Original Article

Survival Rate and Effect of Clinicopathological Characteristics on Survival of Rectal Cancer in Thailand

Phaiboon Pensuwan MD[1], Narongchai Sangsa MD[2], Chitkhet Tomuen MD[3], Chatchawan Wachirametharuch MD[1], Kriengkrai Kovitangkoon MD[4], Nuntiput Putthanachote DrPH[5], Pongdech Sarakran PhD[6]

[1] Department of Surgery, Roi Et Hospital, Roi Et, Thailand
[2] Department of Medicine, Roi Et Hospital, Roi Et, Thailand
[3] Cancer Registry Unit, Roi Et Hospital, Roi Et, Thailand
[4] Department of Pediatrics, Roi Et Hospital, Roi Et, Thailand
[5] Department of Clinical Microbiology, Roi Et Hospital, Roi Et, Thailand
[6] Department of Epidemiology and Biostatistics, Faculty of Public Health, Khon Kaen University, Khon Kaen, Thailand

Objective: To investigate the survival rate and effect of clinicopathological characteristics on survival of rectal cancer in a Thai population.

Materials and Methods: A retrospective cohort study was performed. All data were collected from medical records of patients with rectal cancer at Roi Et Hospital during January 1, 2010 to December 31, 2014. All cases were followed-up until death or to the end of the study (March 31, 2016).

Results: A total of 145 patients had rectal cancer and most of them were men (56.55%), with a mean age of 61.86±12.95 years. The total follow-up time was 6,284 person-months. The median survival time was 55.7 months. Six-month and 1-, 2-, 3- and 5-year survival rates were 97.92%, 92.36%, 86.73%, 77.44%, and 36.67%, respectively. The factors affecting survival included cancer stage III (adjusted HR = 1.45; 95% CI: 1.16 to 2.43), cancer stage IV (adjusted HR = 3.04; 95% CI: 1.25 to 7.41), radiotherapy (adjusted HR = 0.46; 95% CI: 0.23 to 0.95), and chemotherapy (adjusted HR = 0.67; 95% CI: 0.17 to 0.87).

Conclusion: Rectal cancer stage III and IV affect the hazard of death. Patients who receive radiotherapy and chemotherapy have a lower risk of death and better survival rate than those who do not.

Keywords: Rectal cancer; Survival rate, Chemotherapy

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Colorectal cancer is one of the most common cancers diagnosed worldwide, with 746,000 cases in men and 614,000 cases in women. The mortality rate of both sexes is 8.5% and mortality is higher in less developed countries[1]. The incidence of colorectal cancer is high in North America, Europe, Oceania, and Eastern European countries, and is low in Africa, Asia, and South America[2]. The factors effecting survival of colorectal cancer are varied. Most patients with colorectal cancer have a high mortality, especially among advanced stages of this disease.

Rectal cancer occurs in the lower part of colon. The survival rate and factors affecting survival of rectal cancer vary. Previous studies showed that patients who received local treatment had better overall survival and cancer-specific survival than did those who did not receive local treatment[3]. Additionally, patients who underwent local tumor removal had better overall survival than did those who did not undergo this removal. Patients who have a distal resection margin of the tumor less than 1 cm have a 5-year disease-free survival rate of 75.1% and it is 76.3% for a tumor greater than 1 cm[4].

Correspondence to:
Putthanachote N, Department of Clinical Microbiology, Roi Et Hospital, Roi Et 45000, Thailand.
Phone: +66-43-518200; **Fax:** +66-43-527165
E-mail: Nuntiput101@gmail.com

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Previous studies showed that patients who received conventional chemoradiotherapy had a survival rate of 78.0% and short-term radiotherapy had a survival rate of 82.7%[5,6]. Additionally, both types of treatment were important factors for estimating disease-free survival and distant metastasis-free survival of patients at stage N2[5,6]. Many previous studies have reported factors that are associated with rectal cancer and factors affecting survival of patients with rectal cancer.

However, the effect of clinicopathological characteristics on survival of rectal cancer in the Thai population has rarely been reported. Therefore, this study aimed to investigate the survival rate and effect of clinicopathological characteristics on survival of rectal cancer in a Thai population.

Materials and Methods

Patients

We performed a retrospective cohort study. All data were retrieved from medical records of 145 patients and all of them were newly diagnosed with rectal cancer. All of the patients were recruited from those who were admitted and had rectal surgery at Roi Et Hospital, Roi Et Province, Thailand during January 1, 2010 to December 31, 2014. All of the patients had histopathological results to confirm the diagnosis according to the International Classification of Diseases for Oncology (ICD-O 3rd).

Follow-up of the patients

All of the patients were followed up. The time of follow-up started from the date of diagnosis for rectal cancer to follow-up until the patient's death or the end of the study (March 31, 2016). Patients who were lost to follow-up or died from other causes (not death from rectal cancer) were defined as censored. The vital status of the patients was checked from medical records and linkage with the Thai national death registry databases.

Variables

The variables of interest of the study were extracted from medical records, including age at diagnosis, sex, histology grading, stage of disease, histology type, cancer metastasis, cancer extent, radiotherapy, chemotherapy, and supportive treatment.

Statistical analysis

The length of survival time of patients with rectal cancer was calculated from the first date of diagnosis for rectal cancer until the patient's death or the end of the study (March 31, 2016). Descriptive statistics were used to describe demographic variables of the patients. The observed survival rate was determined by using the Kaplan-Meier survival curve and the log-rank test was used to compare between groups. Univariate and multivariate Cox proportional hazard models were used to examine the factors affecting survival of rectal cancer. The crude hazard ratio [HR], adjusted hazard ratio, 95% confident interval [CI], and *p*-value from the partial likelihood ratio test are shown. Statistical significance was set at a *p*-value <0.05 and all data analysis was performed by the Stata version 10.0 (Stata Corp LP, 2007).

Ethical considerations

This research was approved by The Ethical Committee for Human Research of Roi Et Hospital, Roi Et Province, Thailand. The reference number is 004/2560.

Results

Demographics of the patients

Of the 145 patients with rectal cancer, 56.55% were men and 43.45% were women, with a mean age of 61.86$\pm$SD = 12.95 years (Table 1). The marital status was couple in 88.19% of patients. The majority of cases were stage III, followed by stage II, stage IV, and stage I. With regard to histological grading, the highest was well differentiated, followed by moderately differentiated, poorly differentiated, and unknown. Metastasis of the liver was found in 12.41% of patients, in the lungs/pleura in 7.59%, in the brain in 2.07%, and in multiple sites in 4.83% (Table 1).

Survival rate of rectal cancer

The total time of follow-up of the 145 patients with rectal cancer was 6,284 person-months. At the end of the study, 70 patients had died, with an incident rate of 1.11 per 100 person-months. The median survival time was 55.7 months with 6-month, and 1-, 2-, 3, and 5-year survival rates of 97.92%, 92.36%, 86.73%, 77.44%, and 36.67%, respectively (Table 2). The Kaplan-Meier survival curve shows the overall survival time of rectal cancer (Figure 1). Figure 2 to 4 show the survival time of histology grading, extent of cancer, and staging of disease, respectively.

Factors affecting survival of patients with rectal cancer by univariate analysis

Univariate analysis showed that factors affecting survival of rectal cancer were cancer stage III

Table 1. Demographic characteristics of the patients

Variables	Number (n = 145)	Percentage
Sex		
Male	82	56.55
Female	63	43.45
Age (years)		
≤50	31	21.38
51 to 60	27	18.62
61 to 70	52	35.86
>71	35	24.14
Mean ± SD	61.86±12.95	
Minimum: maximum	25:99	
Marital status		
Single	8	5.56
Couple	127	88.19
Divorced	9	6.25
Stage of cancer		
Stage I	10	6.90
Stage II	38	26.21
Stage III	71	48.97
Stage IV	26	17.93
Extent of cancer		
Localized	9	6.21
Direct extension	48	33.10
Regional lymph nodes	64	44.14
Distant metastases	23	15.86
Unknown	1	0.69
Histology grading		
Well differentiated	72	49.66
Moderately differentiated	47	32.41
Poorly differentiated	7	4.83
Unknown	19	13.10
Metastasis		
None	106	73.10
Liver	18	12.41
Lungs/pleura	11	7.59
Brain	3	2.07
Multiple sites	7	4.83

(crude HR = 1.75; 95% CI: 1.08 to 2.84), stage IV (crude HR = 2.86; 95% CI: 1.15 to 7.02), radiotherapy (crude HR = 0.45; 95% CI: 0.22 to 0.90), and chemotherapy (crude HR = 0.73; 95% CI: 0.53 to 0.95). Poorly differentiated cancer, the extent of regional lymph nodes, brain metastasis, and supportive treatment appeared to show an increased hazard of death, but this was not significant (Table 3).

Factors affecting survival of patients with rectal cancer by stepwise Cox proportional hazard regression analysis.

Stepwise Cox proportional hazard regression showed that factors affecting survival of rectal cancer included cancer stage III (adjusted HR = 1.45; 95% CI: 1.16 to 2.43), cancer stage IV (adjusted HR = 3.04; 95% CI: 1.25 to 7.41), radiotherapy (adjusted HR = 0.46; 95% CI: 0.23 to 0.95), and chemotherapy (adjusted HR = 0.67; 95% CI: 0.17 to 0.87) (Table 4).

Discussion

This study aimed to investigate the survival rate and effect of clinicopathological characteristics on survival of patients with rectal cancer among the Thai population. We found that the median survival time of rectal cancer was 55.7 months, with 6-month and 1-, 2-, 3-, and 5-year survival rates of 97.92%, 92.36%, 86.73%, 77.44%, and 36.67%, respectively. Cancer stage III and stage IV were factors that affected survival of patients. This finding is consistent with a previous study from Jordan, which demonstrated that an important factor affecting survival of patients was an advanced stage of rectal cancer[7]. This study also showed that clinicopathological characteristics (stage of disease, histology grading, extent of cancer and cancer metastasis) affected survival of patients, but this was not significant. Our lack of finding is in contrast to several studies that demonstrated that metastasis of cancer to the liver[8], distant metastasis, histological grade[9], poorly differentiated[10] N-status,

Table 2. Survival rate of rectal cancer

Survival time	Median survival time (months)	95% CI	Survival rate (%)	95% CI
6 months	0.9	0.2 to NA	97.92	93.68 to 99.32
1 year	8.0	6.3 to 9.8	92.36	86.63 to 95.70
2 years	NA	NA to NA	86.73	79.98 to 91.32
3 years	43.0	36.3 to NA	77.44	69.24 to 83.71
5 years	57.2	55.7 to NA	36.67	24.97 to 48.41

CI = confident interval; NA = Not applicable

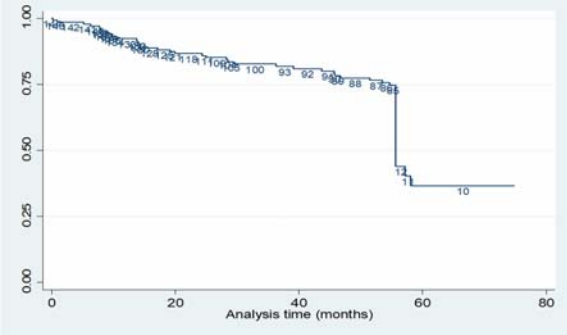

Figure 1. Overall survival time of rectal cancer.

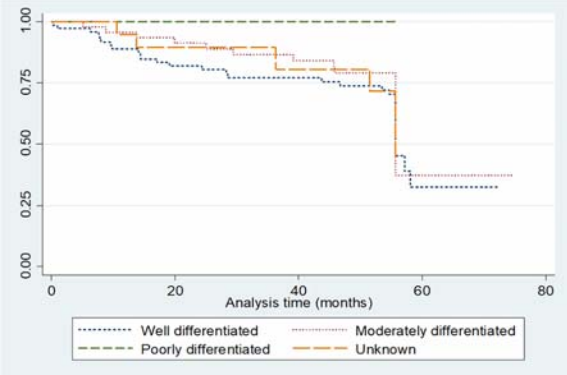

Figure 2. Survival time according to histological grading.

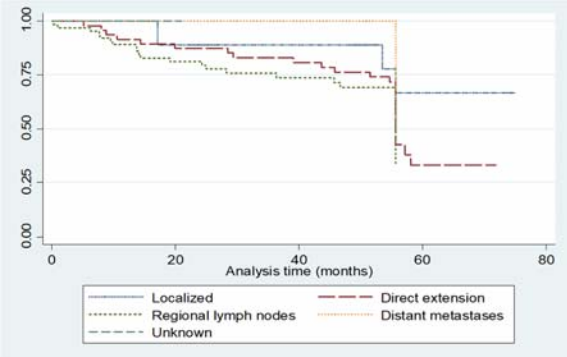

Figure 3. Survival time according to the extent of cancer.

obstruction of the colon[8], signet-ring cell carcinoma, and poor differentiation[11] affected survival of patients. Our study showed that Thai patients who received radiotherapy and chemotherapy had a better survival rate than did those who did not receive these therapies. This finding is similar to many previous studies as

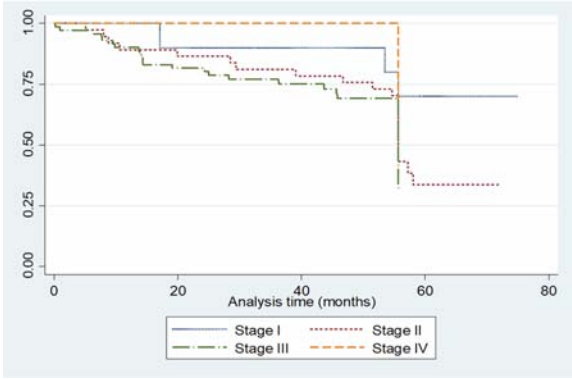

Figure 4. Survival time according to the stage of disease.

follows. A study in Canada showed that stage III colon cancer with complete resection has a better overall survival benefit from combination chemotherapy than monotherapy[12]. A study in China showed that patients with cancer stage II who received adjuvant radiotherapy had a lower risk of death and better survival rate than did those who did not[13]. In Taiwan, patients younger than 70 years old who achieved a pathological complete response and treatment by adjuvant chemotherapy had a better survival benefit than did patients without adjuvant chemotherapy[14]. A Chinese study showed that patients who underwent local tumor surgical resection had better overall survival than patients who did not[15].

The present study has several limitations. First we had no data on the type and cycle of chemotherapy or radiotherapy. This lack of data might have affected the analysis of outcome, with different results from other previous studies. Second, the sample size of this study was relatively small. We also only studied patients who were from Roi Et Province and did not include various populations. Therefore, or study population does not represent overall Thai people or other regions of Thailand because they have different life styles. Third, this study did not examine the quality of life of patients with rectal cancer. Quality of life of patients is an important factor that affects survival of patients and this factor might have affected data analysis. Finally, this study only investigated the effect of clinicopathological characteristics on survival of patients, and did not include other laboratory tests. Abnormal biochemical blood tests might have been associated with survival of patients. Future study is required to include these variables. A strength of our study is that all of the patients were followed-up for

Table 3. Univariate analysis on the factors affecting survival of patients with rectal cancer

Variables	Median time (months)	Person-times	IR/100	Crude HR	95% CI	*p*-value
Sex						
Male	55.70	3,641	1.09	1.00		
Female	55.70	2,642	1.13	1.09	0.62 to 1.73	0.753
Age (years)						
≤60	55.75	2,588	1.04	1.00		
>60	5.70	3,695	1.16	1.08	0.67 to 1.75	0.738
Stage of cancer						
Stage I	NA	571	0.52	1.00		
Stage II	55.70	1,853	1.20	1.11	0.67 to 1.84	0.680
Stage III	55.70	2,772	1.41	1.75	1.08 to 2.84	0.021
Stage IV	NA	1,087	0.46	2.86	1.15 to 7.02	0.024
Histology grading						
Well differentiated	55.70	3,047	1.21	1.00		
Moderately differentiated	55.70	2,220	1.17	1.03	0.64 to 1.68	0.885
Poorly differentiated	NA	258	0.00	1.60	0.56 to 3.12	0.765
Unknown	55.70	758	0.09	0.93	0.42 to 2.04	0.865
Extent of cancer						
Localized	NA	515	0.05	1.00		
Direct extension	55.70	2,305	1.21	1.10	0.68 to 1.79	0.678
Regional lymph nodes	55.70	2,450	1.38	1.61	0.99 to 2.58	0.052
Distant metastases	NA	991	0.05	0.39	0.16 to 1.96	0.241
Unknown	NA	21	NA	NA	NA to NA	NA
Metastasis						
None	55.70	4,704	1.11	1.00		
Liver	NA	526	1.13	1.10	0.46 to 2.56	0.817
Lungs/pleura	55.70	556	0.08	0.73	0.29 to 1.83	0.506
Brain	55.70	139	2.14	1.95	0.61 to 6.2	0.257
Multiple sites	NA	356	0.05	0.44	10.18 to 1.81	0.265
Radiotherapy						
No	55.70	4,704	1.14	1.00		
Yes	NA	1,579	1.01	0.45	0.22 to 0.90	0.024
Chemotherapy						
No	55.70	1,289	1.16	1.00		
Yes	55.70	4,993	1.10	0.73	0.53 to 0.95	0.003
Supportive treatment						
No	55.70	5,565	1.09	1.00		
Yes	55.70	718	1.25	1.33	0.66 to 2.68	0.426

IR = incident rate; CI = confident interval; HR = hazard ratio; NA = not applicable

vital status and all of them had histopathological results.

Conclusion

This study shows the cancer stages III and IV affect the hazard of death of patients. Additionally, patients who receive radiotherapy and chemotherapy have a lower risk of death and better survival rate than those who do not. However, other clinicopathological characteristics factors do not significantly affect the hazard of death. A larger sample size and different population are needed to verify our study findings.

What is already known on this topic?

Chemotherapy, radiotherapy, and local tumor surgical resection reduce the hazard of death in patients with rectal cancer.

What this study adds?

Cancer stages III and IV, radiotherapy, and

Table 4. Final multivariate model analysis of significant factors that independently affected the hazard of death by stepwise Cox proportional hazard regression

Variable	Adjusted HR	95% CI	*p*-value
			0.009
Stage III	1.45	1.16 to 2.43	
Stage IV	3.04	1.25 to 7.41	
Radiotherapy	0.46	0.23 to 0.95	
Chemotherapy	0.67	0.17 to 0.87	

The *p*-value was based on stepwise Cox proportional hazard regression.
HR = hazard ratio; 95% CI = 95% confident interval

chemotherapy affect survival of rectal cancer in the Thai population.

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Potential conflicts of interest

None.

References

1. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015; 136: E359-86.
2. Center MM, Jemal A, Smith RA, Ward E. Worldwide variations in colorectal cancer. CA Cancer J Clin 2009;59:366-78.
3. Zhang Y, Sun Y, Xu Z, Chi P, Lu X. Is neoadjuvant chemoradiotherapy always necessary for mid/high local advanced rectal cancer: A comparative analysis after propensity score matching. Eur J Surg Oncol 2017;43:1440-6.
4. Kang DW, Kwak HD, Sung NS, Yang IS, Baek SJ, Kwak JM, et al. Oncologic outcomes in rectal cancer patients with a </=1-cm distal resection margin. Int J Colorectal Dis 2017;32:325-32.
5. Latkauskas T, Pauzas H, Kairevice L, Petrauskas A, Saladzinskas Z, Janciauskiene R, et al. Preoperative conventional chemoradiotherapy versus short-course radiotherapy with delayed surgery for rectal cancer: results of a randomized controlled trial. BMC Cancer 2016;16:927.
6. Feng YR, Jin J, Ren H, Wang X, Wang SL, Wang WH, et al. Patients with pathological stage N2 rectal cancer treated with early adjuvant chemotherapy have a lower treatment failure rate. BMC Cancer 2017;17:182.
7. Sharkas GF, Arqoub KH, Khader YS, Tarawneh MR, Nimri OF, Al Zaghal MJ, et al. Colorectal cancer in Jordan: Survival rate and its related factors. J Oncol 2017;2017:3180762.
8. Zhang S, Gao F, Luo J, Yang J. Prognostic factors in survival of colorectal cancer patients with synchronous liver metastasis. Colorectal Dis 2010;12:754-61.
9. Mehrkhani F, Nasiri S, Donboli K, Meysamie A, Hedayat A. Prognostic factors in survival of colorectal cancer patients after surgery. Colorectal Dis 2009;11:157-61.
10. Rasouli MA, Moradi G, Roshani D, Nikkhoo B, Ghaderi E, Ghaytasi B. Prognostic factors and survival of colorectal cancer in Kurdistan province, Iran: A population-based study (2009-2014). Medicine (Baltimore) 2017;96:e5941.
11. Siewchaisakul P, Suwanrungruang K, Poomphakwaen K, Wiangnon S, Promthet S. Lack of Association between an XRCC1 gene polymorphism and colorectal cancer survival in Thailand. Asian Pac J Cancer Prev 2016;17:2055-60.
12. Meyers BM, Cosby R, Quereshy F, Jonker D. Adjuvant chemotherapy for stage II and III colon cancer following complete resection: A cancer care Ontario systematic review. Clin Oncol (R Coll Radiol) 2017;29:459-65.
13. Li Q, Li Y, Dai W, Wang S, Xu Y, Li X, et al. Adjuvant radiotherapy improves cause specific survival in stage II, not stage III mucinous carcinoma of the rectum. BMC Cancer 2017; 17: 80.
14. Kuan FC, Lai CH, Ku HY, Wu CF, Hsieh MC, Liu TW, et al. The survival impact of delayed surgery and adjuvant chemotherapy on stage II/III rectal cancer with pathological complete response after neoadjuvantchemoradiation. Int J Cancer 2017;140:1662-9.
15. Zhang CH, Pan YB, Zhang QW, Shi OM, Zheng L, Gui L, et al. The influence of local therapy on the survival of patients with metastatic rectal cancer: a population-based, propensity-matched study. J Cancer Res Clin Oncol 2017.