

## Local Recurrence after Curative Resection of Rectal Cancer in Relation to Various Factors

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**Abstract**—To analyze the relationship between local recurrence and various clinical and pathological features, 339 cases who had undergone curative surgery for rectal cancer during 10 year period were reviewed. Dukes stage, especially extent of lymph node metastasis, and grade of histologic differentiation are associated with risk of local recurrence. Tumor size (5 cm >, 5 cm <) and location (upper, mid, low), duration of symptom (6 month >, 6 month — 1 year, 1 year <) and presence or absence of obstructive symptom are not associated with risk of local recurrence.

To determine the adequate minimal length of distal resection of normal looking rectum, rate of local recurrence and survival of the cases who had undergone sphincter saving operation were analysed according to the length of distal resected rectum (2 cm >, 2-5 cm, 5 cm <). The result shows that to reduce local recurrence, especially anastomotic recurrence, after sphincter saving operation, at least 2 cm of distal rectum should be resected and this is more true in the cases without lymph node metastasis.

**Key words:** *Rectal cancer, Local recurrence, Sphincter-saving operation, Anastomotic recurrence*

### INTRODUCTION

Local recurrence after curative resection for carcinoma of the rectum is a serious problem that might be a direct cause of death. It is particularly distressing for the patients in good general condition without disseminated disease. Therefore prevention and anticipation of local recurrence is very important in the management of rectal cancer.

This study has two major objectives. First, to identify clinical and pathological features associated with an increased risk of local recurrence, we analysed the relationship between local recurrence and various factors such as clinical stage, number of metastatic lymph node(s), tumor size and location, degree of histologic differentiation, duration of symptom and symptoms of obstruction. Second, in the cases who received a sphincter saving operation, we examined to determine whether there is any relationship of length of distal resected rectum to the rate and site of local recurrence and prognosis.

### MATERIAL AND METHODS

From 1973 to 1983, all patients who received a curative sphincter-saving operation or Miles operation for adenocarcinoma of the rectum and rectosigmoid at Seoul National University Hospital were studied retrospectively. We excluded those cases with multiple colorectal cancer, familial polyposis, ulcerative colitis and cases who received preoperative radiation or pelvic exenteration or a Hartmann operation. The decision as to which operation was performed was made by operating surgeon. Neither operative technique nor measures to prevent tumor implantation were standardized.

Patient status was checked at the end of June, 1986 by chart review, direct contact, telephone call or postcards. All the follow up cases had been followed for at least two years. As shown on the Table 1, 339 patients had curative resection during the 10 year period. Of these 110 cases had recurrences and 126 cases were clinically cancer free. Excluding two operative mortality cases the disease status of remaining 101 cases was unknown. Two cases without recurrence died of unrelated cause.

**Table 1.** Follow-up status after curative resection of 339 cases with rectal and rectosigmoid carcinoma (1973-1983)

Follow-up status	Sphincter saving operation		Abdominoperineal resection		Total (%)
Recurrence	34		76		110(32.4)
Alive	5		8		13
Dead	23		65		88
Unknown	6		3		9
No recurrence	51		75		126(37.2)
Alive	50		74		124
Dead*	1		1		2
Status unknown	22		55		77(22.7)
Alive	5		8		13
Dead	17		47		64
Lost to follow-up	9		15		24(7.1)
Operative mortality	0		2		2(0.6)
<b>Total</b>	<b>116</b>	<b>(34.2)</b>	<b>223</b>	<b>(65.8)</b>	<b>339(100.0)</b>

\* Died of unrelated cause

\*\* Follow-up rate; 92.9% (315/339)

Therefore 234 patients who were followed in regards to the disease status, recurrent site and pattern were analyzed. Of these, eighty four patients received a sphincter saving operation-anterior resection or pullthrough operation and coloanal anastomosis-and 150 patients received the Miles operation,

Clinical stage was assessed by conventional Dukes classification based on the pathologic report. Histologic type was also based on the degree of differentiation by the pathologic report. Location of rectal cancer was divided into three groups, upper, mid and low, according to the distance from anal verge to lower margin of tumor. Midrectal cancer involves tumor on 6 to 11.9 cm above from anal verge. The rate of local recurrences was compared between groups according to the tumor size using the criteria of 5 cm of maximum tumor diameter, according to the duration of symptom using the criteria of 6 months and 12 months and presence or absence of obstructive symptom such as constipation or small calibered stool.

Local recurrence has been defined as the recurrence of tumor at or adjacent to the primary site, detected after a potentially curative operation. Intrapelvic recurrence refers to the presence of symptoms and signs, including findings by computerized tomography, ultrasonography and intravenous pyelography. Most other local recur-

rences are biopsy proven. The length of rectum below the lower border of the tumor was measured by the pathologist on formalin fixed specimens that had been pinned out on a cork board to their natural length immediately following removal from the patients.

Statistical comparison was performed utilizing the Chi square test and survival and disease free survival rate were calculated from the date of operation using the life table method. Survival curves were compared using log rank test.

## RESULTS

Of the total 234 cases who were followed up, 110 (47.0%) cases developed recurrence and 75% of these occurred within 2 years. Of 110 recurrent cases, 71 (30.3%) cases developed local recurrence, of which 90% occurred within 2 years after operation. Fig. 1 shows the disease free survival curve after resection of rectal cancer in 234 cases.

Survival curve of 65 patients with local recurrence after detection of local recurrence is shown in Fig. 2. Most patients died within 2 years and median survival was 9.9 months.

Sites of recurrence in 71 cases with local recurrence are shown in Table 2. The major sites are intrapelvic (47.9%), perineal, vagina and the anastomosis site.

Of 71 cases with local recurrence, 20 (23.8%)

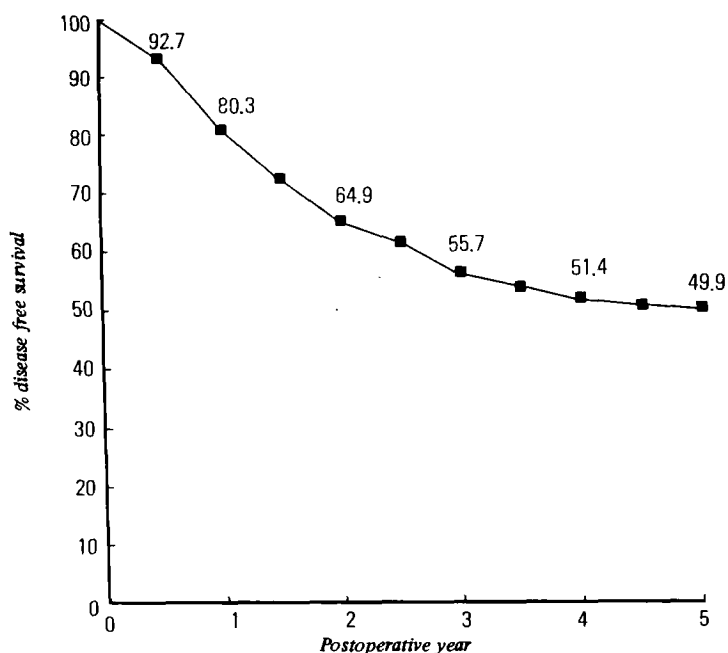


Fig. 1. Disease free survival rate after curative resection of rectal cancer in 234 patients.

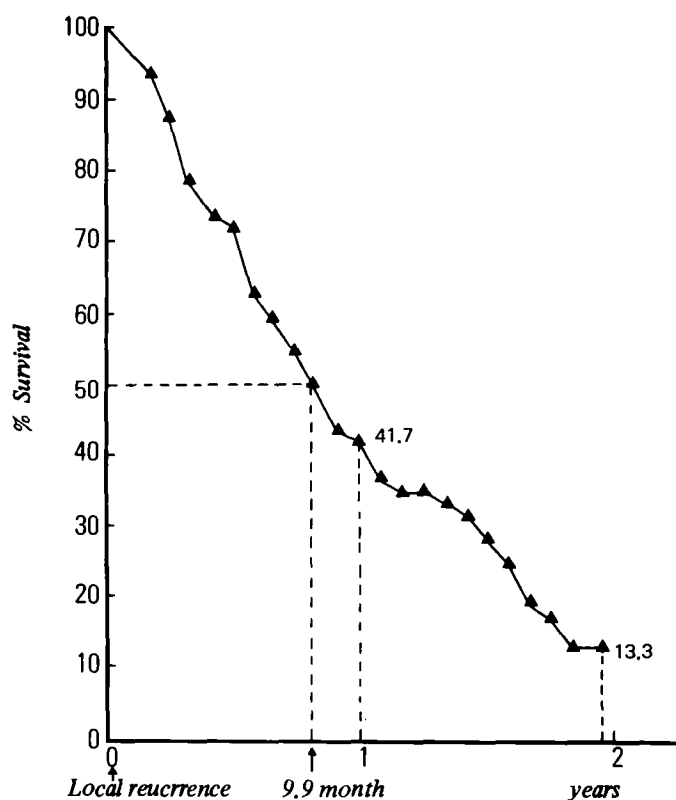


Fig. 2. Survival curve after local recurrence.

cases developed recurrence after sphincter saving operation and 51 (34.0%) cases developed recurrence after abdominoperineal excision. Local recurrence rates according to the Dukes class are shown

Table 2. Sites of local recurrence in 71 cases

Site	No. of cases (%)
Intrapelvic	34 (47.9)
Perineal	18 (25.4)
Vagina	12 (16.9)
Anastomosis	9 (12.7)
Inguinal	5 ( 7.0)
Bladder	5 ( 7.0)
Colostomy	2 ( 2.8)
Miscellaneous*	5 ( 7.0)

\* Main wound, labium, uterus, sacrum

in Table 3. As the cancer stage progresses, the risk of local recurrence is increasing ( $p < 0.05$ ). The cases with lymph node metastasis especially have a significantly higher incidence of local recurrence, regardless of extent of wall invasion. Among the cases with lymph node metastasis, cases with multiple lymph node metastasis, especially over 3 lymph nodes, have higher risk of local recurrence (Table 4) ( $p < 0.005$ ).

Table 5 summarize the relative risk of local recurrence according to the various factors. The cases that the each of these factors could not be checked were excluded. With each of these factors, the table compares the lymph node positive group with lymph node negative group. We compared tumor diameters less and greater than 5 cm, symptoms less than 6 months, 6 to 12 months, over 12 months and the presence or absence of obstructive symptoms. However, no significant difference was noted between groups. In the location of tumor, although the risk of local recurrence of low rectal cancer with lymph node metastasis appears to be higher than those of upper level cancer, as a total, no difference can be found between groups. In the grade of histologic differentiation, differentiated tumors have low risk of local recurrence than the poorly differentiated, mucinous or signet ring cell carcinoma ( $p < 0.05$ ).

To determine the relationship of length of distal resected rectum to risk and site of local recurrence, 84 cases who received a sphincter saving operation were analyzed. Patients are divided into three groups according to the length of distal resected rectum, less than 2 cm, 2 cm to less than 5 cm and over 5 cm. Case numbers with local recurrence are shown in Table 6. Among 84 patients, 20 patients developed local recurrence. Details in-

**Table 3.** Local recurrence and clinical stage

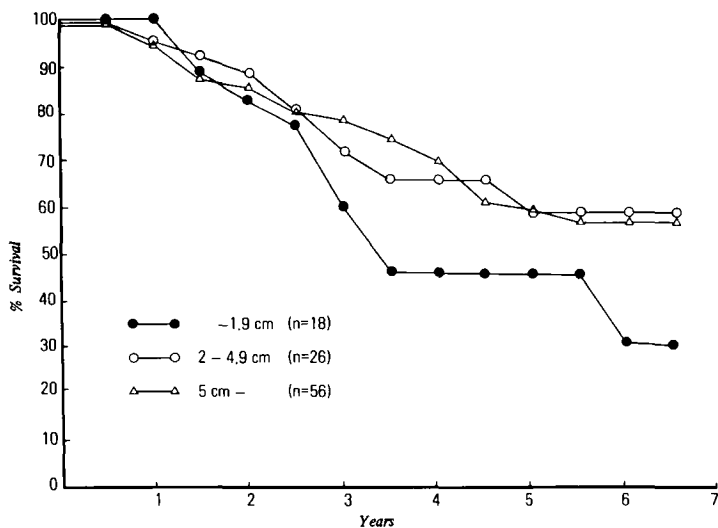
Dukes class	Wall extension	Lymph node metastasis	Number of patients	Number of local recurrence (%)
A	-	--	55	4 ( 7.3)
B	+	-	62	14 (22.6)
C C1	-	+	19	9 (47.4)
C2	+	+	98	44 (44.9)
Total			234	71 (30.3)

\* Relative risk(r) wall extension (+)/(-); r = 2.06  
 LN metastasis (+)/(-); r = 2.94  
 \*\* A vs B or C; p < 0.025, B vs C; p < 0.005

**Table 4.** Number of metastatic lymph node and local recurrence of rectal cancer

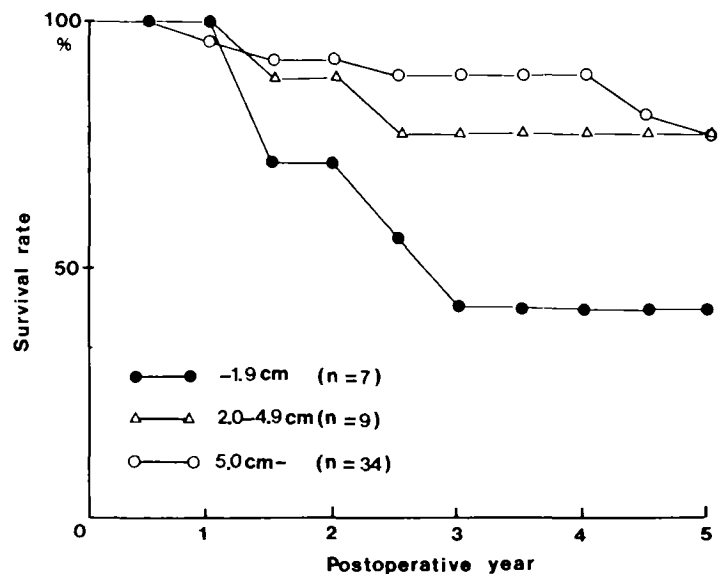
Number of metastatic lymph node	Number of total cases	Number of local recurrence (%)
0	117	18 (15.4)
1 - 3	68	25 (36.8)
4 -	49	28 (57.1)

p < 0.005



**Fig. 3.** Survival curves of patients according to the length of resected distal rectum.

cluding disease free interval and survival of 20 local recurrence cases after the curative sphincter saving operation are displayed in Table 7. Of 20 cases with local recurrence, 3 patients received a second curative surgery. All the cases except three have well to moderately differentiated tumor and the remaining three cases are mucinous carcino-



**Fig. 4.** Survival curves of patients without lymph node metastasis according to the length of distal resected rectum.

ma. The length of distal resected rectum of those three cases with mucinous carcinoma was over 2 cm.

Local recurrence of each group according to the Dukes classification are demonstrated in Table 6. As a total, the higher risk in patients who have less than 2 cm distal resection margin is noted, however, the differences are not clear in each Dukes class. If anastomotic recurrence is considered only, a significant difference is evident in total (p < 0.005) and in each Dukes class (Table 8). This data suggests that at least 2 cm distal resection margin should be resected to reduce the risk of anastomotic recurrence.

Survival status of 100 patients out of 116 pa-

**Table 5.** Local recurrence after curative resection of colorectal cancer in relation to various factors

Factors	Number of local recurrence/Total (%)			Significance of difference in total
	LN (—)	LN (+)	Total	
<b>Maximum diameter of tumor</b>				
5 cm >	10/53(18.9)	20/42(47.6)	30/95 (31.6)	N.S.
5 cm <	10/58(17.2)	31/72(43.1)	41/130(31.5)	
<b>Duration of symptom (month)</b>				
6 >	8/49(16.3)	15/36(41.7)	23/85 (27.1)	X <sup>2</sup> = 1.779 p > 0.1
6 — 12	4/34(11.8)	13/36(36.1)	17/70 (24.3)	
12 <	8/28(28.6)	13/33(39.4)	21/61 (34.4)	
<b>Symptom of obstruction</b>				
(+)	11/57(19.3)	34/75(45.3)	45/132(34.1)	X <sup>2</sup> = 1/405 p > 0.1
(—)	9/56(16.1)	17/41(41.5)	26/97 (26.8)	
<b>Location of tumor (distance from anal verge; cm)</b>				
Upper (12 cm —)	7/32(21.9)	6/18(33.3)	13/50 (26.0)	X <sup>2</sup> = 1.197 p > 0.1
Mid (6 — 11.9 cm)	6/38(15.8)	19/49(38.8)	25/87 (28.7)	
Lower (— 5.9 cm)	5/47(10.6)	28/50(56.0)	33/97 (34.0)	
<b>Hostologic grade</b>				
Well differentiated	8/52(15.4)	12/27(44.4)	20/79 (25.3)	X <sup>2</sup> = 8.690 p < 0.05
Moderately differentiated	5/28(17.9)	12/29(41.4)	17/57 (29.8)	
Poorly differentiated	0/2	3/5 (60.0)	3/7 (42.9)	
Mucinous	3/4 (75.0)	9/18(50.0)	12/22 (54.5)	
Signet ring cell	—	2/3 (66.7)	2/3 (66.7)	

**Table 6.** Local recurrence according to the length of distal resected rectum and Dukes class

Length of Distal resected Rectum (cm)	No. of Local recurrence/Total (%)			
	Dukes A	Dukes B	Dukes C	Total
I — 1.9	0/0	2/4 (50.0)	3/8 (37.5)	5/12(41.7)
II 2.0 — 4.9	1/5 (20.0)	2/5 (40.0)	2/17(11.8)	5/27(18.5)
III 5.0 —	1/8 (12.5)	3/24(12.5)	6/13(46.2)	10/45(22.2)
Total	2/13(15.4)	7/33(21.2)	11/38(28.9)	20/84(23.8)

I vs II + III (p < 0.05)

tients who received sphincter-saving operation were checked. Fifty cases were Dukes B and 50 cases were Dukes C. Survival curves of each group in total, Dukes B and Dukes C cases are shown in Fig. 3, 4 and 5 respectively. Survival curves of each group shows similar pattern to rate of local recurrence. Survival of cases with less than 2 cm

margin appears to be worse than those of cases with over 2 cm margin, but shows statistically non-significant difference by log rank test. This is mainly due to difference in survival of cases without lymph node metastasis. In cases without lymph node metastasis, survival differences are obvious between groups and cases with less than 2 cm

**Table 7.** Disease free interval and survival of local recurrence cases after sphincter saving operation

No.	Sex / Age	Distance from anal verge	Op.	DRM (cm)	Dukes	Degree of differentiation	Site of recurrence	Disease free interval /survival time
1.	F/33	8 cm	CA	7	C	Mu	A+V	10m/1y2m
2.	M/67	20	CA	12	C	W/D	V	2y8m/2y9m
3.	M/24	19	AR	4	C	W/D	P	3y1m/4y7m
4.	M/39	10	CA	6	C	W/D	P	10m/3y10m
5.	F/64	12	AR	1	B	W/D	A	1y8m/2y6m
6.	M/46	7.5	CA	5	A	W/D	A	10m*/5y ↑
7.	F/38	20	AR	5	B	W/D	P	8m/10m
8.	M/52	10	CA	4	B	W/D	P	3y4m/5y ↑
9.	M/46	17	AR	5	C	W/D	P	10m/1y
10.	F/69	20	Ar	9	C	Mu	P	5m/8m
11.	F/27	23	AR	5.5	B	W/D	P	10m/?
12.	M/36	20	AR	7	C	M/D	P	2y9m/4y2m
13.	M/60	18	AR	4	A	M/D	A	1y4m*/2y
14.	M/30	13	AR	5	B	W/D	A	1y11m/?
15.	M/75	16	AR	1.5	B	W/D	A+P	6m/1y
16.	F/46	6	Ar	1.5	C	W/D	A	2y/2y11m
17.	F/46	6	AR	1	C	M/D	A	1y*/1y9m
18.	F/34	6	AR	2	C	Mu	P	11m/?
19.	M/48	12	AR	2.5	B	W/D	P	8m/2y2m
20.	F/47	7	AR	1	C	M/D	A	3m/?

CA; coloanal anastomosis, AR; anterior resection, DRM; distal resection margin, A; anastomotic site, P; extraluminal intrapelvic, V; vagina, \*; second curative op. Mu; mucinous, W/D; well differentiated, M/D; moderately differentiated

**Table 8.** Anastomotic recurrence according to the length of distal resected rectum and Dukes class

Length of Distal resected Rectum (cm)	No. of anastomotic recurrence/Total (%)			
	Dukes A	Dukes B	Dukes C	Total
I — 1.9	0/0	2/4 (50.0)	3/8 (37.5)	5/12(41.7)
II 2.0 — 4.9	1/5 (20.0)	0/5	0/17	1/27( 3.7)
III 5.0 —	1/8 (12.5)	1/24( 4.2)	1/13( 7.7)	3/45( 6.7)
Total	2/13(15.4)	3/33( 9.1)	4/38(10.5)	9/84(10.7)

I vs II or III (p < 0.005)

margin have worst prognosis (Fig. 5). Survival difference between the cases with over 5 cm margin and those with less than 2 cm margin is statistically significant (log rank test chi square = 10.139, p = 0.0014). In Dukes C, no significant difference in survival between groups is found.

### DISCUSSION

There are two main types of curative operation

for adenocarcinoma of rectum, abdominoperineal resection and a type of sphincter-saving operation such as anterior resection, pullthrough operation or abdominosacral excision. For the choice of proper surgical procedure among these, several points should be considered. Although operative mortality and morbidity is associated with the extent of operation, anastomosis and other operative technique, curability and rate of recurrence are of prime im-

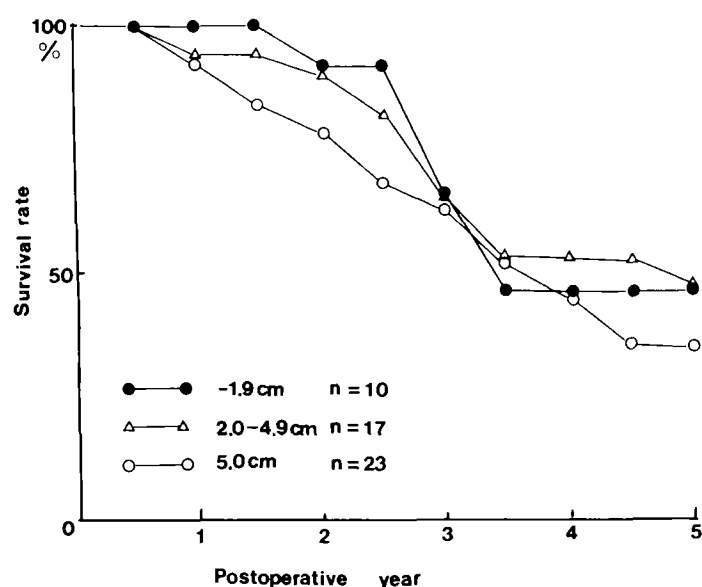


Fig. 5. Survival curves of patients with lymph node metastasis according to the length of distally resected rectum.

portance because the rate of above complication that skillful surgeons make would be acceptable.

According to the principle of standard cancer surgery that surrounding normal tissue should be removed together with tumor itself, adequate length of normal bowel segment proximal and distal to the primary cancer of colorectum should be resected to prevent local recurrence. Both the proximal and distal bowel to colon cancer and the proximal bowel to rectal cancer are redundant and would be no problem. However, because the length of distally resected rectum is critical to determine whether the sphincter and anus can be saved, it is very serious to define the optimum extent of distal resection.

To define the optimum length of distally resected normal rectum, it would be necessary to understand the mode of tumor spread and extent and direction of intramural, extramural and lymphatic invasion. In the past, many surgeons who believed that distal spread as well as proximal spread is important, insisted that at least 5 to 7 cm length distal bowel should be resected (Goligher *et al.* 1951; Manson *et al.* 1976). Therefore, most of the patients with rectal cancer had undergone Miles operation that had been considered as an only type of operation for rectal cancer. However, many pathologists had reported that distal tumor spreading beyond the 1 cm margin is rare and spreading beyond 2 cm margin is extremely rare (Goligher *et*

*al.* 1951). On the basis of those pathologic and clinical study, many surgeons came to believe that 2 to 5 cm is enough (Pollet and Nicholls 1983). As the sphincter saving operation became a popular procedure, the length of the distal margin tended to be shortened more and more. Several reports said that rate of local recurrence and survival of patient are not influenced by the length of distally resected rectum (Pollet and Nicholls 1983; Grinnell 1954; Segall *et al.* 1981; Slanetz *et al.* 1972; Wilson and Beahrs 1976).

There are several different ways of measuring bowel length. It can be either the length in natural position, length after mobilization or under the tension and either the length just after removal or the length in the formalin fixed specimen. Surgeon mobilize the intrapelvic rectum and secure the length of rectum needed. If he can secure the sufficient length, he would proceed the sphincter saving procedure. If not, he should move to the Miles operation. However, Miles operation is desirable to reduce local recurrence and to tolerate the radiation therapy in the case with anaplastic carcinoma or extensive pelvic local invasion because early recurrence is expected.

Anastomosis between proximal and distal bowel after anterior resection of upper rectal cancer would have no problem. After excision of mid or low rectal cancer, anastomosis is not easy to perform technically. Introduction of EEA makes it more feasible to perform low pelvic anastomosis (Goligher 1979; Heald 1980). Pullthrough or abdominosacral excision can be alternatives. Extent of local invasion, degree of histologic differentiation, the distance from anal verge have been thought to be associated with risk of local recurrence after curative surgery and still debated though (Manson *et al.* 1976; Segall *et al.* 1981; Gunderson *et al.* 1983; Morosn *et al.* 1963; Enker and Pilipshen 1983; Stearns and Brinkley 1953; Cass *et al.* 1976; Floyd *et al.* 1965; Lofgren *et al.* 1957). In this study, tumor size, duration of symptom, presence or absence of obstruction symptom and location of tumor did not show any relationship with risk of local recurrence, but clinical stage and degree of differentiation influenced the rate of local recurrence. If the patients were subdivided into more groups using different criteria of tumor size or duration of symptom, gross difference between groups might be seen. But statistical significance would not be obtained due to small size of groups.

Many cases in this study received adjuvant ther-

apy such as chemotherapy and radiation therapy postoperatively. The effect of radiation therapy to control local recurrence was not mentioned in the result of this study. We almost always recommend postoperative radiation therapy to the patients with Dukes B or Dukes C rectal cancer, however, not a small number of patients do not receive that therapy for some reasons. Therefore, the rate of local recurrence and survival was compared retrospectively between patients who received radiation therapy and those who did not and the result showed that radiation therapy did improve neither local control nor patients survival. More standardized prospective trial is needed to ascertain any advantage of adjuvant therapy to control local recurrence. If low rectal cancer that Miles operation usually indicated, is excluded, there is no difference in risk of local recurrence between Miles operation and sphincter-saving operation (Slanetz *et al.* 1972; Nicholls *et al.* 1979). But in low rectal cancer, rate of local recurrence after sphincter-saving operation have been reported to be higher than after Miles operation (Enker and Pilipshen 1983; Cass *et al.* 1976). Despite the above fact, because early detection is possible and second chance of curative surgery can be secured, more and more cases with mid or low rectal cancer undergo sphincter saving operation rather than Miles operation (Segall *et al.* 1981; Pheils *et al.* 1983; Lockart-Mummary *et al.* 1976).

Most of the recurrence, especially local recurrence, are developed within 2 to 3 years after operation and those developed beyond that period are distant metastasis (Cass *et al.* 1976; Lofgren *et al.* 1957; Welch and Donaldson 1978). As shown in Fig. 1, 90% of recurrence cases developed recurrence within 2 years after operation. Two of major causes of death in patients with local recurrence are uremia and intestinal obstruction that are mainly due to local recurrence (Welch and Donaldson 1979). Survival of local recurrence group is not better than that of distant metastasis group and once the local recurrence is occurred, median survival is less than 10 months (Welch and Donaldson 1978; Polk and Spratt 1971). Therefore preventive and therapeutic measures to control local recurrence are more important in those cases than in others.

The results of analysis of local recurrence according to the length of distal resected rectum shows grossly increased risk of local recurrence in cases with less than 2 cm margin and shows evidently that cases with less than 2 cm margin

have significantly higher risk of anastomotic recurrence in each Dukes class and poorer prognosis after curative surgery. Moreover, all the cases with less than 2 cm margin had moderately to well differentiated tumor. Therefore, to reduce the rate of local recurrence and to obtain more favorable outcome, at least over 2 cm length of distal rectum should be resected together with tumor mass. Survival difference can not be seen obviously in Dukes C cases, but Dukes B cases. It means that determination of the extent of distal clearance is more important in the cases without lymph node metastasis. And it may mean that once regional lymph nodes are involved, they would have poor outcome regardless of the extent of distal clearance.

In summary, among the clinical and pathological features examined in this study, clinical stage, especially extent of lymph node metastasis, and grade of histologic differentiation are influencing the development of local recurrence after curative resection of rectal cancer. Tumor size and location, duration of symptom and presence or absence of obstruction symptom are not associated with risk of local recurrence. To reduce risk of local recurrence, especially anastomotic recurrence after sphincter-saving operation, at least over 2 cm of distal rectum below lower margin of tumor should be resected. This is more true in the cases without lymph node metastasis.

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= 국문초록 =

## 직장암수술후 국소재발의 유발인자에 관한 연구

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직장암에 있어서 여러가지 임상적, 병리학적 소견이 근치적 수술후 국소재발에 미치는 영향을 알아보기 위해서 1973년 부터 1983년 까지 10년간 본교실에서 직장암으로 수술받은 339예를 분석하였다. Dukes임상기, 암세포의 분화도 등이 국소재발율에 영향을 미쳤으나 종양의 크기 (5 cm >, 5 cm <), 종양의 위치 (상, 중, 하), 수술전 증상호소기간 (6 month >, 6 month << 1 year, 1 year <), 폐쇄증상 유무 등은 국소재발율과 관계가 없었다.

괄약근보존술식을 하는 경우 적당한 원위부 직장절제 길이를 알아보기 위하여, 본 교실에서 괄약근보존술식을 받은 환자를 절제된 원위부 직장길이 (2 cm >, 2-5 cm, 5 cm <)에 따라 세군으로 분류하여 각군의 국소재발율과 생존기간을 알아보았다. 그 결과 괄약근보존술식후 국소재발, 특히 문합부재발을 줄이기 위하여 적어도 2 cm 이상의 원위부 직장이 절제되어야 하고, 특히 이것은 임파선 전이가 없는 증례에서 더욱 뚜렷한 것을 알 수 있었다.