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Nodal Metastasis in the Distal Mesorectum: Need for Total Mesorectal Excision of Rectal Cancer

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Locoregional failure of rectal cancer is a troublesome problem and a major cause of morbidity and mortality following curative surgery. The mesorectum has been regarded as an important site in local failure after surgery of rectal cancer. Total mesorectal excision (TME) has been raised by some colorectal surgeons to prevent early local recurrence. This study was performed to ascertain the incidence of metastatic lymph nodes in the distal mesorectum (DMR) of the colorectal cancer patient. We also examined the clinicopathologic risk factors of distal mesorectal metastasis. Eight of 53 patients had positive metastatic lymph nodes in DMR. Twenty-seven patients were Dukes B and 26 patients were Dukes C stage. Out of 26 Dukes C patients, 8 patients (30.8%) had metastatic lymph nodes in the DMR. However, there was no significant difference in risk factors between DMR positive and DMR negative patients with Dukes C stage. In conclusion, the incidence of metastatic lymph nodes in DMR was about 30.8%, therefore the mesorectum especially the DMR should be removed completely by total mesorectal excision to eradicate the metastatic lymph nodes which may cause local recurrence.

Key Words: Rectal cancer, total mesorectal excision, distal mesorectum

Local recurrence is a persistent troublesome problem in the treatment of rectal cancer following curative surgery (a term denoting the removal of all visible tumors). Because the local recurrence of rectal cancer after curative surgery had been found to be more common than colon cancer (Pihl *et al.* 1981), at posterior location (Hardy *et al.* 1971), or in Dukes C patients (Morson *et al.* 1963; Pihl *et al.* 1981; Tonak *et al.* 1982), the mesorectum distal to the lower border of the tumor has been regarded as having a primary foci of early local tumor recurrence after surgery of rectal cancer (Heald *et al.* 1982). The "*en bloc*" dissection of the rectum and entire mesorectum (total mesorectal excision, TME) was declared to decrease local recurrence (Heald *et al.* 1982). We designed this study to ascertain the incidence of node metastasis in the distal mesorectum (2 cm distal to lower border of tumor) and to examine its relation with clinicopathologic risk factors.

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MATERIALS AND METHODS

From January 1994 to June 1996, patients of pathologically proven rectal cancer were examined. Surgery for rectal cancer was done by a single surgeon (JS Min) with curative intent including total mesorectal excision (TME). The TME was defined as the com-

plete excision of the distal mesorectum down to the level of the levators (Heald *et al.* 1982). The term 'curative intent' used in the present study was defined as having all the macroscopic tumor removed and negative lateral margin involvement in pathologic examination and with no evidence of distant metastasis at the time of surgery. Fifty-three patients were enrolled.

The clinicopathologic characteristics of the patients are summarized in Table 1. Thirty-eight patients underwent a low anterior resection (LAR), 14 patients underwent an abdominoperineal resection (APR), and 1 patient underwent a Hartmann's procedure respectively.

Fifty-two patients had adenocarcinoma. The remaining one patient had mucinous carcinoma. The histologic grades of the adenocarcinomas were moderately well differentiated in 43 patients, well differentiated in 6 patients, and poorly differentiated in 3 patients.

Twenty-seven patients were Dukes stage B, and 26 patients were stage C according to Astler-Coller's modification.

Five patients showed microvascular invasion by the tumor (2 patients in Dukes B, 3 patients in Dukes C). Three patients showed 7 solitary tumor deposits in DMR (1 patient in Dukes B, 2 patients in Dukes C). The length of the distal resection margin varied from 1.0 cm to 8.0 cm (mean±SD; 3.5±2.0 cm). Ten patients had the distal resection margin of less than 2 cm and had negative tumor involvement in the distal margin. All of three patients had moderately differentiated adenocarcinomas. Five patients had a 1.0 cm, 4 patients with a 1.5 cm, and 1 with a 1.7 cm distal margin respectively.

The fresh surgical specimen was opened along the midline of anterior wall, avoiding the cross section of the tumor. It was washed with saline and pinned to a woodblock with the mucosal surface down. The transverse line was made on the mesorectal tissue 2 cm below the lower margin of the tumor. The distal mesorectum was defined as a mesorectum located below this line. The distal mesorectum was carefully dissected and all the lymph nodes in the distal mesorectum were examined to determine the presence of metastasis.

Table 1. Clinicopathologic characteristics of all patients(n=53)

Parameter	Mean of values or No. of patients	
Age(years)*	55.8±10.4	
Size of tumor(cm)*	5.0± 1.8	
Preop. CEA(ng/ml)*	7.0±15.4	
Sex Male	28	
Female	25	
Gross type of tumor		
Ulcerative	25	
Fungating	24	
Annular constrictive	4	
Location of tumor		
Anterior	14	
Lateral	10	
Posterior	29	
Depth of invasion		
T2	11	
T3	42	
Level of tumor		
Upper	16	
Mid	25	
Lower	12	
Fixity of tumor		
Mobile	48	
Fixed	5	
Pathology of tumor		
Adenoca.	52	
Well		6
Moderate		43
Poor		3
Mucinous ca.	1	
Vascular invasion**		
Negative	35	
Positive	5	
Solitary tumor deposit in DMR		
Present	3	
Absent	50	

*: Numbers mean mean±standard deviation.
**: Vascular invasion was evaluated in 40 patients.

Patients with Dukes C stage were divided into those who had metastatic lymph nodes in the distal mesorectum (Group I, n=8) and others without metastatic lymph nodes in the distal mesorectum (Group II, n=18).

The clinicopathologic parameters for risk

factor analysis of lymph node metastasis in the distal mesorectum were age and gender of the patient, preoperative level of the plasma carcinoembryonic antigen (CEA), size of the tumor, gross morphology of the tumor, location of the tumor along the rectal circumference, depth of tumor invasion (T stage) according to the TNM system, level of the tumor from the anal verge, fixity of the tumor by digital rectal examination, pathology of the tumor, and microvascular invasion of the tumor.

The one-way ANOVA (analysis of variances) test and chi-square test were used for statistical analysis.

RESULTS

Lymph node status after surgery

The mean number of lymph nodes obtained from a patient in toto and from the distal mesorectum after the APR were 29.1 and 1.7 respectively, whereas the mean number of lymph nodes from a patient in toto and from distal mesorectum after the LAR were 25.9 and 1.8 respectively. There was no significant difference in the number of surgically obtained lymph nodes between the two operative methods (Table 2).

In the Dukes B patients, the mean number of lymph nodes were obtained from single patient were 27.6 and a mean of 1.6 nodes were obtained from the distal mesorectum. In the Dukes C patients, a mean of 26.1 nodes from single patient and a mean of 1.8 nodes from the distal mesorectum were obtained. There was no significant difference between Dukes B and C patients in the number of surgically obtained lymph nodes (Table 3).

Clinicopathologic features

In Group I, 4 patients were men and 4 patients were women, whereas 9 patients were men and 9 patients were women in Group II.

The age of patients (mean±SD) was 55.4±9.4 years (range: 39~69 years) in Group I and 53.9±11.6 years (range: 23~70 years) in Group II.

The size of the tumor (mean±SD) was 4.8±1.2 cm (range: 2.5~6.0 cm) in Group I and 4.4±1.5 cm (range: 2.0~7.0 cm) in Group II. The preoperative levels of plasma CEA (mean±SD) were 6.1±10.1 ng/ml (range: 1.2~30.9 ng/ml) in Group I and 7.6±14.9 ng/ml (range: 0.1~64.0 ng/ml) in Group II.

The gross morphology of tumors in Group I was fungating in 3 patients, ulcerative in 4 patients, and annular constrictive in 1 patient, whereas in Group II, the tumor was fungating in 7 patients, ulcerative in 10 patients, and annular constrictive in 1 patient. In Group I, the tumor was located at the anterior rectal wall in 2 patients, lateral in 1 patient, and posterior in 5 patients. In Group II, the tumor was located at the anterior rectal wall in 6 patients, lateral in 4 patients, and posterior in 8 patients.

One patient in Group I and 4 patients in Group II had tumors that were confined to the rectal wall and did not penetrate into the

Table 2. Result of lymph node dissection in different types of surgery

Surgery	Number of lymph nodes*	
	Total	Distal mesorectum
Abdominoperineal resection (n=14)	29.1±17.7	1.7±1.6
Low anterior resection(n=38)	25.9±11.4	1.8±1.6
Hartmann's procedure(n=1)	35.0	1.0

*: $p>0.05$

Numbers mean mean±standard deviation.

Table 3. Result of lymph node dissection according to stage

Dukes stage	Number of lymph nodes*	
	Total	Distal mesorectum
B(n=27)	27.6±13.6	1.6±1.1
C(n=26)	26.1±12.9	1.8±1.9

*: $p>0.05$

Numbers mean mean±standard deviation.

Table 4. Difference of clinicopathologic parameters of Dukes C patients according to lymph node metastasis in distal mesorectum(n=26)

Parameter		Group-I(n=8)	Group-II(n=18)
Age(years)*		55.4± 9.4	53.9±11.6
Size(cm)*		4.8± 1.2	4.4± 1.5
Pre-op. CEA(ng/ml)		6.1±10.1	7.6±14.9
Sex	Male	4	9
	Female	4	9
Gross type of tumor	Ulcerated	4	10
	Fungated	3	7
	Annular	1	1
Location of tumor	Anterior	2	6
	Lateral	1	4
	Posterior	5	8
Depth of invasion**	T2	1	4
	T3	7	14
Level from anal verge	Upper(12~15 cm)	2	4
	Mid(8~12 cm)	4	10
	Lower(4~8 cm)	2	4
Fixity of tumor	Mobile	8	16
	fixed	0	2
Pathology***	Differentiated	6	17
	De-differentiated	2	1
Vascular invasion	Present	2	1
	Absent	6	17

All parameters showed no significant difference between group I and II.
*: Numbers mean mean±standard deviation.
**: T2=tumor does not penetrate entire rectal layer.
T3=tumor penetrates all layer of rectal wall.
***: Differentiated− well to moderate differentiation.
Dedifferentiated− poorly differentiation, mucinous carcinoma.

entire muscle layer (T2), whereas 7 patients in Group I and 14 patients in Group II had penetrating tumors (T3). In Group I, the tumors were located in the upper rectum (12~15 cm above anal verge) in 2 patients, mid rectum (8~12 cm above anal verge) in 4 patients, and lower rectum (4~8 cm above anal verge) in 2 patients. In Group II, the tumors were located in the upper rectum in 4 patients, mid rectum in 10 patients, and lower rectum in 4 patients. Tumors were movable from the pelvic wall in 8 patients of Group I and 16 patients in Group II.

In Group I, 6 patients had differentiated (well to moderately differentiated) tumors and 2 patients had dedifferentiated (poorly differentiated and mucinous carcinoma) tumors. In Group II, tumors were differentiated in 17 patients and dedifferentiated in one patient. There were 2 microvascular invasion of the tumor in group I and one case in Group II.

The difference between Group I and II according to the listed clinicopathologic parameters showed no statistical significance (Table 4).

DISCUSSION

Local recurrence of rectal cancer is common after surgery and probably influences the patient's survival. Because most local recurrence occurs as a direct result of incomplete tumor

resection (Heald and Ryall, 1986; Adam *et al.* 1994; McCall *et al.* 1995), the frequency of local recurrence varies according to the attending surgeon. The mesorectum has been regarded as an important loophole for the local failure of rectal cancer surgery because it contains a nest of adenocarcinoma cells or metastatic nodes (Heald *et al.* 1982). Many interesting clues were presented regarding the role of the mesorectum in the local failure of rectal cancer in the literatures. First, local suture-line recurrences are most commonly found posteriorly (Hardy *et al.* 1971) and only from tumors of the rectum with the highest incidence in the lowest tumors (Morson *et al.* 1963). Second, the initial tumor is almost invariably a Dukes C lesion with evident lymphatic deposits (Morson *et al.* 1963). Last, at least half of the recurrent rectal cancers that recur do so within the pelvic cavity (Silen, 1983).

Because the probability of the extrarectal spread of cancer would be confined at first within the mesorectum, TME was declared by Heald (Heald *et al.* 1982) and it also has been advocated as the appropriate procedure to manage carcinoma of the rectum, especially for mid and lower rectal cancer (Scott *et al.* 1995).

Until recently, it was the general concept that APR was more radical than LAR in the treatment of the mid to lower rectal cancer (Vlasak *et al.* 1989). Whereas, there are many studies that prove no superiority in radicality of APR to LAR in decreasing local recurrence (Fick *et al.* 1990; Amato *et al.* 1991; Tuscano *et al.* 1992; Enker *et al.* 1995; Nymann *et al.* 1995).

The conventional LAR may leave a variable amount of mesorectum beside the rectal stump (Anderberg *et al.* 1984). The tendency to 'cone' the dissection plane toward the rectal wall posteriorly and laterally is a common technical error which may be dangerous in context of local recurrence (Anderberg *et al.* 1984; Reid *et al.* 1984; Heald and Ryall, 1986).

In this study, we used the TME and the results revealed no significant difference between the the APR and the LAR in the extent of lymph node dissection. We identified a total number of 29.1 ± 17.7 and 25.9 ± 11.4 nodes per patient during the APR and the LAR, respectively. This corresponds with the result of 23.1 ± 1.18 nodes per patient which was obtained by fat clearance technique in the Guildford group (Cawthorn *et al.* 1986). This suggested that if the distal mural margin is pathologically acceptable or if the lateral surgical margin is not involved by the tumor, mid to lower rectal cancer may be treated by TME alone with curative intent. And, we bring up the hypothesis with care that the widely accepted concept that the APR is a more radical procedure than the LAR may be changed.

Disappointing results from more traditional surgical practices have led to clinical trials of various regimens of radiotherapy and chemotherapy (Galandiuk *et al.* 1992; Izar *et al.* 1992). The preoperative radiotherapy has a superiority over postoperative radiotherapy for reducing local recurrence (Pahlman *et al.* 1985). The best reported result in the recurrence after curative surgery for rectal cancer was from the North Central Cancer Treatment Group (NCCTG) from conventional surgery plus radiotherapy or combination chemoradiotherapy, and in the NCCTG control arm, surgery plus radiotherapy produced a 5-year local recurrence rate of 25% and an overall recurrence rate of 62.7% and an addition of chemotherapy reduced these figures to 13.5% and 42 %, respectively (Krook *et al.* 1991). The local recurrence rate was from 3.7% (Heald and Ryall, 1986) to 5% (MacFarlane *et al.* 1993) in 5 years with TME and the results from the TME alone were substantially superior to the results of the NCCTG. Such large differences may imply that viable local tumor residues or lymph nodes remained more frequently after operation in NCCTG's studies than in the patients who underwent TME (MacFarlane *et al.* 1993). These results may suggest that the usual field of spread of rectal cancer is confined within the mesorectal envelope and that rectal cancer is far more curable by surgery alone than has generally been believed or currently accepted.

The extramural distal metastasis to the lymph nodes or tumor deposit were found from 8.6% (Grinnell, 1954), to 20% (Scott *et al.* 1995) of rectal cancer patients. In the present

study, we performed the TME in 53 patients and 8 patients (15.1% of all patients, 30.8% of Dukes C patients) had positive nodes in the distal mesorectum and 7 tumor deposits were found in the distal mesorectum in another 3 patients (1 patient in Dukes B, 2 patients in Dukes C) without difference between Dukes B and C patients by any risk factors studied.

The local recurrence after surgery for rectal cancer was influenced not only by the TME but the circumferential lateral margin involvement of tumor was also important. And even if the TME was undertaken, patients with positive lateral margin had high risk of local recurrence and their prognosis was poor (Quirke *et al.* 1986; Cawthorn *et al.* 1990; Wolff, 1992; Ng *et al.* 1993; Adams *et al.* 1994).

We excluded anyone who had a positive lateral resection margin and cannot evaluate the role of lateral margin involvement of the tumor.

The useful methods to ascertain lymph node metastasis in DMR preoperatively are digital rectal examination and pelvic computerized tomography (Nicholls *et al.* 1982; Beynon *et al.* 1989). Recently, the endorectal ultrasonography has also been used with high accuracy for accessing regional lymph nodes and determining the depth of the invasion of the tumor in preoperative staging of the patient (Kim *et al.* 1994).

The local recurrence after curative surgery for rectal cancer may be influenced by distal resection margin and there were many arguments for determining the length of the distal resection margin. Even though some reports revealed extensive intramural spread (Handley, 1910; Cole, 1913) and the rule of a 5 cm margin was advocated (Grinnel, 1954), recently a general rule of a 2 cm margin has been accepted by many surgeons (Black and Waugh, 1948; Deddish and Sterns, 1961) as well as a less than 2cm margin which does not affect survival or local recurrence (Pollett and Nicholls, 1983).

Authors preferred that distal resection margin was satisfactory with a minimal 2 cm from the lower border of the tumor. But 10 patients of our series had a less than 2 cm of distal resection margin and 9 patients of them underwent the LAR. They all had moderately differentiated adenocarcinoma and the frozen section of the distal resection margin revealed negative tumor invasion. Because the distal intramural spread below the palpable edge of a rectal cancer is unusual and may be a sign of very advanced or highly malignant disease, reduction of the resection margin with TME does not increase local recurrence or compromise survival (Karanjia *et al.* 1990; Heald and Karanjia, 1992). Our experiences of short distal resection margin and the LAR for a very low setting rectal tumor is possible under this basis.

We found frequency of lymph node metastasis in the DMR was high. But we were not able to define the risk factor for the DMR metastasis of the rectal cancer. We concluded that the mesorectum especially the DMR should be removed completely to eradicate the metastatic nodes which may cause local recurrence.

Because of the short term of follow up of rectal cancer patients in this study, we are not able to suggest whether the TME may decrease local failure rate over conventional surgery for rectal cancer. But the supplement of cases and follow up data will prove the efficacy of the TME.

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