

— J. Korean Soc Ther Radiol Oncol : Vol. 15, No. 4, December, 1997 —

* , † , ‡ , §

* . * . * . * . * . *

† . ‡ . ‡ . ‡ . § . *

The Role of Adjuvant Postoperative Radiotherapy in Curative Resectable Sigmoid Colon Carcinoma

Won Park, M.D.*, Jinsil Seong, M.D.*, Ki Chang Keum, M.D.*
Chang Ok Suh, M.D.*, Sang Wook Lee, M.D.*, Ji Hoon Lim, M.D.*
Jin Sik Min, M.D. †, Jae Kyung Roh, M.D. ‡, Joo Hang Kim, M.D. ‡
Hyun Cheol Chung, M.D. ‡, Kang Kyu Lee, M.D. § and Gwi Eon Kim, M.D.*

*Department of Radiation Oncology**, *General surgery†*, *Internal Medicine‡*,
Yonsei University College of Medicine, Yonsei Cancer Center,
Department of Radiation Oncology§, Yonsei University, Wonju College of Medicine

Purpose: To evaluate the role of postoperative radiation therapy after curative resection of sigmoid colon cancer

Materials and Methods: From 1988 to 1993, a total of 93 patients with curative resectable sigmoid colon cancer of modified Astler-Coller (MAC) stage B2, B3, C2, C3 was divided into two groups on the basis of those who received radiation treatment and those who did not. Forty-three patients who treated by surgery alone were classified as postop RT (-) group. The remaining 50 patients who underwent postoperative radiotherapy were classified as postop RT (+) group. In all patients in postop RT (+) group, radiation therapy was delivered using 4 or 10 MV linear accelerators to treat the tumor bed with approximately 5cm margin to a total dose 50.4-61Gy (median 54Gy) in 1.8Gy per fraction. Thirty-two patients were treated with 5-Fluorouracil based adjuvant chemotherapy at least 3 cycles, but these was no significant difference between two groups. Treatment failure pattern, 5year local failure-free survival rates (LFFS), and 5year disease-free survival rates (DFS) were compared between two groups.

Results: Five year LFFS and DFS were 85.1%, 68.5%, respectively. In postop RT (-) group, LFFS was 76.2%, compared with 91.7% in postop RT (+) group. Improved LFFS and DFS were seen for patients with stage C3 sigmoid colon carcinoma with postoperative radiation therapy compared with postop RT (-) group ($P=0.01$, $P=0.06$ respectively). In stage B3, LFFS was

1997 9 5 1997 11 5
: , 134

higher in postop RT (+) group than that in postop RT (-) group, although it was not significant. Especially, local control was higher in stage T4 in postop RT (+) group than that in postop RT (-) group.

Conclusion : This study showed significantly improved LFFS and DFS in MAC Stage C3 and improved tendency of LFFS and DFS in MAC Stage B3 disease. Large scale prospective study is required to verify the role of adjuvant radiation therapy in resectable sigmoid colon cancer.

Key Words : Sigmoid colon cancer, Postoperative radiation therapy

가
 9-13),
 , 가
 가
 가
 가
 가
 가
 가
 30%
 1-8), Modified Astler-Coller(MAC) Stage B2-C
 5-
 fluorouracil(5-FU) 가
 14-21% 9-11),
 B3-C 10-13), MAC Stage
 30%
 가
 5-FU 가
 가
 MAC Stage C 5-FU levamisole Kopelson 가 23),
 가 14-19),
 natural history 가
 가 2023),
 가
 가
 1988 1 1993 12
 MAC Stage B
 가
 가 1-3)

가 23 , 가 3 1 2 , 5
 3 , 4 가 93 가 40 , 가 53 (Table 1).
 103 가 93 가 58 .

Table 1. Enrolled Patients in Resectable Sigmoid Colon Cancer

Cases	Number	() 43	() 50
Total number of cases	133		
Cases Excluded From Analysis	40		
Metastatic disease or palliative resection	23		
Operation refusal	3	85	Hartmann's
Preoperative radiation treatment	4	procedure가 8	
Synchronous/metachronous primary	3		
Postoperative death	2		
Positive resection margin	5	50	
Cases for analysis	93		

Table 2. Patients Characteristics Between Postop RT(-) Group and Postop RT(+) Group in Sigmoid Colon Cancer

	Postop RT(-) (N=43)	Postop RT(+) (N=50)	Statistical Significance*
Age(years)			NS
Range(median)	39-77(63)	35-78(60)	NS
Male/Female ratio	18/25	22/28	
Pathologic differentiation			NS
Well	7(16.3%)	14(28.0%)	
Moderate	30(69.8%)	27(54.0%)	
Poor	0	3(6.0%)	
Unknown	6(14.0%)	6(12.0%)	
Tumor size			NS
5cm	27(62.8%)	32(64.0%)	
5cm<	11(25.6%)	13(26.0%)	
Unknown	5(11.6%)	5(10.0%)	
MAC stage			NS
B2	19(44.2%)	17(34.0%)	
B3	6(14.0%)	7(14.0%)	
C2	14(32.6%)	17(34.0%)	
C3	4(9.3%)	9(18.0%)	
T stage			NS
T3	40(93.0%)	46(92.0%)	
T4	3(7.0%)	4(8.0%)	
LN number			NS
0	25(58.1%)	24(48.0%)	
1-3	12(27.9%)	18(36.0%)	
4	6(14.0%)	8(16.0%)	
Operation method			NS
Sigmoid colectomy	40(93.0%)	45(90.0%)	
Hartmann's procedure	3(7.0%)	5(10.0%)	
Chemotherapy			NS
Yes	13(30.2%)	19(38.0%)	
No	30(69.8%)	31(62.0%)	

* : Independent samples T-test, NS : not significant

가
45Gy
: 54Gy)

1.8Gy 5
45Gy
50.4Gy-61Gy(

clipping
samples T-test
Kaplan-Meier method
Log rank test

Independent

가
. 93 32
4

3
5-FU(500mg/m²/day), leukovorin(20mg/m²/day)
levamisole

1.
93 29
31.2%
3-68 (: 17)
26 (89.7%)가 36
(41.4%)

가 19
가
(Table 2).

3
40%,
60%

carcinoembryonic antigen
X
21%,
가 20%
35%
가 14%

가

1-144
53 (: 51)
가 93 90
96.8%

2.5

(Fig. 1).

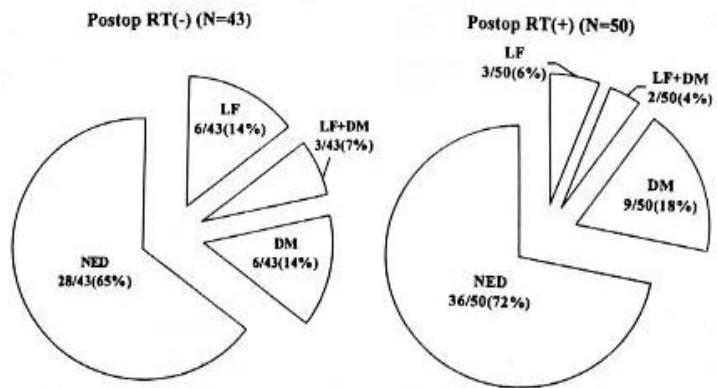


Fig. 1. Analysis of failure patterns in resectable sigmoid colon cancer (NED : no evidence of disease, LF : local failure, DM : distant metastasis)

85.1%
 MAC Stage B2, B3, C2, C3
 93.9%, 85.1%, 76.9%, 69.2%
 가
 가
 5
 87.5% 가 (P=0.02).
 가

3.5
 68.5%
 MAC Stage B2, B3, C2, C3
 88.1%, 61.5%, 56.7%, 51.9% 가
 (P=0.05),
 가

76.2% 91.7% 가 15%
 가

MAC , T
 5
 Table 3
 . MAC Stage B2, C2
 가 , MAC Stage B3
 19%
 MAC Stage C3
 88.9%
 25.0%
 (Fig. 2).
 (T4 Stage)

Table 3. Comparison of Five year Local Failure-Free Survival Rate between Postop RT (-) Group and Postop RT (+) Group in Sigmoid Colon Cancer

	Postop RT(-) (N=43)(%)	Postop RT(+)(N=50)(%)	Statistical Significance
MAC stage			
B2	17/19(87.4)	16/17(91.7)	NS
B3	4/ 6(66.7)	6/ 7(85.7)	NS
C2	12/14(82.5)	15/17(87.4)	NS
C3	1/ 4(25.0)	8/ 9(88.9)	P=0.01
T stage			
T3	33/40(79.8)	36/46(93.3)	NS
T4	1/ 3(33.3)	3/ 4(75.0)	NS
Number of involved LN			
0	21/25(81.7)	22/24(95.8)	NS
1-3	9/12(69.3)	16/18(87.7)	NS
4	4/ 6(66.7)	7/ 8(87.5)	NS

* : Log rank test
 NS : not significant

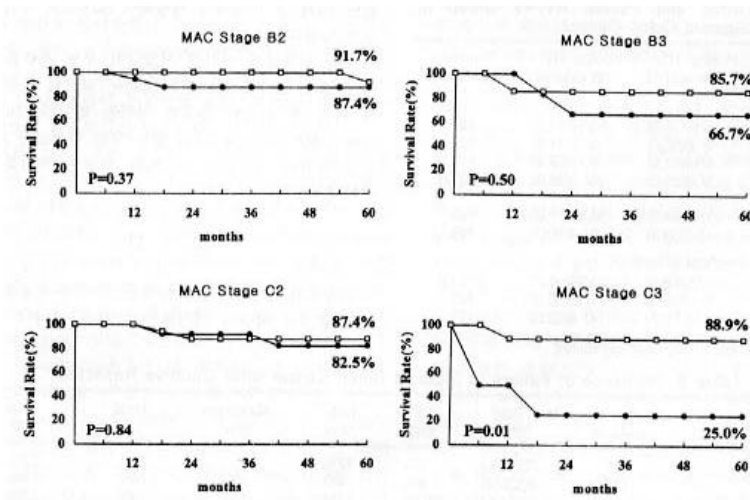


Fig. 2. Local failure-free survival rates according to MAC Stage in respectable sigmoid colon cancer (postop RT (-) : - - - - postop RT (+) : - - - -)

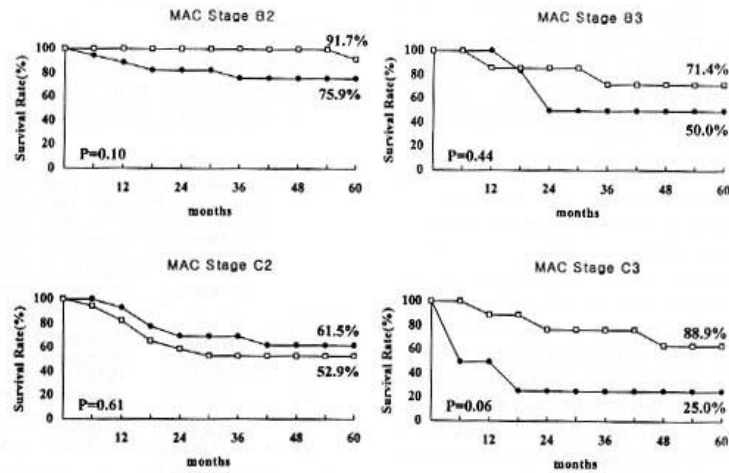


Fig. 3. Disease free-survival rates according to MAC Stage in resectable sigmoid colon cancer
 (postop RT(-) : - - - - postop RT(+) : - - - -)

Table 4. Comparing of Five year Disease-Free Survival Rate between Postop RT(-) Group and Postop RT(+) Group in Sigmoid Colon Cancer

	Postop RT(-) (N=43)(%)	Postop RT(+) (N=50)(%)	Statistical Significance*
MAC stage			
B2	15/19(75.9)	16/17(91.7)	NS
B3	3/ 6(50.0)	5/ 7(71.4)	NS
C2	9/14(61.5)	9/17(52.9)	NS
C3	1/ 4(25.0)	6/ 9(88.9)	P=0.06
T stage			
T3	27/40(64.3)	36/46(75.8)	NS
T4	1/ 3(33.3)	2/ 4(50.0)	NS
Number of involved LN			
0	18/25(68.8)	21/24(91.7)	P=0.09
1-3	6/12(45.5)	11/18(59.8)	NS
4	4/ 6(66.7)	4/ 8(50.0)	NS

* : Log rank test NS : not significant

44 19 가
 55.4% 49 10
 80.6% 가
 (P=0.02).
 61.9%, 73.7% T Stage,
 MAC Stage C3 (Table 4).
 63.5% 25.0%
 (Fig. 3).

Table 5. Incidence of Failure in Sigmoid Colon Cancer after Curative Resection

	No. of patients	Total failure	LF [*] only	DM [†] only	Abdomen only	Total LF	Total DM
Willet ^{10, 11)}	211	70(33%)	5%	12%		21%	28%
Minsky ¹²⁾	115	30(26%)	4%	4%	9%	14%	13%
Malcolm ¹³⁾	88	30(34%)	10%	11%	1%	19%	22%
Park [‡]	43	15(35%)	14%	14%		21%	21%

* : Local Failure † : Distant Metastasis ‡ : This study

가 , levamisole 5-FU
 가 66% 74%
 가 levamisole
 가 15, 16)
 가 5-FU levamisole 가
 가 17, 18), levamisol leukovorin
 가 19)
 가
 가
 . Gunderson
 1 2nd look operation
 91 48%(
 22%), 30% (: 7.7%),
 21% (: 7%)
 가
 1, 2, 9), 20-22),
 23),
 Duttonhaver 9, 20) 32
 80
 43-63Gy . 80
 14-21% (: 4-10%), 26 (33%) 16%(
 13- 28% (: 4-12%) : 9%)
 가 MAC Stage B3-C
 6-25% , 5
 가 MAC Stage B3 51%
 Gunderson 78% , C2 39% 57% , C3 29%
 49% MAC Stage
 20-50% B3-C
 가 10-13)
 . Willet 21, 22) 98
 203
 50.4-54Gy
 . NCCTG Mayo clinic 93%,
 401 (7%) 72% 69%, 47%
 levamisole
 levamisole 5-FU
 50%, levamisole 5-FU 가 60%
 52%, 43% ,
 가
 MAC Stage B 가 53%
 14). Intergroup study 1296
 MAC Stage C 가
 929 levamisole
 49% 65% , 1cm

가 가 5-FU 가

Kopelson²³⁾ 85 17

4-6 45-51Gy

가 9% 30% , MAC Stage B2-3 5

64% 100% (P<0.05), MAC Stage C2-3

MAC Stage B2, B3

가 MAC Stage B3, C3 . MAC Stage B3 가 86% , MAC Stage C3 89% , MAC Stage C3 가 가 가 18%

가 Willet 21, 22) 가 가 30%

가 가 가

Stgae B3, C3 - , MAC 가

1. Rich T, Gunderson LL, Lew R, Galdibini JJ, Cohen AM, Donaldson G. Patterns of recurrence of rectal carcinoma after potentially curative surgery. *Cancer* 1983; 52:1317-1329
2. Gunderson LL, Sosin H. Areas of failure found at reoperation (second or symptomatic look) following "curative surgery" for adenocarcinoma of the rectum : clinicopathologic correlation and implication for adjuvant therapy. *Cancer* 1974; 34:1278-1291
3. Minsky BD, Mies C, Recht AR, Rich TA, Chaffey JT. Resectable adenocarcinoma of the rectum: II. the influence of blood vessel invasion. *Cancer* 1988; 61:1417-1424
4. Tepper JE, Cohen AM, Wood WC, Orlow EL, Hsiedberg SE. Postoperative radiation therapy of rectal cancer. *Int J Radiat Oncol Biol Phys* 1987; 135-10
5. Gastrointestinal Tumor Study Group. Prolongation of the disease-free interval in surgically treated rectal carcinoma. *N Eng J Med* 1986; 312:1465-1472
6. Gastrointestinal Tumor Study Group. Survival after postoperative combination treatment of rectal carcinoma. *N Eng J Med* 1986; 315:1294-1295
7. Krook JE, Moertel CG, Gunderson LL, et al. Effective surgical adjuvant therapy for high-risk rectal carcinoma. *N Eng J Med* 1991; 324:709-715
8. Fisher B, Wolkmark N, Rockette HE, et al. Postoperative adjuvant chemotherapy or radiation therapy for rectal cancer: results from NSABP protocol R-01. *J Natl Cancer Inst* 1988; 80:21-9
9. Gunderson LL, Sosin MS, Levitt S. Extrapelvic colon-areas of failure in a reoperation series: implication for adjuvant therapy. *Int J Radiat Oncol Biol Phys* 1985; 11:731-741
10. Willet CG, Tepper JE, Cohen AM, Orlow E, Welch CE. Failure pattern following curative resection of colonic carcinoma. *Ann Surg* 1984; 200:685-690
11. Willet CG, Tepper JE, Cohen AM, Orlow E, Welch C, Donaldson G. Local failure following curative resection of colonic adenocarcinoma. *Int J Radiat Oncol Biol Phys* 1984; 10:645-651
12. Minsky BD, Mies C, Rich TA, Recht A, Chaffey JT. Potentially curative surgery of colon cancer: patterns of failure and survival. *J Clin Oncol* 1988; 6:106-118
13. Malcolm AW, Perencevich NP, Olson RM, Hanley JA, Chaffey JT, Wilson RE, et al. Analysis of recurrence patterns following curative resection for carcinoma of the colon and rectum. *Surg Gynecol Obstet* 1981; 152:131-136
14. Laurie JA, Moertel CG, Fleming TR, et al. Surgical

- adjuvant therapy of large bowel carcinoma: an evaluation of levamisole and the combination of levamisole and fluorouracil. *J Clin Oncol* 1989; 7: 1447-1456
15. **Moertel CG, Fleming TR, MacDonald JS, et al.** Levamisole and fluorouracil for adjuvant therapy of resected colon carcinoma. *N Eng J Med* 1990; 322: 352-358
 16. **Moertel CG, Fleming TR, MacDonald JS, Haller D, Laurie J.** The intergroup study of fluorouracil (5-FU) plus levamisole and levamisole alone as adjuvant therapy for stage C colon cancer. *Proc Am Soc Clin Oncol* 1992; 11:161
 17. **NIH Consensus Conference.** Adjuvant therapy for patients with colon and rectal cancer. *JAMA* 1990; 264:1444-50
 18. **Lopez M.** Adjuvant therapy of colorectal cancer. *Dis Colon rectum* 1994; 37(suppl):S86-S91
 19. **Wolmark N, Rockette HE, Fisher B, Wickerham DL, Redmond C, Fisher ER, et al.** The benefit of leukovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer : results from NSABP protocol C-03. *J Clin Oncol* 1993; 10: 1879-1889
 20. **Duttenhaven JR, Hoskins RB, Gunderson LL, Tepper JE.** Adjuvant postoperative radiation therapy in the management of adenocarcinoma of the colon. *Cancer* 1986; 57:955-963
 21. **Willet CG, Tepper JE, Shellito PC, Wood WC.** Indication for adjuvant radiotherapy in extrapelvic colonic carcinoma. *Oncology* 1989; 3:25-31
 22. **Willet CG, Fung CY, Kaufman DS, Efird J, Shellito PC.** Postoperative radiation therapy for high risk colon carcinoma. *J Clin Oncol* 1993; 11: 1112-1117
 23. **Kopelson G.** Adjuvant postoperative radiation therapy for colorectal carcinoma above the peritoneal reflection:1.sigmoid colon. *Cancer* 1983; 51:1593-1598

= =

* , † , ‡
 † , § , *

:

가 ,
 가

: 1988 1 1993 12
 93 가

43

가 가 50

1-2

가

5cm

4 MV

10 MV

가

1.8Gy

50.4Gy-

61Gy

5-Fluorouracil

32

가

:5

85.1%, 68.5%

76.2%

91.7%

. MAC Stage C3

($P=0.01$, $P=0.06$). MAC Stage B3

가

(Stage T4),

:

MAC Stgae B3, C3 -

가

가