The Role of Postoperative Pelvic Radiation Therapy in Rectal Cancer

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To evaluate the role of postoperative pelvic radiation therapy in rectal cancer, a retrospective analysis was done on 189 patients with modified Astler-Coller stages B2+3, C1, and C2+3 who were treated from February 1979 to June 1986. Forty-seven patients were staged as B2+3, 17 as C1, and 125 as C2+3. As a curative resection, 41 received low anterior resection, 143 received abdomino-perineal resection, and five received pelvic exenteration. The survival and disease-free survival rates of the total patients at five year were 45.3% and 44.1%, respectively. The stage was an important prognostic factor for survival and disease-free survival: the survival rates at five year were 63.4% in stage B2+3, 62.4% in C1, and 37.2% in C2+3 (p<0.005); the disease-free survival rates at five year were 55.7% in B2+3, 65.7% in C1, and 36.4% in C2+3, respectively (p<0.01). The liver was the most frequently involved organ of recurrence followed by the lung and the perineum. The patients who received low anterior resection achieved better disease-free survival but were more prone to late radiation bowel morbidities than those who received abdominoperineal resection. Postperative pelvic radiation therapy proved to be effective in locoregional disease control but did not prevent the appearance of distant metastasis, which was of major concern in advanced stages. Patterns of treatment failure, and factros relating to radiation morbidity are discussed, and therapeutic options for better results are proposed.

Key Words: Rectal cancer, Postoperative radiation therapy

INTRODUCTION

The rectum is partially peritonealized in its upper portion while the rest of it lacks peritoneal coverings. Cancers arising in the middle or lower rectum may spread to the perirectal tissue with more ease because of absence of the anatomic barrier, the peritoneum. As a treatment method radical surgery plays a major role, but local and/or regional relapse has been the frequent problem.

In early stages of rectal cancer, i.e., in modified Astler-Coller (MAC) stages A and B1, postoperative adjuvant radiation therapy is not usually recommended because the risk of locoregional relapse is usually less than 10% after curative resection¹⁻⁴). In more advanced stages, form MAC B2 upto MAC C3, the risks of locoregional relapse are in the range of 25% to 50% or even higher with curative surgery alone^{3,4}), and so the addition of postoperative adjuvant pelvic radiation therapy has been generally recommended with the aim to decrease locoregional relapse and to improve survival.

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Meanwhile, the effectiveness of postoperative radiation therapy in the reduction of locoregional recurrence has been proven by many retrospective studies^{5~10)} and prospective studies^{11~15)}, but they usually shows little or no survival benefits.

In the previous reports presented from our hospital^{5,6)}, the role of postoperative radiation therapy in the reduction of locoregional recurrences had been clarified. And through this study we attempt to reevaluate and confirm this role, to view the patterns of treatment failure and major complications, by an updated data with longer follow-up periods, and to suggest future treatment directions for better result.

MATERIALS AND METHODS

Two hundred and thirty-one patients received pelvic radiation therapy between February 1979 and September 1986 at the Department of Therapeutic Radiology, Seoul National University Hospital, under the diagnosis of rectal cancer. Of these, 42 patients were excluded in this analysis because of various reasons: incomplete radiation dose to the pelvis (less than 30 Gy) due to poor compliance

of the patients in 12; early stage (MAC B1) that usually dose not need adjuvant radiation therapy in 11; metastatic disease (MAC D) recognized at the operation in 8; gross residual tumor after incomplete surgical resection in 5; radiation therapy given for the purpose of symptom palliation produced by local or regional relapse after previous curative surgery in 4; and histologic types other than adenocarcinoma in 2. One hundred and eighty-nine patients were thought to be eligible for the evaluation of effectiveness of postoperative pelvic radiation therapy in rectal adenocarcinoma and formed the basis of this study.

All the patients were restaged according to the modified Astler-Coller (MAC) staging system¹⁶ (Table 1) after thorough review of the medical and radiation therapy records. MAC stages B3 and C3 constituted only minor proportions and showed unusually better survival than expected, so for the purpose of simplicity we analysed these groups together with B2 and C2 groups, respectively.

Radiation therapy was usually commenced three to four weeks postoperatively when there was no wound problem, and the interval between surgery and radiation therapy did not exceed 12 weeks. Irradiation was delivered to cover the whole pelvis with or without inclusion of the perineum according to the estimated risk decided on an individual base, using megavoltage equipments (60 Co teletherapy unit, 6 MV or 10 MV linear accelerators) with a conventional fractionation schedule (180 cGy per day, five fractions per week). Generally AP-PA two field parallel opposing technique with the patients supine or three field technique using right and left lateral fieds plus PA portal with the patients prone were used. The prescribed dose to the whole pelvis was in the range between 45 Gy and 55 Gy (median dose was 50 Gy), and when necessary, small field boost irradiation to the tumor bed area was given in the range of 6 Gy and 12 Gy. In cases with tumors located near the anus, direct perineal boost irradiation using 60 Co γ -ray or electron beam was done with the patients in lithotomy position.

The patterns of failure were defined as locoregional when recurrence was confined to the pelvic cavity, as distant when there was metastasis outside the pelvic cavity, and as combined if both of these two components occurred together in one patients. If the patients needed hospitalization and/ or surgical correction during the follow-up period because of conditions thought to be related to postopertive radiation therapy, we regarded these as the major complications.

The base of follow-up was the date of definitive operation, and the median follow-up period in the survivors was 54 months ranging from four to 128 months. Survival period was to the time of death or to the time of the last follow-up, and the disease-free survival period was to the time of recurrences. The results were analysed as of October 31, 1990. Only seven patients were lost to follow-up within two years postoperatively, and the percentage of adequate follow-up (known final outcomes and/or observation for longer than two years) reached 97%. The survival rates and the cumulative risks of recurrences were calculated using the actuarial life table mehtod¹⁷⁾ and the comparisons of the survival rates were done using logrank chi-square test¹⁸⁾.

RESULTS

Age of the patients ranges from 21 to 70 years with the median of 49. As shown in Table 2, rectal cancer tends to occur more often with increasing age. Both sexes are thought to be equally affected with the male to female ratio of 1.15: 1 (53% vs 47%). Two-thirds were staged as having MAC C2+3 disease, one-fourth was staged as having MAC B2+3, and MAC stage C1 constituted only minority

Table 1.	Modified	Astler -Coller	Staging	System	(MAC)
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Stage		Definition
A	Nodes negative ;	lesion limited to the mucosa
B1	Nodes negative ;	extension of lesion through the mucosa but still within the bowel wall
B2	Nodes negative ;	extension of lesion beyond the entire bowel wall
В3	Nodes negative ;	surgical or pathologic adherence to or invasion of surrounding organs or structures
C1	Nodes positive;	lesion within the bowel wall
C2	Nodes positive;	extension of lesion through the entire bowel wall
СЗ	Nodes positive ;	surgical or pathologic adherence to or invasion of surrounding organs or structures

Table 2. Characteristics of Patients

Characteristic	Number	%
Age (γears)		
- 30	10	5.3
31 - 40	32	16.9
41 — 50	54	28.6
51 60	65	34.4
61 —	28	14.8
Median	49	
Range	21 —	70
Sex		
Male	101	53.4
Female	88	46.6
Stage		
B2 + 3	47	24.9
C1	17	9.0
C2 + 3	125	66.1
Histology		
Adenoca	168	88.9
W/D	78	
M/D	50	
P/D	5	
not speci*	35	
Mucinous	17	9.0
Signet ring	3	1.6
Papillary	1	0.5

^{*} Differentiation not specified

(9%) of this patient population. Histologically, adenocarcinoma constituted the vast majority of the patients (89%), and the variant types were diagnosed in the remainder (11%) (Table 2).

One hundred and forty-eight patients (78%) received sphincter-sarificing procedures (143 combined abdominoperineal resection and five pelvic exenteration), while 41 patients (22%) received sphincter-preserving low anterior resection. The type of operation was decided on according not only to the location of the tumor but to the operative finding and the desire of the patient (Table 3).

The survival and disease-free survival rates of the entire patient group at five year were 45.3% and 44.1%, respectively. The prognostic implication of modified Astler-Coller staging system was shown clearly: the survival rates at five year according to MAC stages were 63.4% in stage B2+3, 62.4% in

Table 3. Type of Operation by Tumor Location

	Distance from Anal Verge			
Operation	Within 6 cm	Above 6 cm	Unknown	Total (%)
LAR*	7	26	8	41 (22)
APR.**	111	29	3 .	143 (76)
PE #	2	2	1	5 (2)
Total	120 (64)	57 (30)	12 (6)	189 (100)

- * Low anterior resection
- ** Abdomino-perineal resection
- # Pelvic exenteration

Table 4. Patterns of Failure by Stage

Stage	LR*	DM#	LR+DM	Total
B2+3	9 (53%)	7 (41%)	1 (6%)	17 (100%)
C1	2 (40%)	3 (60%)	0 (0%)	5 (100%)
C2+3	17 (25%)	45 (66%)	6 (9%)	68 (100%)
Total	28 (31%)	55 (61%)	7 (8%)	90 (100%)

^{*} Locoregional failure, # Distant metastasis

C1, and 37.2% in C2+3, with statistical significance (p<0.005); the disease-free survival rates by stage groups were 55.7%, 65.7%, and 36.4%, respectively, with statistical significance also (p<0.01) (Fig. 1). The survival and disease-free survival figures in C1 group were relatively good compared to those in B2+3 group, which might have some drawbacks in interpretation because of small sample size.

We tried to verify the impact of tumor location on the disease-free survival with the assumption that the more distally located the tumor, the more frequently the locoregional failures should occur because of absence of the anatomic barrier, the peritoneal coverings. But there was no statistically meaningful difference according to the location of the tumor (within vs beyond 6 cm from the anal verge). On the contrary, there was a statistically survival significant difference in disease-free between sphincter-preserving and sphinctersacrificing operations (71.2% vs 36.8%; p<0.005). And there was a marginally significant difference between these two groups in survival (59.3% vs 41. 1%: 0.05) (Fig. 2). The stage distributionsaccording to operation types were not different from each other (0.5 by chi-square test).

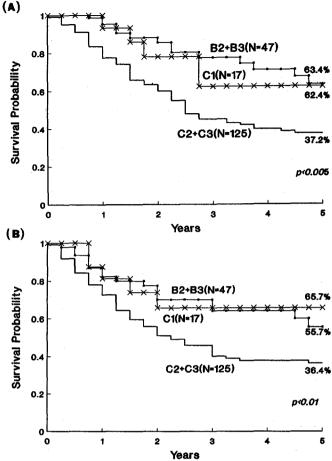


Fig. 1. Survival and disease-free survival according to modified Astler-Coller stages. Lymph node involvement with the same depth of invasion was a bad prognostic factor affecting not only survival rates (A), but also disease-free survival rates (B) at five year significantly. The survival and disease-free survival rates in C1 group were comparable with those in B2+3 group probably because of the small sample size.

One hundred and nine relapses were identified in 90 patients throughout this analysis. The patterns of failure as a function of stage is shown in Table 4. Of these, 28 patients (31%) experienced locoregional failures only, 45 patients (61%) experienced distant failures only, and seven (8%) experienced combined failures. It is evident that distant failure in C2+3 group was much more frequent than in lower stage grups (Table 4). The frequent sites of locoregional failures were the perineum in 13 patients, the pelvic lymph nodes in 12, and the adjacent pelvic organs in six (Table 5). And the most frequent site of distant failure was the liver in 25 patients, foll-

owed by the lungs in 18, the distant lymph nodes in 11, and the bones in 10 (Table 6). We reevaluated the radiation therapy technique applied to these patients by careful review of the radiation therapy records together with the simulation films in order to find the reason for more recurrences in the perineum than usually expected, which disclosed: that all of those failing in this site received abdominoperineal resection; that the perineum was entirely or partially omitted in the radiation portals in all of them (i.e., inadequate dose to the perineum); and that variant histologic subtypes, which comprised only about one-tenth in all patient popu-

Table 5. Sites of Locoregional Recurrence

Site	Number
Perineum	13
Pelvic LN	12
Pelvic organ	6
Anastomosis	4
Stoma	1
Total	36

Table 6. Sites of Distant Metastasis

Site	Number	
Liver	25	
Lung	18	
Distant LN	11	
Bones	10	
Peritoneum	5	
Brain	4	
Total	73	

Table 7. Perineal Recurrence vs Histologic Subtype in Patients Reciving Abdomino-Perineal Resection

Histologic	Perineal re		
subtype	Present	Absent	Total
Classic types	4	16	20
Variant types*	9	119	128
Total	13	135	148

Variant types include mucinous, signet ring, and papillry types.

0.05 by chi-square (X²) test.

Table 8. Bowel Complication vs Operation

Bowel	Operation			
Complication	LAR*	APR#	Total	
Absent	35	145	180	
Present	6	3	9	
Total	41	148	189	

Low anterior resection

lation (Table 2), were relatively frequent among these patients (4/13, 31%), where 2 mucinous types, one signet ring cell type, and one papillary type were encountered (Table 7).

The cumulative risks of locoregional and distant failures by stage were calculated using actuarial method¹⁵⁾, which indicated: that the cumulative risk of locoregional failure in each stage group was much alike, with majority occurring within the first two years (p>0.5 at 2 year and p>0.25 at 5 year) (Fig. 3); but that the cumulative risk of distant failure was much higher in C2+3 group than in B2+3 and C1, which increased continuously with the elapse of time (p<0.005 both at 2 and 5 year postoperatively) (Fig. 3).

There were ten cases with major complication which needed hospitalization for surgical correction and/or medical management. The median time to the occurrence of complication from the base of follow-up was nine months (range: 5-34 months). Intestinal obstruction was the most frequent type affecting eight individuals, while colonic perforation occurred in one patient and urethral stricture occurred in another one. Excluding the last patient with urethral stricture who received combined abdominoperineal resection, nine patients suffered from complication related to the bowel. The numbers of bowel complication according to operation type are shown on Table 8. The radiation dose to the whole pelvis in these patients was rather uniform (4,860 cGy-5,075 cGy), which is not different from that in the patients without complication. Of the ten, eight patients were operated on to correct the problem and no recurrence was found, and remaining two were managed conservatively.

DISCUSSIONS

The disease-free survival rates at five year according to stage after curative surgery alone, reported by Rich et al.4, were 76.9% in stages A+B1, 42.4% in stages B2+3, 25.0% in stage C1, and 22.5% in stages C2+3, respectively. The same parameters analysed in our study are higher by about 15% in B2+3 and 20% in C2+3 than those reported by these authors (Fig. 1). Tepper et al.9 in Massachusetts General Hospital (MGH) analysed 5 year treatment results of rectal cancer by comparing the historical control group receiving surgery alone with the group receiving postoperative radiation therapy as well, all of who were treated at the same hospital, and demonstrated that postoper-

[#] Abdomino perineal resection

P < 0.001 on chi-square (X^2) test

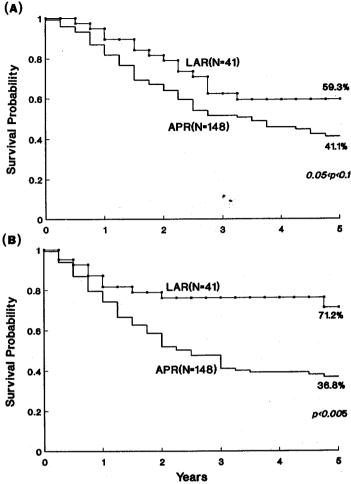


Fig. 2. Survival and disease-free survival according to operation type. There was a marginally significant difference in survival between those receiving sphincter-preserving and those receiving sphincter-sacrificing operations (A), and there was a statistically significant difference in disease-free survival between these two groups (B).

ative radiation therapy improved local control from 77% to 91% in B2 disease, and from 53% to 79% in C2 disease. The locoregional disease-free survival rates at five year in our study were 71% in B2+3 group and 72% in C2+3 group (Fig. 3), which were comparable with those reported at MGH series when radiation therapy was added. Though the analysis done at MGH was not prospectively designed, the improvements in local control by 14% in B2 and 26% in C2 should be attributed to postoperative radiation therapy. The survival rates at five year after surgery alone, reported by Minsky et al., 30 were around 60% in B2+3, and about 35% to 40% in C2+3, which do not seem different from

our study which used postoperative radiation therapy in addition to surgery (Fig. 1). From these informations, we may conclude that the addition of postoperative pelvic radiation therapy can improve disease-free survival but not survival.

Rich et al.⁴⁾ reported that the type of operation did not influence the incidence of pelvic failure. But according to the report by Minsky et al.³⁾, the type of operation affected survival significantly, showing better survival in those receiving low anterior resection than that in those receiving abdominoperineal resection (80% vs 60%, p=0.02). But if corrected for stage, there was no significant difference according to the operation type. In our

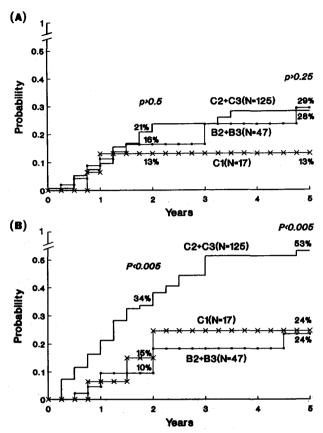


Fig. 3. Cumulative risks of recurrence according to the failing site and modified Astler-Coller stage. The cumulative risk of locoregional recurrence in each stage group was much alike, with majority occurring within the first two years (A), while that of distant metastasis showed marked differences according to stage (B); in stage C2+3, the risk was much greater than in earlier stages, and it rised continuously with the elapse of time after two years postoperatively.

study, the sphincter-sacrificing procedures adversely affected the disease-free survival at 5 year significantly (37% vs 71%, p<0.005) (Fig. 2), though the stage distributions according to operation type were essentially the same.

Rich et al.⁴), in their retrospective analysis of the recurrence patterns in rectal cancer after potentially curative surgery without adjuvant treatment, reported that the incidences of pelvic failure and of distant failure at five year were 30.5% and 28.8% in stage B2+3, and 50.5% and 47.5% in stage C2+3, respectively. The relative proportions of the pelvic and the distant components were virtually equal to one another within the same stage group when no adjuvant modality was added. In our analysis, the

cumulative actuarial risk of locoregional recurrence in each stage group showed differences neither in the slope nor in the shape of the curve (Fig. 3), while the cumulative risk of distant metastasis in each group showed marked differences both in the slope and the shape of the curve (Fig. 3), reaching a statistically significant level as early as two years postoperatively. These findings that there was little or no significant difference in the risk of locoregional failure between B2+3 and C2+3 groups in our study and that the risk of locoregional failure in C2+3 group in our study was much lower than the Rich's data⁴⁾ in the coresponding stage group, which employed no radiation therapy, strongly suggest that postoperative pelvic radia-

tion therapy did contribute to the decrement of locoregional failure quite effectively. But the pity is that it did not work in preventing or decreasing the incidence of distant metastasis, which was the major problem in the advanced stage group (C2+3).

As the frequent sites of locoregional failure the perineum was ranked in the first in our study, which might have been prevented if more cares had been taken of to irradiate this site electively with adequate doses. It would be reasonable to include the perineum withih the radiation portals with the same dose to that prescribed to the whole pelvis, if any risk factors such as close proximity of tumor to the anal verge, intraoperative tumor spilage, and documentation of variant subtypes histologically were present in the patients who received abdominoperineal resection. In fact, after the use of three field technique including the perineum within the irradiated volume, recurrences in this site seldom occurred. The liver was the most commonly affected organ of distant metastasis likewise in various other reports3,4,12,13). And if we take into account of intraabdominal lymph node metastasis and peritoneal seeding together with metastasis to the liver, about half of the failures outside the pelvis occurred within the abdominal cavity.

In both the patient groups treated with surgery alone and surgery plus postoperative radiation therapy, the incidence of small bowel obstruction requiring laparotomy was usually in the order of 5% according to the report by Tepper et al.9). Nine bowel complications needing surgical correction out of 189 total patients (4.8%) in our study seemed to correspond well to the above report. Factors related to the bowel related late radiation morbidity are known to be radiation technique, irradiated volume, dose to the normal bowel, and other conditions such as past history of pelvic surgery or pelvic inflammatory disease¹⁹⁾. According to Gunderson et al.20), radiation therapy technique may contribute to the incidence of small bowel complication, which was about 10% to 12% when AP/PA two parallel opposing technique was used in MD Anderson Hospital, but it was less than 5% when four field box technique was used in MGH. In our study, six (including one bowel perforation) out of nine bowel related complications needing reoperation were observed in those who received low anterior resection and radiation therapy using AP/PA parallel opposing technique (Table 8). Considering that two-thirds of those suffering from major complication received low anterior resection while all receiving low anterior resection comprised only one-fifth of the total patients analysed here, it can be concluded that the technique of radiation therapy together with the volume of the small bowel irradiated are the main determinants in the occurrence of this type of complication (p<0.001 by chi-square (x^2) test) (Table 8). To decrease the volume of the small bowel within the radiation portals, informations regarding the location and mobility of the small bowel with small bowel radiographs taken postoperatively may be useful in the radiotherapy treatment planning²⁰. Setting the patient on prone position with the urinary bladder distended during the irradiation may also help decrease the small bowel volume irradiated.

The radiation dose to the small bowel exceeding 45 Gy to 50 Gy, which is thought to be the tolerance limit of the normal small bowel, is related to the appearance of late bowel complications. In our study, though not meaningfully higher than those without complications, the doses to the whole pelvis were about 50 Gy (4,860 cGy-5,075 cGy). Devereux et al.21) demonstrated that tumoricidal radiation dose averaging 55 Gy may be safely delivered with excellent locoregional disease control (two locoregional recurrences out of 19 patients with C3 stage) but with no bowel related complications, when intestinal sling procedure, elevating the small bowel out of the pelvis and hence out of future radiation portals, was added at the time of primary surgery.

In advanced stages, usually sages between B2 through C3, curative surgery followed by postoperative pelvic radiation therapy is generally recommended, which, as in this study, resulted in significant reduction of locoregional recurrences. Devereux et al.21) employed higher dose than usual (55 Gy) with an excellent local disease control but could not prevent the appearance of distant metastasis. Tepper et al.22), in an attempt to improve the local control and survival in patients with locally advanced rectal cancer, have used a combination of high-dose preoperative radiation therapy upto 5,040 cGy followed by surgical resection and intraoperative electron beam radiation therapy (IORT) when there were visible or palpable residual tumors, microscopically positive surgical margins, or persisting tumor adherence. The local control and survival in the patients treated by this method for the control of primary tumors appeared favorable compared to other series in the literature and they suggested a benefit to the use of IORT as a boost technique. But this approach did not prevent

and reduce the incidence of distant metastasis either.

To overcome the problem of distant metastasis. adjuvant chemotherapy with or without radiation therapy was designed and tried in some prospective randomized studies. According to the report by the Gastrointestinal Tumor Sudy Group (GITSG)13,14), combined modality arm employing concomitant administration of 5-flourouracil (5-FU) plus methyl-CCNU and pelvic radiaion therapy showed significant advantages not only in disease-free survival but also in survival. Meanwhile, the results reported by the NSABP (protocol R-01)12) showed that only the adjuvant chemotherapy arm employing 5-FU, methyl-CCNU, and vincristine (MOF) was superior to the control arm both in disease-free and overall survivals, whose benefits were confined to the males only, while the postoperative radiation therapy arm reduced the incidence of locoregional recurrence but failed to be a better option in terms of disease-free and overall survivals. In interperting the results from these two studies, it should be noted that there was no combined modality arm in the NSABP study, and the agents used in the latter study were very similar to those used in the GITSG, which demonstrated no value for chemotherapy alone arm. From these unbalanced conclusions we feel that the results reported by the NSABP should be accepted cautiously until a separate prospective study solve this complicated problems²³⁾. But, in summary, it seems manifest that the combination of radiation and chemotherapy may offer the greatest survival advantage in regionally advanced rectal cancer. The uncertainties are: which agents are to be chosen; by which route and how long these drugs should be administered; and what is the best schedule in the combination of drugs and irradiation²⁴). In practice, it may be reasonable and safe to administer 5-FU, which seems to be the most effective agent, together with pelvic radiation therapy. And this type of combination may be recommended for those at high risk of locoregional and distant failure after curative surgery. With regard to the high cumulative risk of distant metastasis in C2+3 group in this study (Fig. 3), combination of systemic chemotherapy and pelvic radiation therapy might have been a reasonable option to improve survival. Recently, trial of this combined modality adjuvant therapy using 5-FU plus radiation therapy for those with locoregionally advanced rectal cancer (MAC B2 through C3) is under progress at our hospital as a prospective non-randomized study. Though the preliminary data analysis of this trial did not show marked reduction in distant metastasis¹⁵⁾, it is not wise to abandon this trial because the follow-up period was too short to derive any conclusions. We anticipate to present a better results with this new option.

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= 국문초록 ==

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직장암의 치료에 있어서 골반부위에 대한 수술후 방사선치료의 역할을 검증하기 위하여 1979년 2월부터 1986년 6월사이에 치료를 받은 modified Astler-Coller 병기 B2+3, C1, 및 C2+3의 직장암 환자 189명에 대한 후향적 분석조사를 시행하였다. B2+3 병기의 환자는 47명이었으며, C1 병기는 17명, 그리고 C2+3 병기는 125명이었다. 근치적 수술로 41명이 전방절제술을, 143명이 복부회음절제술을, 그리고 5명은 골반장기적출술을 시행받았다. 전체환자군의 5년 생존율 및 5년 무병생존율은 각각 45.3% 및 44.1%였다. 각 병기별 5년 생존율은 B2+3에서 63.4%, C1에서 62.4%, C2+3에서 37.2%로서 이는 통계적으로 유의한 차이를 보였으며 (p<0.005), 5년 무병생존율2+3에서 55.7%, C1에서 65.7%, C2+3에서 36.4%로서 이것도 역시 통계적으로 유의한 차이를 보여 (p<0.01) 병기가 생존율 및 무병생존율에 있어 중요한 예후인자임을 알 수 있다. 재발시 가장많이 침범되는 장기는 간이었으며, 그 다음으로는 폐 및 회음부였다. 전방절제술을 시행받은 환자군에서 복부회음절제술을 시행받은 환자군보다 보다 좋은 무병생존율을 보였고 방사선에 의한 장합병중의 위험이 더 높았다. 수술후 방사선치료로 국소재발억제에는 좋은 효과가 있었으나 진행된 병기에서 주로 문제가 되는 원격전이의 발생은 예방하지 못하였다.