radiotherapy as planned and were excluded from this study. Remaining 8 of 21 patients

who did not receive postoperative radiotherapy, presented with recurrence at the time of referral.

All patients were retrospectively restaged according to the Modified Astler-Coller Staging System (Table 1).

The male to female ratio in 19 patients was 5.3:1 (16 male and 3 female).

The median age was 50 years with a range from 29 to 77 years (mean 47 years).

Distribution by initial site and stage of 19 patients is listed in Table 2. Ten of 19 patients had right-sided lesions, 9 of 19 patients had left-sided lesions and there was no patients with tumors arising from transverse colon. The cecum was the most frequent site of primary disease (6/19).

Periodic physical examination, CBC, guaiac test, liver function test and carcinoembryonic antigen determination were routinely performed during the follow-up and barium enema or colonos-

copy done, if necessary.

The median follow-up period was 26 months with a range of 4 to 124 months (mean 32 months).

Pattern of failure was documented with clinical symptoms and signs and radiographic studies including CT scan. Local failure was defined as any tumor regrowth within the original tumor bed, operative field including the anastomotic sites. Definite parenchymal liver involvement by tumors was considered to be liver failure. Peritoneal seeding was defined as multifocal tumor studding of peritoneal surfaces or serosal surfaces of abdominal viscera.

Distant metastasis was defined as any remote recurrence in the extraabdominal organs.

Eleven of 13 patients completed their courses of postoperative radiotherapy as initially planned. The radiation therapy was given to the entire abdomen in 7 patients with a moving strip technique and to the local field in 4 patients employing telecobalt 60 or 10 MeV linear accelerator (as shown in Table 3). The treatment was given 5 times a week, 2 fields per day. A daily tumor dose was 180 to 200 cGy. Local field size was determined by multiple factors such as the preoperative barium enema, operative and pathological findings. An attempt was made to include regional lymph node, if the residual tumors suspected in this area. The treatment position of the patients was depended on the location of the primary tumors. For instance, patients with right or left-sided lesions were treated in the decubitus position and patients with sigmoid tumors were treated in the prone position with full distension of bladder in order to displace the small bowel from the irradiation. To spare uninvolved tissue, the shrinking field technique was used. Total tumor dose for entire abdomen was 2000 cGy to 2600

Table 1. Astler-Coller Staging System

Stage	Criteria
A	Tumor confined to mucosa, lymph node negative
B1	Tumor extends into but not through bowel wall (muscularis, lymph node negative)
B2	Tumor penetrates full thickness of bowel wall (through muscularis and serosa, lymph node negative)
B3	Tumor penetrates full thickness of bowel wall with adherence to or invasion of adjacent organs, lymph node negative.
C1	Same as B1 except lymph node positive.
C2	Same as B2 except lymph node positive.
C3	Same as B3 except lymph node positive

Table 2. Distribution by Site and Stage (19 Patients)

Stage	B2	B3	C1	C2	C3	Stage unknown	Total
Cecum	1	1	1	1	1	1	6
Ascending colon	1			1		1	3
Hepatic flexure						1	1
Splenic flexure					2	1	3
Descending colon	1				1		2
Sigmoid colon	1		1	1	1		4
Total	4	1	2	3	5	4	19

cGy and for local field was 5040 cGy to 5500 cGy.

Acute and late complications were carefully monitored during the treatment and follow-up periods.

Summary of radiotherapy in 11 patients with postoperative radiotherapy is listed in Table 3.

RESULT

The time to failure ranged from 4 months to 52 months with a median of 20 months.

Four of 11 patients who received postoperative radiotherapy had relapse (36%). Local failure was only one among 11 patients. Three other patients

had relapse in the brain.

Patterns of initial failure by stage and location of primary disease are shown in Table 4.

Local failure rate in 11 patients with postoperative radiotherapy was 9% (1/11). In these 11 patients, local failure rates by stage are shown in Table 5.

Only one among total of 19 patients failed in the liver. Among 8 patients who did not receive postoperative radiotherapy, 4 patients (50%) relapsed in the abdomen, retroperitoneum and liver.

The actuarial 3 year and 5 year survival rates in 11 patients with postoperative radiotherapy were 73% and 55%, respectively.

Table 3. Summary of Radiotherapy in 11 Patients with Postoperative Radiotherapy

	Age	Location	Stage	Field	Radiation source	Total dose
1	29	Sigmoid colon	C1	Entire abdomen	10 MeV L. A	2600 cGy
2	49	Descending colon	B2	Entire abdomen	10 MeV L. A	2250 cGy
3	32	Ascending colon	C2	Entire abdomen	CO-60	2000 cGy
4	52	Ascending colon	B2	Entire abdomen	CO-60	2250 cGy
5	56	Cecum	C1	Entire abdomen	CO-60	2000 cGy
6	30	Cecum	C2	Entire abdomen	CO-60	2250 cGy
7	36	Splenic flexure	C3	Entire abdomen	CO-60	2000 cGy
8	62	Sigmoid colon	B2	Local field	10 MeV L. A	5040 cGy
9	42	Cecum	B3	Local field	10 MeV L. A	5040 cGy
10	77	Sigmoid colon	C2	Local field	10 MeV L. A	5500 cGy
11	51	Descending colon	C3	Local field	10 MeV L. A	5040 cGy

L. A ; Linear Accelerator

Table 4. Patterns of Initial Failure by Stage and Location

	Stage						Total number	Location of primary disease					
	B2	B3	C1	C2	C3	Un-known		Cecum	Ascending colon	Hepatic flexure	Splenic flexure	Descending colon	Sigmoid
Number of patients failing	(1)	[1]	[1]	[1]	[1]	(4)	(8)	(3)	(1)	(1)	(2)	(1)	
Patterns of failure	(1)			[1]	(1)	(1)	[1](3)	(2)	[1]			(1)	
Local						(1)	(1)			(1)			
Liver													
Peritoneal seeding	(1)*						(1)*	(1)*					
Distant metastasis					(2)	(2)	(4)	(1)	(1)		(2)		
		[1]	[1]		[1]		[3]	[2]			[1]		

() : number of patients who did not receive postoperative radiotherapy.

[] : number of patients with postoperative radiotherapy.

* : coexist with local recurrence at the time of initial relapse.

Table 5. Local Failure Rates by Stage in 11 Patients with Postoperative Radiotherapy

Stage	Local failure rate
B2 + B3	0 (0/4)
C1 + C2 + C3	14% (1/7)
C1	0 (0/2)
B2 + C2	17% (1/6)
B3 + C3	0 (0/3)

Table 6. 5-Year Survival by Stage

	B2 + B3	C1 + C2 + C3	Over all
Our patients	67%	42%	55%
Historic control group with surgery alone			
Willet, et al ¹⁰⁾	61%	38%	51%
McGlone, et al ²¹⁾	53%	31%	45%
Cass et al ⁶⁾	47%	24%	37%
Murray, et al ²²⁾	59%	44%	54%
Falterman, et al ²³⁾	53%	32%	42%
Copeland et al ²⁴⁾	52%	22%	41%

Significant complications were not observed in all 11 patients with postoperative radiotherapy. However, mild diarrhea and/or vomiting were developed in 6 patients.

DISCUSSION

Radical surgical resection remains the primary therapeutic modality in the curative management of adenocarcinoma of the colon. The use of adjuvant radiation for colonic cancer excluding rectal cancer has not been extensive.

Although histologically indistinguishable from rectal tumors, these tumors may behave quite differently because of anatomic factors that determine patterns of disease dissemination. The ascending and descending colon, splenic and hepatic flexures and frequently the cecum are similar to the rectum in that they are relatively immobile structures that lack a mesentery and usually lack a peritoneal covering (serosa) on the posterior and lateral surfaces.

A lesion that extends through the entire bowel wall in these areas has the potential of involving adjacent organs and structures as does rectal carcinoma and result in a narrow circumferential

surgical margin, especially with posterior or lateral extension.

In contrast, the transverse and sigmoid colon are freely suspended on a mesentery and consequently are freely mobile except for their proximal and distal segments. For carcinoma that involve a mobile portion, the risk of peritoneal seeding of malignant cells may be greater than the likelihood of local recurrence. In these bowel location, the risk of inadequate operative removal is probably greatest when there is tumor adherence to or invasion of surrounding organs or tissues.

Adenocarcinoma of the colon arise in the mucosa of bowel wall and spreads earliest by direct invasion of muscularis propria. Metastasis to regional lymph node is uncommon in tumors confined to the mucosa and muscularis¹¹⁾. Once the tumor has penetrated through the muscularis to involve serosa, regional lymph node involvement is more common.

When hematogenous dissemination occurs, it is most frequently to the liver via the portal circulation, exclusively. The liver represents the first capillary filter encountered by blood-borne tumor emboli. In this study, only one patient failed in the liver. This finding may be insignificant because of small number of patients.

Once the primary tumors has penetrated the serosa, exfoliated malignant cells may implant on the peritoneum and serosal surface of the abdominal viscera.

Patients with stage A and B1 adenocarcinoma of the colon have a high likelihood of cure. The risk of recurrence is exceeded by their risk of dying of intercurrent disease or developing second primary tumors, and adjuvant therapy is not indicated. However, patients with more advanced stages are at substantial risk of recurrence and effective adjuvant therapy with minimal toxicity is clearly desirable.

Local recurrence in the original tumor bed or operative field represents a major component of a failure after surgery with curative intent in patients with stage B2, B3 or C of adenocarcinoma of various sites of the colon⁶⁻¹²⁾.

Risk of local failure¹²⁾ escalates with progressive penetration of the bowel wall by the primary tumors and anatomic immobility of colonic segment and with higher histologic grade.

Willet, et al¹⁰⁾ from Massachusetts General Hospital reported that with surgery alone local recurrence was not found to be a problem in stage A, B1 or C1 lesions.

Several centers have reported a reduced local failure¹³⁻¹⁶⁾ and improvement of survival^{13,14,17)} in selected patients (i.e. anatomically immobile sites and stage B3, C2, C3 especially).

Autopsy study by Russel et al²⁰⁾ revealed that local failure rate in the patients treated with curative surgery alone was 38% and 47%, 35% for stage B, C respectively and 0, 27%, 69% for stage C1, B2+C2, B3+C3 respectively.

Our results showed that patients with postoperative radiotherapy appeared to be improved in local recurrence when compared with this autopsy study, although there was no statistical significance.

As far as survival rate is concerned, comparing with the historic control group who underwent curative surgery alone, our survival rates in patients with postoperative radiotherapy appear to be slightly improved.

The 5 year survival rate by stage in the historic control group and our patients with postoperative radiotherapy is listed in Table 6.

It is interesting to speculate on the potential value of adjuvant whole abdominal irradiation in patients with high risk of relapse.

The literature⁶⁻¹¹⁾ have shown that a majority of failures are limited to the abdominal cavity. Entire abdominal radiotherapy produce substantial acute morbidity and possibility of delayed radiation damage to critical normal tissue.

It would be difficult to justify whole abdominal treatment in all patients subgroup for that reason.

The risks of peritoneal seeding were highest in the stage C3 group of patients¹⁾. Trials evaluating whole abdominal treatment should probably be limited initially to patients with pathologic extension to a free peritoneal surface, positive peritoneal cytologic finding¹⁸⁾ or stage C3 disease.

Since the liver may be at risk even when peritoneal cavity is not, questions regarding liver prophylaxis will have to be addressed.

The demonstration of early dissemination to structures that are not adequately addressed by radical surgical therapy is the most rational method of selection of patients for potentially toxic adjunctive therapy.

CONCLUSION

From March 1970 to December 1984, 21 patients treated initially with curative surgery for adenocarcinoma of the colon, referred to the Department of

Radiation Oncology, College of Medicine, Yonsei University, were analyzed retrospectively.

1. Local failure rate was 9% (1/11) in patients with postoperative radiotherapy.

2. Local failure rates by stage were 0 (0/4), 14% (1/7) for stage B2+B3, C1+C2+C3 respectively and 0 (0/2), 17% (1/6), 0 (0/3) for stage C1, B2+C2, B3+C3 respectively.

3. The actuarial 3 year and 5 year survival rates in patients with postoperative radiotherapy were 73 %, 55% respectively.

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＝ 국문초록 ＝

대장선암의 치료에 있어 수술후 방사선 치료의 역할

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대장선암의 근본적인 치료는 외과적 절제술로 알려져 있으나 이 경우 직장선암과 마찬가지로 수술후 국소재발이 문제시 되어 왔다.

직장선암의 경우 수술후 국소재발의 위험성이 높은 환자에 수술후 방사선치료를 병용함으로써 국소제어율 및 나아가서 생존율까지도 상당히 개선된다고 알려져 있다.

그러나 대장선암의 경우 국소제어율 및 생존율의 개선이 보고되고 있기는 하나 아직 널리 알려져 있지는 못하다.

이에 저자는 1970년 3월부터 1984년 12월까지 대장선암으로 진단받고 일차적으로 근치적 수술을 시행한 후 연세대학교 의과대학 치료방사선과에 내원한 21명의 환자를 후향성 분석하여 다음과 같은 결과를 얻었다.

1. 21명의 환자중 수술후 방사선 치료를 병용하여 계획대로 무사히 마친 환자는 11명이었다.
2. 수술후 방사선 치료를 병용한 환자들의 전체적인 국소실패율은 9%(1/11)이었고 병기별로는 B2+B3가(0/4), C1+C2+C3가 14%(1/7)였고 C1이 0(0/2) B2+C2가 17%(1/6), B3+C3가 0(0/3)였다.
3. 수술후 방사선 치료를 병용한 환자들의 5년 생존율은 55%였다.