Prognostic Factors for Survival in Colorectal Cancer Patients

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Objective: To determine the prognostic value for survival of pretreatment characteristics and treatments in stage I-IV colorectal cancer (CRC) patients.

Material and Method: The present retrospective cohort study was conducted by reviewing 287 files of stage I-IV CRC patients. Fifteen clinical variables were investigated through analysis as prognostic factors for survival.

Results: The median survival time for CRC patients, colon and rectal cancer patients were 37.2, 43.2, and 29.5 months respectively. The 5-year survival rates of CRC patients were 38.6%. 5-year stage-specific survivals for stage I, II, III and IV CRC were 100%, 68%, 44%, and 2% respectively (p < 0.001). Sixty eight percent of CRC patients were in stages III and IV. Multivariate analysis revealed age ≥ 60 years old, WHO performance status 3, stage III and IV disease and poorly differentiated histology as poor prognostic factors for survival, whereas treatment with complete surgical resection and adjuvant chemotherapy was a good prognostic factor for survival in CRC.

Conclusion: As the majority of patients were in advanced stages with poor prognosis, early stage disease identification and treatment with newer agents would likely improve survival of high-risk CRC patients.

Keywords: Colorectal cancer, Prognostic factor

Colorectal cancer (CRC) is the third most common cancer and the fourth most common cause of cancer death in the world[1]. In the year 2002, it was estimated that over one million new colorectal cancer cases would be diagnosed worldwide, and about 529,000 patients would die from CRC[1]. CRC is more common in developed countries. The highest incidence rate of colon cancer in males is in Japan [age-standardized incidence rates (ASR) = 55.54], and for females is in New Zealand (ASR = 28.61)[2]. In rectal cancer, the highest incidence rates for males is in Japan (ASR = 27.4), and for females is in Singapore Chinese (ASR = 12.10)[2]. The incidence rate of CRC in Thailand is low when compared with other countries, that is, ASR was 8.8 for males and was 7.6 for females. For the period 1998-2000, the incidence rate of CRC in Thailand was the third highest in frequency in males after liver and lung cancer, and the fifth highest after cancer of the cervix, breast, liver and lung for females[3].

Prognostic factors for patients with CRC are important for the determination of high-risk groups for recurrent disease in early stages, and for overall survival in both early stage and advanced stage CRC patients. Prognosis in CRC is affected by a large number of factors, the most important of which are the clinical stage of presentation, surgical quality, for example, ability to perform curative or palliative operation, location of tumor, pathologic stage and histology grade, and type of treatment[4-6]. Many studies have been published about the prognostic factors in CRC patients studied in Western countries. However, only a few studies of prognostic factors for survival in colorectal cancer have been conducted in Thailand. Rajavithi Hospital is one of the tertiary care hospitals where many cancer patients, especially from Bangkok and the central region of Thailand, are referred for cancer treatment. This provided an important opportunity to do a retrospective study of colorectal cancer patients treated in the Department of Medicine,

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Rajavithi Hospital, to determine the prognostic value for overall survival of various pretreatment characteristics and types of treatment in Thai patients.

Material and Method

The present study was an ambispective cohort study. This retrospective cohort study was conducted through examining selected medical files of patients with colorectal cancer stage I, II, III, and IV treated in the Oncology Unit, Department of Medicine, Rajavithi Hospital for 9 years, between January 1, 1995 and December 31, 2003 as approved by the Ethics Committee on Research Involving Human Subjects, Rajavithi Hospital, Bangkok, Thailand. Patient's status was followed until August 31, 2004, from medical records and the population registration database, Ministry of Interior.

At enrollment in the Unit, demographic and clinical data from each patient were systematically collected. Fifteen primary variables were collected, coded and entered into a computer statistical program. The 14 variables retrospectively studied as potential pretreatment prognostic variables included age, sex, World Health Organization performance status (WHO PS), location of primary tumor, tumor obstruction, tumor perforation, histologic type (adenocarcinoma/mucinous adenocarcinoma/signet ring cell carcinoma), histologic grade, lymphatic invasion, blood vessel invasion, TNM stage, primary tumor (T), regional lymph node (N), and distant metastasis (M). One potential therapeutic prognostic variable also included in the analyses was type of treatment patients received including, curative surgery, adjuvant chemotherapy, adjuvant radiation, neo-adjuvant radiation, palliative surgery, palliative chemotherapy, palliative radiation, and best supportive care.

Most stage I, II, III colon and rectal cancer patients received standard treatments based on disease stage including surgery, adjuvant chemotherapy, and adjuvant radiation. Most CRC patients received adjuvant intravenous 5-fluorouracil plus intravenous calcium leucovorin (Mayo clinic regimen), while a few patients received oral UFT plus oral leucovorin. Patients with stage IV colorectal cancer at first diagnosis, and stage II-III colorectal cancer who subsequently developed metastatic disease, received appropriate palliative chemotherapy. Palliative chemotherapy regimens were intravenous 5-fluorouracil plus intravenous calcium leucovorin (Mayo clinic regimen) or oral UFT plus oral leucovorin or oral capecitabine or oxaliplatin based chemotherapy.

Most stage IV CRC patients were assessed for tumor response after the first regimen of chemotherapy. Some patients who had disease progression after first line chemotherapy and still had good performance status were offered additional second line chemotherapy regimens. Palliative radiation and surgery were given to patients having relevant indications.

Response evaluation was based on World Health Organization (WHO) criteria[7]. A complete response was defined as complete disappearance of all disease on radiographic and physical examination for a minimum of 4 weeks. Partial response was defined as a greater than 50% reduction in the sum of the products of the perpendicular diameters of all measurable lesions for a minimum of 4 weeks. Stable disease was defined as no detectable change in the tumor volume of all the lesions. Progressive disease was defined as a greater than 25% increase in the sum of the products of the perpendicular diameters of all the measurable lesions or by the appearance of new lesions. All patients enrolled were monitored for response, and time to death. Overall survival time was calculated from the date of entry into the present study and time to death was defined as time to death or time to last follow-up.

Statistical analysis

Chi-square test or Fishers' exact test was used to compare between colon cancer and rectal cancer group. Overall survival time was estimated using the method of Kaplan and Meier[8]. Fifteen variables were included for analyses to identify prognostic factors for survival. Comparisons of cumulative survival were obtained by univariate analyses using the log-rank test[9] and multivariate analyses were performed using Cox regression analysis. A p-value of less than 0.05 was considered statistically significant.

Results
Outcome of the treatment for the entire group

From January 1995 through December 2003, 287 patients with early stage CRC treated with surgery alone or surgery plus adjuvant and/or neo-adjuvant treatment, and with advanced stage CRC treated with palliative treatment were identified. The characteristics of the 287 CRC patients are listed in Table 1. There were 142 men and 145 women, with a median age of 61 years and a median WHO PS of 1. Location of primary tumor was the colon in 204 patients (71%) and the rectum in 83 patients (29%). Fifty nine percent of patients lived in Bangkok and its surroundings.

Table 1. Patient characteristics

Variable	Colorectal cancer	Colon cancer	Rectal cancer	p-value*
Number of patients	287	204	83	
Sex: male/female (no.)	142/145	101/103	41/42	0.986
Age median (years)	61	61	59	0.942
Age (%): < 50/50-59/60-69/≥ 70	23/23/29/25	25/20/30/25	19/33/26/22	0.942
WHO performance status (%): 0/1/2/3	14/51/29/6	15/52/29/4	11/49/30/10	0.316
Tumor obstruction (%): no/yes	69/31	63/37	85/15	<0.001
Tumor perforation (%): no/yes	99/1	99/1	100/0	0.275
Histopathologic type (%)				
Adenocarcinoma/mucinous adenocarcinoma/ signet ring cell carcinoma	96/3.5/0.5	95.5/4/0.5	98/2/0	0.661
Histopathologic grade (%)				
Well/moderately/poorly differentiation	62/33/5	63/34/3	60/31/9	0.222
Lymphatic invasion (%): no/yes	95/5	94/6	97/3	0.269
Blood vessel invasion (%): no/yes	98/2	99/1	95/5	0.039
TNM staging (%): I/II/III/IV	2/30/32/36	3/35/31/31	2/18/33/47	0.023
Primary tumor (T) (%): T1/T2/T3/T4/Tx	0.5/4/23/69/3.5	0.5/3/21/71/4.5	0/6/28/65/1	0.282
Regional lymph node (N) (%): N0/N1/N2/Nx	41/31/25/3	46/29/21/4	28/34/36/2	0.013
Distant metastasis (M) (%): M0/M1	64/36	69/31	53/47	0.012
Treatment (%)				
Stage I: CS /CS + NR +ACT	86/14	100/0	50/50	-
Stage II: CS / CS + ACT/ CS+AR or NR +ACT	10/78/12	13/87/0	0/33/67	-
Stage III: CS / CS + ACT/ CS+AR or NR + ACT/ PS +PCT	13/66/20/1	16/84/0/0	7/22/67/4	-
Stage IV: PCT/BSC	90/10	89/11	92/8	-

p-value*: comparison between colon cancer and rectal cancer was analysed by Chi-square test or Fishers' Exact test
CS: curative surgery, ACT: adjuvant chemotherapy, AR: adjuvant radiotherapy, NR: neo-adjuvant radiotherapy, PS: palliative surgery, PCT: palliative chemotherapy, BSC: best supportive care

Thirty one percent of CRC patients had tumor obstruction, with more tumor obstruction in the colon than rectal cancer, 37% vs. 15%, p < 0.001. The predominant histology type was adenocarcinoma (96%) and grade was well differentiated (62%). Five percent of rectal cancer cases had blood vessel invasion, more than in colon cancer cases (1%), p = 0.039. Colon cancer patients presented at stage I, 3%, stage II, 35%, stage III, 31%, and stage IV, 31%. Rectal cancer was more commonly first diagnosed with stage IV than in colon cancer, 47% vs. 31%, p = 0.023. Around 90% of both colon and rectal cancer patients presented with T3-T4 disease. Rectal cancer cases presented with N2 disease more frequently than colon cancer cases, 36% vs. 21%, p = 0.013, and had distant metastasis (M1) more often than colon cancer cases, 47% vs. 31%, p = 0.012.

Regarding treatment, five patients of stage I colon and one patient of rectal cancer received curative surgery. One patient with stage I rectal cancer received curative surgery after neo-adjuvant radiation, followed by adjuvant chemotherapy. Among stage II colon cancer patients, nine patients (13%) received only curative surgery, and 62 (87%) received curative surgery and adjuvant chemotherapy. Stage II colon cancer patients received adjuvant chemotherapy in high percentage due to their high risk features. Primary tumor T4 and tumor obstruction were found in 78% and 35% of patients respectively. Among stage II rectal cancer patients, five patients (33%) received curative surgery and adjuvant chemotherapy and 10 (67%) received curative surgery and adjuvant or neo-adjuvant radiation and adjuvant chemotherapy.

Among stage III colon cancer patients, 10 patients (16%) received only curative surgery while 54 (84%) received curative surgery and adjuvant chemotherapy. Among stage III rectal cancer patients, two patients (7%) received curative surgery only, six (22%) received curative surgery and adjuvant chemotherapy, and 18 (67%) received curative surgery

and adjuvant or neo-adjuvant radiation and adjuvant chemotherapy while one patient (4%) received only palliative surgery and palliative chemotherapy. The most commonly used regimen of adjuvant chemotherapy in the present study (98%) was low dose 5-fluorouracil plus calcium leucovorin, (Mayo clinic regimen). Oral UFT plus oral leucovorin was used in only 2% of patients receiving adjuvant chemotherapy.

Fifty seven patients (89%) of those initially diagnosed with stage IV colon cancer and 36 patients (92%) with stage IV rectal cancer received palliative chemotherapy. Best supportive care only was given to seven patients (11%) with stage IV colon cancer and three patients (8%) with stage IV rectal cancer who could not tolerate or refused active treatment.

Recurrent or metastatic disease occurred in 64 of 177 stage II and III colorectal cancer patients, with 36% developing recurrent disease during the surveillance period. Stage II and III colon cancer patients developed recurrent disease 28% and 44% respectively, while stage II and III rectal cancer patients developed recurrent disease 13% and 52% respectively. Common sites of metastasis for 103 stage IV colorectal cancer patients at first diagnosis were the liver (71%), intra-abdominal organ (33%), intra-abdominal lymph nodes (15%) and lung (14%). In comparison, common sites of metastasis for 64 recurrent stage II and III colorectal cancer patients were the intra-abdominal organ (47%), liver (33%), intra-abdominal lymph nodes (23%), and lung (19%). One hundred twenty eight of 167 stage IV colorectal cancer patients (76.6%) were treated with palliative chemotherapy. The first line chemotherapy regimens used in the present study were a combination of intravenous 5-fluorouracil and leucovorin (Mayo clinic regimen) in 95 patients (74%), oral UFT and oral leucovorin in 19 patients (15%), oral capecitabine in six patients (5%), and oxaliplatin-based treatment in four patients (3%). Median number of cycles of first line chemotherapy was six cycles. Forty-two patients (33%) received a second line chemotherapy and nine patients (7%) received third line chemotherapy. The objective response rate for the first line of 5-fluorouracil based regimen was 17%, with 10% partial responses and 7% complete response, with 25% stable disease and 52% progressive disease. Second line chemotherapy was given to 42 patients (33%). The regimens included oral UFT plus oral leucovorin in 27 patients (64%), oxaliplatin-based chemotherapy in nine patients (21%), irinotecan in two patients (5%) and other regimens in four patients (10%). Objective responses were found

in four patients receiving second line chemotherapy, with one complete response in a patient receiving oxaliplatin based regimen. Partial response was found in three patients receiving either irinotecan single agent or oxaliplatin-based or oral UFT plus oral leucovorin.

Survival analysis

Overall, 145 cases of 287 colorectal cancer patients died. One hundred and forty-two patients (49.48%) were alive through the present study period. The median survival time of 287 patients was 149 weeks (37.2 months), with 5-year and 7-year survival, 38.6% and 37.6% respectively. Median survival time of colon cancer patients was longer than for rectal cancer patients, 43.2 vs. 29.5 months, but did not reach statistical significance, $p = 0.093$; (Fig. 1, Table 2).

The stage-specific overall survival curve for colorectal cancer is shown in Fig. 2, with a median survival time of 201 weeks for stage III and 69 weeks for stage IV CRC patients. Stage I had better survival than stages II, III, and IV, with 5-year survival rates of 100%, 68%, 44%, and 2% respectively, and 7-year survival rates of 100%, 68%, 41%, and 2% respectively ($p < 0.001$) (Table 2).

Treatment-specific five-year survival for those colorectal patients receiving curative surgery plus adjuvant chemotherapy, curative surgery plus adjuvant or neo-adjuvant radiation plus adjuvant chemotherapy, curative surgery only, and palliative chemotherapy was 63% 53%, 45%, and 4% respectively.
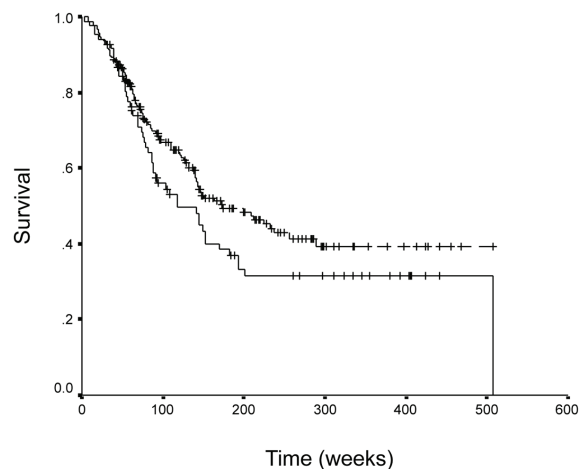
Fig. 1 Overall survival curve, median survival time for all stages of colon and rectal cancer was 173 weeks (43.2 months) and 118 weeks (29.5 months), respectively ($p = 0.093$)

Stage IV colorectal cancer patients who received palliative chemotherapy and best supportive care only had median survival times of 78 weeks and 20 weeks, respectively (Table 2).

Univariate analyses

The authors collected pre-therapeutic and therapeutic data from 204 colon cancer and 83 rectal cancer cases, totaling 287 colorectal cancer patients.

Table 2. Univariate survival analysis of possible prognostic factors in colorectal cancer

Variable	No.	5-year survival rate %	7-year survival rate %	Median survival (weeks)	p-value (log-rank test)
Overall	287	38.6	37.6	148.9	
Colon	204	41.4	39.4	173.2	0.093
Rectum	83	31.6	31.6	118.3	
Sex					0.825
Male	142	40.5	38.7	151.1	
Female	145	37.0	37.0	148.9	
Age at diagnosis (years)					0.008
< 50	67	54.3	54.3	>500	
50-59	67	52.5	48.1	289.4	
60-69	83	24.9	24.9	139.7	
$\geq$ 70	70	26.4	26.4	120.2	
WHO performance status					<0.001
0	39	82.6	82.6	>500	
1	148	43.6	41.5	181.9	
2	83	14.2	14.2	87.0	
3	17	7.1	7.1	76.7	
Stage of tumor					<0.001
Stage I	7	100.0	100.0	>500	
Stage II	86	68.3	68.3	>500	
Stage III	91	44.2	41.2	201.2	
Stage IV	103	2.1	2.1	68.6	
Degree of differentiation					0.003
Well	175	40.3	40.3	171.9	
Moderately	93	40.9	37.5	141.4	
Poorly	14	11.1	11.1	55.7	
Primary tumor (T)					<0.001
T1 + T2	11	90.0	90.0	>500	
T3	66	39.9	40.0	143.9	
T4	199	37.9	36.4	148.9	
Tx	10	0.0	0.0	44.0	
Regional lymph node (N)					<0.001
N0	117	55.8	55.8	>500	
N1	88	37.8	34.7	139.7	
N2	73	19.0	19.0	78.4	
Nx	9	0.0	0.0	34.3	
Distant metastasis (M)					<0.001
M0	184	57.7	56.1	>500	
M1	103	2.1	2.1	68.6	
Treatment					<0.001
CS + ACT + PCT + PR	127	62.9	59.9	>500	
Curative surgery only	20	45.3	45.3	131.7	
CS + AR/NR + ACT	29	53.2	53.2	>500	
Palliative chemotherapy	101	4.2	4.2	78.4	
Best supportive care	10	10.0	10.0	19.6	

CS = curative surgery; ACT = adjuvant chemotherapy; AR = adjuvant radiotherapy; NR = neoadjuvant radiotherapy; PCT = palliative chemotherapy; PR = palliative radiotherapy
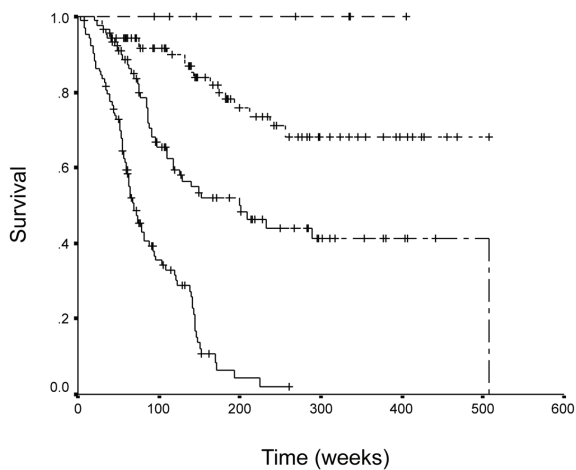
Fig. 2 Overall survival curve, median survival time for stage I, II colorectal cancer was not reached, median survival time for stage III and IV was 201 weeks and 69 weeks respectively. 5-year survival rate for stage I, II, III, IV colorectal cancer patients was 100%, 68%, 44% and 2% respectively (p < 0.001)

The 15 variables analyzed as potential prognostic factors were age, sex, WHO performance status, location of primary tumor (colon vs. rectum), tumor obstruction, tumor perforation, histologic type (adenocarcinoma/mucinous adenocarcinoma/signet ring cell carcinoma), histologic grade, lymphatic invasion, blood vessel invasion, TNM stage, primary tumor (T), regional lymph node (N), distant metastasis (M), and type of treatment received.

In colorectal cancer, univariate survival analysis by Kaplan Meier and log-rank test showed that significant prognostic factors for longer survival were age < 50, p = 0.008; WHO performance status 0, p < 0.001; early clinical stage (I and II), p < 0.001; well differentiated grade, p = 0.003; primary tumor T1 and T2, p < 0.001; no regional lymph node involvement (N0), p<0.001; no distant metastasis (M0), p < 0.001; stage I-IV colorectal cancer patients receiving curative surgery and adjuvant chemotherapy, and subsequent palliative chemotherapy and radiation, p < 0.001 (Table 2).

Multivariate analyses

Survival duration was further modeled with multivariate Cox regression analysis employing a proportional hazard rate hypothesis. The 15 variables analyzed as potential prognostic factors using univariate analyses were also examined using multivariate analyses. In colorectal cancer stage I-IV, multivariate survival analyses showed that older age, poor WHO performance status, high TNM staging, poor histologic grade of tumor and receiving only best supportive care were statistically significant for decreased survival (Table 3). In addition, multivariate survival analysis of stage IV colorectal cancer patients was also performed and demonstrated that patients with WHO performance status 3 and receiving only best supportive care treatment were statistically significant factors for poor survival, with hazard ratios of 6.11 (p = 0.001) and 7.1, (p = 0.001) respectively.

Table 3. Parameters that correlate with survival of colorectal cancer stage I-IV in multivariate analysis (n = 287)

Variable	Harzard ratio	95% confident interval	p-value
Age at diagnosis (years)			
< 50 years	1		
50-59 years	0.94	0.52-1.70	0.846
60-69 years	1.77	1.06-2.97	0.029
≥70 years	1.73	1.01-2.99	0.049
WHO performance status			
0-1	1		
2	1.42	0.97-2.09	0.075
3	5.06	2.67-9.59	<0.001
Stage			
Stage I + II	1		
Stage III	2.93	1.64-5.26	<0.001
Stage IV	8.31	2.55-27.12	<0.001
Degree of differentiation			
Well	1		
Moderately	1.17	0.80-1.71	0.412
Poorly	3.28	1.67-6.43	0.001
Treatment			
CS + ACT + PCT + PR	1		
Curative surgery	2.22	0.95-5.17	0.064
CS + AR/NR + ACT	1.15	0.53-2.45	0.726
Palliative chemotherapy	1.44	0.50-4.16	0.497
Best supportive care	7.90	2.02-30.98	0.003

Cox regression analysis included variables in table plus sex, location of primary tumor, tumor obstruction, tumor perforation, histologic type, lymphatic invasion, blood vessel invasion, primary tumor (T), regional lymph node (N), and distant metastasis (M)
CS = curative surgery; ACT = adjuvant chemotherapy; AR = adjuvant radiotherapy; NR = neoadjuvant radiotherapy; PCT = palliative chemotherapy; PR = palliative radiotherapy

Colon cancer versus rectal cancer

The 5-year survival rates were not statistically significantly different for colon and rectal cancer. Overall stage-specific survival of colon cancer as 5-year survival rate for colon cancer in stages I plus II and III were 67% and 50% with no patients at stage IV surviving after 5 years of follow-up (p < 0.001). Stage-specific overall survival of rectal cancer as 5-year survival rate for stages I plus II, III, and IV were 84%, 30%, and 4% respectively (p < 0.001). Median survival time for stage IV colon cancer and rectal cancer were 64 weeks and 74 weeks respectively.

In the univariate analysis of colon cancer, WHO performance status, TNM stage, primary tumor invasion, lymph node involvement, distant metastasis, and type of treatment were prominently significant prognostic factors (p < 0.001). Histologic grade was moderately significant (0.001 < p < 0.05). For rectal cancer, age, WHO performance status, TNM stage, histologic grade, lymph node involvement, distant metastasis, and type of treatment were significant prognostic factors (Table 4).

When multivariate survival analysis was performed for colon cancer, WHO performance status 0-1, stage I plus II, well differentiated grade and treatment with curative surgery plus adjuvant chemotherapy plus subsequent palliative chemotherapy and radiation were significant, good prognostic factors for survival (Table 5). For rectal cancer, multivariate survival analysis showed that age < 50 years old, WHO performance status 0-1, stage I plus II, and well differentiated grade were significantly associated with longer survival (Table 5).

Discussion

The present study was carried out to identify prognostic factors for dying of colorectal cancer in patients treated in the Oncology Unit, Department of Medicine, Rajavithi Hospital. Analysis showed that rectal cancer presented at a significantly more advanced stage (stage III and IV) and with more blood vessel invasion than in colon cancer. Colon cancer had more tumor obstruction than rectal cancer. The most common site of metastases of initially diagnosed stage IV colorectal cancer was the liver (71%), which is comparable with a previous retrospective study in Thai patients that found the liver as a common site of metastases (61%)[10]. In contrast, stage II and III

Table 4. Univariate survival analysis of prognostic factors and 5-year survival rates in colon, and rectal cancer stage I-IV

Variables	5-year survival (%) (p-value)	
	Colon cancer	Rectal cancer
Sex		
Male vs. female	41 vs. 42 (0.942)	7 vs. 26 (0.851)
Age		
Age < 50 vs. age ≥70	48 vs. 36 (0.332)	65 vs. 6 (<0.001)
WHO PS		
PS 0 vs. 3	86 vs. 0 (<0.001)	74 vs. 12 (<0.001)
Stage		
Stage I + II vs. IV	67 vs. 0 (<0.001)	84 vs. 4 (<0.001)
Degree of differentiation		
Well vs. Poorly	41 vs. 0 (0.003)	39 vs. 19 (0.027)
Primary tumor		
T1-2 vs. T4	100 vs. 38 (<0.001)	75 vs.30 (0.063)
Regional lymph node		
N0 vs. N2	53 vs. 33 (<0.001)	67 vs. 7 (<0.001)
Distant metastasis		
M0 vs. M1	59 vs. 0 (<0.001)	51 vs. 4 (<0.001)
Type of treatment		
Colon: CS + ACT vs. BSC	63 vs. 0 (<0.001)	53 vs. 3 (<0.001)
Rectum: CS + AR/NR + ACT vs. BSC		

CS = curative surgery; ACT = adjuvant chemotherapy; AR = adjuvant radiotherapy; NR = neoadjuvant radiotherapy; BSC = best supportive care; PS = performance status

Table 5. Multivariate survival analysis of prognostic factors compared between colon cancer and rectal cancer

Variable	Harzard ratio	95% confident interval	p-value
Colon			
WHO Performance status			
0-1	1		
2	1.66	1.03-2.67	0.036
3	12.08	4.85-30.10	<0.001
Stage			
Stage I + II	1		
Stage III	2.72	1.34-5.53	0.006
Stage IV	7.97	1.96-32.38	0.004
Degree of differentiation			
Well	1		
Moderately	0.85	0.53-1.37	0.500
Poorly	4.06	1.64-10.09	0.003
Treatment			
CS + ACT + PCT + PR	1		
Curative surgery	2.06	0.77-5.50	0.151
Palliative chemotherapy	1.48	0.43-5.05	0.536
Best supportive care	15.19	2.78-83.09	0.002
Rectum			
Age at diagnosis (years)			
< 50 years	1		
50-59 years	2.12	0.62-7.27	0.234
60-69 years	4.78	1.53-14.92	0.007
≥ 70 years	8.12	2.46-26.77	0.001
WHO performance status			
0-1	1		
2	1.22	0.59-2.52	0.591
3	4.34	1.50-12.60	0.007
Stage			
Stage I + II	1		
Stage III	10.16	2.01-51.35	0.005
Stage IV	6.00	0.41-88.06	0.191
Degree of differentiation			
Well	1		
Moderately	2.93	1.34-6.36	0.007
Poorly	3.07	0.96-9.82	0.059

Cox regression analysis included variables in table plus sex, location of primary tumor, tumor obstruction, tumor perforation, histologic type, lymphatic invasion, blood vessel invasion, primary tumor (T), regional lymph node (N), and distant metastasis (M)
CS = curative surgery; ACT = adjuvant chemotherapy; AR = adjuvant radiotherapy; NR = neoadjuvant radiotherapy; PCT = palliative chemotherapy; PR = palliative radiotherapy

colorectal cancer patients who developed subsequent recurrent disease (36%) found the common site of recurrences was the intra-abdominal organs (47%).

The high incidence of intra-abdominal organ recurrence in the present study could be due to 29% of stage II and 33% of stage III rectal cancer patients did not receive adjuvant radiation and 7% of stage III rectal cancer did not receive both adjuvant chemotherapy and radiation.

Regarding survival, 5-year stage-specific survivals of colorectal cancer patients were 100% for stage I, 68% for stage II, 44% for stage III, and 2% for stage IV. This finding is consistent with a report from Korea showing that the 5-year stage-specific survivals of colorectal cancer patients were 89% for Dukes' stage A, 75% for Dukes' stage B, 49% for Dukes' stage C, and 12% for Dukes' stage D[11]. Colon cancer patients had a trend to live longer than rectal cancer patients but not statistically significantly different.

In colon cancer, 5-year stage-specific survivals of patients in the present study were 67% for stage I and stage II, 50% for stage III, and 0% for stage IV patients. When compared with a study from the United States Surveillance, Epidemiology, and End Results (SEER) data, the 5-year stage-specific survivals of colon cancer in American's study were 93% for stage I, 82% for stage II, 59% for stage III, and 8% for stage IV patients[12]. This present study had 5-year stage-specific survivals of colon cancer approximately 10% lower than the results of the American study. This could be due to not all, but only 80-90% of patients in the present study received adjuvant and palliative chemotherapy. Another possibility for the difference outcome of survival in the present study could be due to a lot lower number of patients in the present study compared with US SEER data studies[12]. However, stage II and III colon cancer patients receiving curative surgery plus adjuvant chemotherapy in the present study had 5-year survival rates of 63% which is comparable with 5-year survival rates of colon cancer patients receiving 5-FU based adjuvant chemotherapy (66%) reported by the Intergroup 0089 study[13]. For stage IV colorectal cancer, median survival time was 17 months, which is not inferior to the results of Phase III studies of oxaliplatin and irinotecan-based chemotherapy as first line treatment, previously reported with median survival times of 16-17 months[14,15].

In rectal cancer, 5-year survival rates for stage I plus II, and stage III were 84% and 30%. This is comparable with the 5-year survival rates of rectal cancer treated with adjuvant treatment, ranging from 37% to 79%[16]. Results also demonstrate that younger

colorectal and rectal cancer patients had significantly longer survivals compared to older patients, which is consistent with results of a previous Korean study[11]. Among clinical factors, a survival difference was not found by location of tumor or sex, but age older than 60 and advanced stage were related to poorer prognosis for colorectal cancer in both univariate and multivariate analyses for colorectal cancer and rectal cancer. The present finding is consistent with other reports[5,17]. The authors also demonstrated that a WHO performance status greater than 2 was also an important negative prognostic factor in colorectal cancer in both univariate and multivariate analyses, which has not been seen in previous studies[5,6,11,17].

In the evaluation of pathological factors, high tumor grade, lymph node involvement and distant metastases were associated with poor outcome in univariate analysis for both colon and rectal cancer. Depth of tumor invasion was associated with prognosis only in univariate analysis for colon cancer. However, only degree of differentiation was significant for survival in multivariate analysis for both colon and rectal cancer. The present results, which are in agreement with those from other reports[17-20], suggest that pathological grade significantly affects patient survival.

In evaluating the impact of treatment on survival, adjuvant treatment after surgery is a good prognostic factor through both univariate and multivariate analyses for colorectal and colon cancer. This finding is consistent with reports of pooled analysis of adjuvant chemotherapy for early stage colon cancer that shows that adjuvant therapy produces beneficial treatment effects across all subsets of patients[20]. Adjuvant treatment was found to be a prognostic factor for rectal cancer only in univariate analysis, but not in multivariate analysis in our study. The present result is similar to a previous study of intermediate to high risk early stage rectal cancer which demonstrated that surgery plus chemotherapy, or surgery plus chemotherapy plus radiation had superior survival when compared with surgery alone or surgery plus radiation alone[16]. As expected, palliative chemotherapy also had an impact on survival for stage IV colorectal cancer in both univariate and multivariate analysis in the present report.

The results of other studies on prognostic factors for colon and rectal cancer treated with resection only, and determined by multivariate analyses, showed age, sex, stage, histology grade, direct spread of tumor, venous invasion, and rectal location were prognostic factors for colorectal cancer[5,6,17,18]. The results of previous studies are similar to the present results. However, sex, direct spread of tumor, venous invasion, and rectal location were not found to be prognostic factors in the presented multivariate analysis. Other studies using multivariate analyses of variables in prognosis among rectal cancer patients demonstrated that age, sex, stage, histology grade, direct spread of tumor, and venous invasion were prognostic factors for survival[5,19], which is comparable to the present results. However, in the present study, multivariate analysis did not show that sex, direct spread of tumor, and venous invasion were independent prognostic factors for rectal cancer. This could be due to the smaller number of patients in the present study compared with other studies.

In conclusion, the present study suggests that CRC patients of older age, advanced stage, and poor histology grade and WHO performance status should be considered at high-risk for short survival. In order to improve survival outcome, early stage CRC patients with poorly differentiated histology should be treated with high potency adjuvant chemotherapy regimens (for example, oxaliplatin-based chemotherapy[21]). For stage IV CRC patients, oxaliplatin- or irinotecan-based palliative chemotherapy in conjunction with a new anti-angiogenesis treatment should be considered for good performance status patients. In this present study, the authors had a small number of CRC patients in early stages, and a substantial number of patients who did not receive adjuvant or palliative chemo-therapy. Therefore, to improve quality of cancer care in Thailand, better identification of early stage CRC patients should be provided by improving public awareness of prevention and for early detection and treatment of colorectal cancer. Despite numerous studies on prognostic factors performed worldwide, some inconsistency results were still found. In conjunction with advances in molecular biology and new treatment modalities of CRC, further studies of prognostic factors are still needed to identify the role of various clinical and pathological factors, and new treatment factors in colorectal cancer prognosis.

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ปัจจัยพยากรณ์ที่มีผลต่อการรอดชีพของผู้ป่วยโรคมะเร็งลำไส้ใหญ่และเรคตัม

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วัตถุประสงค์: เพื่อศึกษาหาปัจจัยพยากรณ์ที่มีผลต่อการรอดชีพของผู้ป่วยมะเร็งลำไส้ใหญ่และเรคตัม ระยะที่ I ถึง IV โดยศึกษาวิเคราะห์ปัจจัยก่อนการรักษาและวิธีการรักษา

วัสดุและวิธีการ: เป็นการศึกษา retrospective cohort โดยการทบทวนเวชระเบียนของผู้ป่วยมะเร็งลำไส้ใหญ่ และเรคตัม 287 ราย โดยวิธีเคราะห์ 15 ปัจจัยที่อาจพยากรณ์การรอดชีพของผู้ป่วย

ผลการศึกษา: ค่ามัธยฐานของการรอดชีพของผู้ป่วยมะเร็งลำไส้ใหญ่และเรคตัม, มะเร็งลำไส้ใหญ่, มะเร็งเรคตัม เท่ากับ 37.2, 43.2 และ 29.5 เดือนตามลำดับ อัตราการรอดชีพที่ 5 ปี ของผู้ป่วยมะเร็งลำไส้ใหญ่และเรคตัมเท่ากับร้อยละ 38.6 อัตราการรอดชีพที่ 5 ปี แบ่งตามระยะของ ผู้ป่วยมะเร็งลำใส้ใหญ่และเรคตัมระยะ I, II, III และ IV เท่ากับร้อยละ 100, 68, 44 และ 2 ตามลำดับ (p < 0.001) ร้อยละ 68 ของผู้ป่วยมะเร็งลำใส้ใหญ่และเรคตัมเป็นระยะ III และ IV การวิเคราะห์ชนิด multivariate พบว่าอายุมากกว่าหรือเท่ากับ 60 ปี, WHO performance status 3, ระยะที่ III และ IV ของโรค และพยาธิวิทยาพบชิ้นเนื้อ poorly differentiated เป็นปัจจัยพยากรณ์โรคที่ไม่ดี ขณะที่การรักษา ด้วยการผ่าตัดที่สมบูรณ์ ร่วมกับการให้ยาเคมีบำบัดเสริมเป็นปัจจัยพยากรณ์โรคที่ดีในมะเร็งลำไส้ใหญ่และเรคตัม

สรุป: เนื่องจากผู้ป่วยส่วนมากอยู่ในระยะลุกลามที่มีการพยากรณ์โรคที่ไม่ดี ดังนั้นการค้นหาผู้ป่วยระยะเริ่มแรก และการรักษาด้วยยาชนิดใหม่ที่มีประสิทธิภาพสูง จะทำให้การรอดชีพของผู้ป่วยมะเร็งลำไส้ใหญ่ และเรคตัมของไทย ดีขึ้นได้