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Original Article

Factors Determining Circumferential Resection Margin of Rectal Cancer at Maharat Nakhon Ratchasima Hospital

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Abstract

Background: **Total mesorectal excision (TME) has recently achieved excellent oncological outcomes for patients with rectal cancer. The TME procedure aims at free circumferential resection margins (CRM), which has been found to be an acceptable surrogate endpoint for loco-regional and disease-free survival.**

Objective: **To assess factors affecting rates of CRM involvement after rectal cancer excision.**

Patients and Methods: **The prospective study of 80 rectal carcinoma patients who have definitive operation from January 1, 2009 to July 31, 2010 at Maharat Nakhon Ratchasima Hospital.**

Results: **Eighty rectal cancer patients (65%) were male with mean age of 62.2 years. The majority of cases (46.3 %) were in stage III disease. In T category, the majority of cases (81.3 %) were in T3 stage and 49% were in N0 stage. The most common location of cancers (40%) was the lower rectum followed by the upper and middle rectum at 30% equally. Univariate analysis of various clinicopathological parameters showed that sex, age > 50 yrs, mucin production, poorly differentiation, presence of neural or lymphovascular invasion, lymph node status, tumor stage III or IV, location of rectal cancer, type of operation, preoperative radiotherapy or even the length of surgeon experience did not influence the CRM involvement. The only factor that significantly affected CRM involvement.was T4 category cancer (P = 0.01).**

Conclusions: **Advanced T stage was found to significantly affect the CRM involvement.**

Key words: **circumferential resection margin, rectal cancer, total mesorectal excision**

Introduction

The incidence of colorectal cancer in Thailand is low compared with those of other countries. It is the third in frequency in males after the cancers of liver and lung, and the fifth after cancers of the cervix, breast, liver and lung in females[1]. The number of cases of colorectal cancer in both sexes is rapidly increasing from 22,857 patients in 1990 to 59,171 in 2008.[2]

Total mesorectal excision (TME) is a surgical technique that demands precise dissection according to the anatomical structures in the pelvic cavity[3,4] along the fascia propria of the rectum without damage. TME represents the current gold standard for surgical treatment of invasive cancers locating within the middle and lower rectum.[5,6] TME has recently achieved excellent oncological outcomes for patients with rectal cancer.[5] Hence the oncological outcome of rectal

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cancer is usually worse than that of colon cancer; one reason for this is the higher locoregional recurrence (LRR) rate after curative resection for rectal cancer[7]. TME in rectal cancer patients has played a major role in reducing LRR and improving overall survival (OS).[8-10] The TME procedure aims to achieve free circumferential resection margins (CRM) which is an acceptable surrogate endpoint for LRR and disease-free survival (DFS).[11-13] LRR dropped by 50% with TME procedure compared with conventional surgery (11% vs 27% at 5 years).[9,14] LRR in rectal cancer remains a significant clinical problem associated with severe morbidity, low salvage likelihood, and eventual death in the majority of patients.[15,16]

The CRM has been known as the major cause of LRR. Criteria for CRM involvement[14] is defined as positive when presence of tumor cells ≤ 1 mm and negative when tumor cells > 1 mm. Patients with positive CRM have LRR rate 78% and 5-year DFS rate 15% while the negative CRM patients have LRR rate 10% and 5-year DFS rate 66%.[14,17]

The present study was designed to assess factors affecting rates of CRM involvement after rectal cancer excision and to determine the CRM involvement rates for patients undergoing anterior resection (AR), low anterior resection (LAR) and abdominoperineal resection (APR).

Patients and Methods

The prospective study of 80 rectal cancer patients who had definitive operation from January 1, 2009 to July 31, 2010 at Maharat Nakhon Ratchasima Hospital was conducted. We collected demographic data, pathological feature, TNM staging, level of tumor location, type of operation, pre-operative radiation, surgical experience of surgeon, and CRM. Statistical analyses were expressed as mean ± SD, Chi-square with Yates' correction, odds ratio and 95% confidence interval (CI). The protocol was approved by the Ethical Committee Board of Surgical Department. A written informed consent was obtained from each patient.

Results

Table 1 showed detailed demographic data of patients admitted during January 2009 and July 2010.

Table 1 Demographic data (N = 80 cases)

Characteristics	Number (%)
Sex	
male: female	52 (65.5) : 28 (35)
Age (years) (mean ± SD) (range)	62.2 ± 12.88 (28-84)
Pathological features	
mucin producing and poor differentiation	2 (2.5)
neural invasion	5 (6.3)
lymphovascular invasion	16 (20)
T category	
T1	0
T2	9 (11.3)
T3	65 (81.3)
T4a	4 (5)
T4b	2 (2.5)
N category	
N0	36 (45)
N1a	17 (21.3)
N1b	8 (10)
N1c	0
N2a	9 (11.3)
N2b	10 (12.5)
M category	
M0	72 (90)
M1a	7 (8.8)*
M1b	1 (1.2)**
TNM stage	
I	5 (6.3)
IIa	28 (35)
IIb	1 (1.3)
IIIa	4 (5)
IIIb	25 (31.3)
IIIc	8 (10)
IVa	7 (8.8)
IVb	1 (1.2)
CRM ≤ 1 mm.	16 (20)

*liver metastasis, **liver and lung metastasis

Sixty five percent were male and 35 % were female with mean age of 62.2 ± 12.8 years (mean ± SD). Pathological features of mucin producing and poorly differentiation accounted for 2.5% and neural or lymphovascular invasion accounted for 26.3% of the cases. The majority of the cases (46.3%) were in stage III of the disease with 36.3% and 8% in stage II and IV, respectively.

In T category, the majority of the cases, 81.3%, were in T_3 stage with 11.3% and 7.5% in T_2 and T_4, respectively. None of the cases included in this study has T_1 staging. In N category, the majority (49%) of the cases were in N0 stage, with 31.3% in N_1 and 23.7% in N_2, respectively. CRM was positive in 20% of the

Table 2 Location, Treatment, Surgeon experience (N = 80 cases)

Location of tumor and treatment characteristics	Number (%)
Level of tumor	
Upper rectum	24 (30)
Middle rectum	24 (30)
Lower rectum	32 (40)
Type of operation	
Anterior resection	25 (31.3)
Low anterior resection	33 (41.2)
Abdomino-perineal resection	22 (27.5)
Preoperative radiotherapy	7 (8.8)
Surgical experience of surgeon > 2 years	69 (86.3)

cases with 31.8% having APR and 8% having AR.

The most common location of cancer was the lower rectum (40%) followed by upper and middle rectum at 30%, equally. Some patients (8.8%) received preoperative radiotherapy. LAR was the major operation performed (41.2%), followed by AR (31.3%) and APR (27.5%) respectively. Most of the operations (86.3%) were performed by surgeons with > 2 years experience as shown in Table 2.

The univariate analysis of risk factors on CRM (Table 3) showed that sex, age > 50 yrs, mucin production or poorly differentiation, presence of neural or lymphovascular invasion, lymph node status, tumor

Table 3 Univariate analysis of risk factors on CRM (N = 80 cases)

Clinicopathological parameters	CRM		P	Odds ratio (95% CI)
	< 1 mm.	> 1 mm.		
Age			0.83	1.44 (0.32-6.09)
< 50 years	4	12		
> 50 years	12	52		
Mucin producing and poorly differentiated	2	0	0.10	9.14 (0.58-275.69)
Well and Moderately differentiated	14	64		
Neural invasion or lymphovascular invasion			0.66	0.59 (0.12-2.62)
positive	3	18		
negative	13	46		
T4 lesion	4	2	0.01*	10.33 (1.38-93.70)**
T1-T3 lesion	12	62		
LN status			0.50	10.33 (0.42-5.24)
positive	10	34		
negative	6	30		
N_2 status	4	15	0.84	1.09 (0.25-4.44)
N_0, N_1 status	12	49		
M_1	1	7	0.93	0.54 (0.02-5.09)
M_0	15	57		
Stage III or IV	11	35	0.31	1.82 (0.50-6.88)
Stage I or II	5	29		
Level of tumor			0.14	2.29 (0.66-8.03)
Lower rectum	9	23		
Upper and middle rectum	7	41		
APR	7	15	0.19	2.54 (0.70-9.22)
AR, LAR	9	49		
APR or LAR	14	41	0.07	3.93 (0.74-27.49)
AR	2	23		
Preoperative radiotherapy	3	4	0.28	3.46 (0.53-21.83)
No Preoperative radiotherapy	13	60		
Surgical experience of surgeon				
> 2 years	13	56	0.81	0.62 (0.12-3.44)
≤ 2 years	3	8		

*Statistical significance ($P < 0.05$), **Clinical significance

stage III or IV, location of rectal cancer, type of operation, preoperative radiotherapy or even the length of surgeon experience do not influence the CRM involvement. The only factor that significantly affects the CRM involvement was T_4 category cancer (P = 0.01).

Discussion

In the study, the demographic data showed that patients with rectal cancer had a mean age of 62.2 years which was similar to the study by Wang et al[18] in China of 59.9 years. Studies in Europe[19-21] reported higher mean ages ranged 70-79 years. T category, N category and TNM stage were found to be similar to those reported[19-21] in the studies mentioned above with T_3, N_0 and TNM Stage III being the most common findings.

The most common location of rectal cancer reported was in the lower rectum. The main operative treatment was LAR with only 8.8% of the cases receiving preoperative radiotherapy. In contrast, Marling et al[15] reported 49% of the cases having pre-operative radiotherapy. The reason for the difference in the proportion of preoperative radiotherapy may be due to disinclination from the patients and trepidation regarding the side effects from the surgeons.

The CRM was positive in 20% of the cases in this study with 31.8% and 8% in those with APR and AR respectively. Tilney et al[22] reported CRM positive in 17.6% of APR and 6.2% of AR. Wibe et al[21] reported 9.44% CRM positive with ARP and AR technique combined and Bernstein et al[20] reported 15.5% CRM positive at ≤ 2 mm.

The univariate analysis of risk factors on CRM involvement in this study demonstrated that advanced T category (T_4) was the only risk factor associated with CRM involvement. Other factors such as type of operation or length of surgeon's experience had no effect on the CRM involvement. Martling et al[19] reported a reduction of LR after the surgeons received APR training. However, they had to operate at least 12 operations per year. In contrast, Wang et al[18] found that the location of rectal cancer, tumor differentiation, T category or even lymph node status were risk factors for CRM involvement. Similarly, Tinley et al[22] reported that T category, lymph node status and operative procedure were risk factors for CRM involvement. Bernstein et al[20] also reported that T category (T2, T3) in middle or upper rectum was a risk factor for CRM involvement but the definition of CRM positive was at ≤ 2 mm. In addition, Bernstein et al[20] also advised that pre-operative radiotherapy should be given in this group of patients. All studies mentioned above reported that T category was a vital risk factor for CRM involvement.[18,20,22] T staging helps define the depth of invasion of cancer, hence, the higher the T stage, the nearer the cancer cells are to the fascia propria which is close to the margin of APR technique leading to an increase in the risk of CRM positive.

In summary, the present study demonstrated that advanced T stage was the only risk factor for CRM involvement.

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