

# Rectal Cancer in Naresuan University Hospital: 2010 to 2018, Hospital Based Registry Population

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**Objective:** To determine the outcome of rectal cancer in Naresuan University Cancer Program and the effect of healthcare coverage schemes on patient outcome.

**Materials and Methods:** The retrospective study was conducted by reviewing 163 patients, diagnosed with rectal cancer, from the cancer registry, based on Thai Cancer Based Version 6.2, between January 1, 2010 and August 31, 2018. Kaplan-Meier survival curve was applied for cumulative survival analysis.

**Results:** The overall 1-year, 3-year, and 5-year survival time for all rectal cancer were 87.03%, 64.94%, and 50.21%, respectively. The median survival time for stage IV was 1.60 years (95% CI 1.19 to 2.06). Liver metastasis was the most common single organ metastasis and associated with the worse outcome. There was no significant difference in patient survival between patients in Government Benefit scheme and patients in Universal Healthcare Coverage scheme.

**Conclusion:** The stage of disease and site of metastasis are the factors that significantly affect patient survival. Further studies with higher number of patients should be performed to evaluate the outcomes of rectal cancer treatments in different healthcare coverage schemes.

**Keywords:** Rectal cancer, Metastasis, Survival analysis, Healthcare coverage

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Colorectal cancer is the third most common cancer in terms of incidence and the second in terms of mortality worldwide<sup>(1)</sup>. Naresuan University Hospital is a tertiary health care center, providing a multidisciplinary team for cancer patient care, responsible for patients in the lower northern region of Thailand. All cancer patient data had been recorded in the cancer registry system since 2010. Naresuan University Hospital has provided healthcare services accommodating all types of healthcare schemes. There are currently three major healthcare schemes in Thailand. First, the Government Medical Benefit Healthcare scheme for government officers and their immediate families; second, the Social Security Healthcare scheme for workers in any organization,

and lastly, the Universal Healthcare scheme for Thais who are not covered under any of the previously mentioned schemes. All rectal cancer patients in this region should have an appropriate care covered in the cancer treatment program. However, the chemotherapy regimens for advanced stage rectal cancer are different in each healthcare scheme.

The standard treatment for stages I is surgery alone, while for stages II, III, and IV are a combination of surgery and chemotherapy ± radiation therapy<sup>(2)</sup>. The chemotherapy treatment is comprised of either FOLFOX (folinic acid, fluorouracil, and oxaliplatin) covered under the Government Medical Benefit Healthcare scheme; or de Gramont/Mayo (folinic acid and fluorouracil) for Universal Healthcare coverage. There is a public concern that the outcome under the latter may be inferior to that of the former. However, the outcome of rectal cancer treatment in Naresuan University Cancer Program for these healthcare coverage schemes had never been systematically evaluated. Therefore, the authors conducted the present study to evaluate the outcome of Naresuan

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University Cancer Program and the impacts of the different healthcare coverage schemes on the result of rectal cancer treatments.

## Materials and Methods

The authors performed a retrospective cohort study to determine the survival of rectal cancer patients in Naresuan University Hospital cancer program. The hospital cancer registry system, based on Thai Cancer Based Version 6.2 (reference available from <http://tcb.nci.go.th>, 2016), was used as a database for the present study. Patients diagnosed with rectal cancer between January 1, 2010 and August 31, 2018 were enrolled in the study. The diagnosis of rectum cancer was based on tissue pathology. Patient information, including age, sex, date of diagnosis, staging, health coverage scheme, and date of last visit or death were reviewed. The patients with incomplete information, unknown staging, or no follow-up were excluded. The protocol of the present study was reviewed and approved by the Naresuan University Hospital Ethics Committee.

### Statistical analysis

Data were presented as median, mean  $\pm$  standard deviation (SD), or percentage, as appropriated. Kaplan-Meier survival curve was applied for cumulative survival analysis. Patient's death caused by other reasons or recurrence of rectal cancer was considered for survival analyses of the outcome of treatment. Log-rank test was applied for comparing survival rates between groups. Crude hazard ratio (HR) and 95% confidence interval (CI) from the partial likelihood ratio test were determined. The length of survival time of patients with rectal cancer was calculated from the first date of diagnosis of rectal cancer to the patient's death or the end of the study. Patients who have failed follow-up were classified in a censored group. A p-value of less than 0.05 was considered statistically significant.

## Results

Between January 1, 2010 and August 31, 2018, there were 184 patients diagnosed with rectal cancer and registered at the Naresuan Hospital Cancer Program. Twenty-one patients were excluded from the study due to erroneous encoding of ICD-10 or incomplete data for analysis. Only 163 patients were enrolled in the present study. Demographic data of patients diagnosed with rectal cancer are shown in Table 1. The data showed higher incidence of colorectal cancer in males than in females. The

**Table 1.** The demographic data of rectal cancer patients (n=163)

	n (%)
Sex	
Male	106 (65.03)
Female	57 (34.97)
Age (year), Mean $\pm$ SD	60.75 $\pm$ 10.67
Male	62.45 $\pm$ 11.11
Female	57.60 $\pm$ 9.02
Cancer staging	
I	12 (7.36)
II	19 (11.66)
III	78 (47.85)
IV	54 (33.13)
Metastatic sites (n=54)	
Multiple sites	18 (33.33)
Liver	19 (35.19)
Lung	8 (14.82)
Lymph node	7 (12.96)
Peritoneum	1 (1.85)
Other	1 (1.85)
Health care coverage	
Government medical benefit scheme	91 (55.83)
Universal health-care coverage scheme	62 (38.03)
Social security scheme	5 (3.07)
Self-payment	5 (3.07)

SD=standard deviation

age at which the rectal cancer diagnoses was also higher in males than in females. Most patients were diagnosed with advanced stages, 78 patients (47.9%) in stage III and 54 patients (33.1%) in stage IV. In stage III patients, there were 16 patients (20.51%), 28 patients (35.90%), and 34 patients (43.50%) who were classified in pre-operative chemoradiation group, post-operative chemoradiation group, and others, which had insufficient data, respectively. One-third of the patients had multiple site metastasis. Liver was the most common site for single organ metastasis, followed by lungs and lymph nodes. Patients classified according to their healthcare coverage schemes are shown in Table 2. Patients diagnosed with stage I rectal cancer and covered under the Universal Healthcare coverage were statistically predominant than those who were covered under the Government Medical Benefit scheme. The distribution of metastatic organs

**Table 2.** Patient characteristics classified by health-care coverage schemes

Variables	Universal healthcare coverage scheme (n=62) n (%)	Government medical benefit scheme (n=91) n (%)	p-value
Sex			0.980
Male	41 (66.13)	60 (65.93)	
Female	21 (33.87)	31 (34.07)	
Age (year), Mean±SD	58.26±1.46	62.92±0.96	0.006
Stage			0.037
I	9 (14.52)	3 (3.30)	
II	5 (8.06)	14 (15.38)	
III	25 (40.32)	45 (49.45)	
IV	23 (37.10)	29 (31.87)	
Metastatic site	(n=23)	(n=29)	0.157
Lung	2 (8.70)	5 (17.24)	
Lymph node	2 (8.70)	5 (17.24)	
Multiple site	12 (52.16)	6 (20.69)	
Liver	6 (26.09)	12 (41.38)	
Peritoneum	1 (4.35)	0 (0.00)	
Other	0 (0.00)	1 (3.45)	

SD=standard deviation

**Table 3.** Survival rate of rectal cancer patients

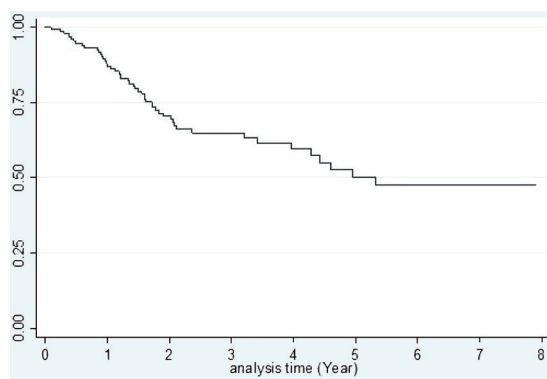
Survival time	95% CI	Survival rate (%)
1 year	0.80 to 0.92	87.03
2 years	0.61 to 0.78	70.39
3 years	0.55 to 0.73	64.94
4 years	0.49 to 0.69	59.51
5 years	0.38 to 0.61	50.21
6 years	0.35 to 0.59	47.57
7 years	0.35 to 0.59	47.57

CI=confidence interval

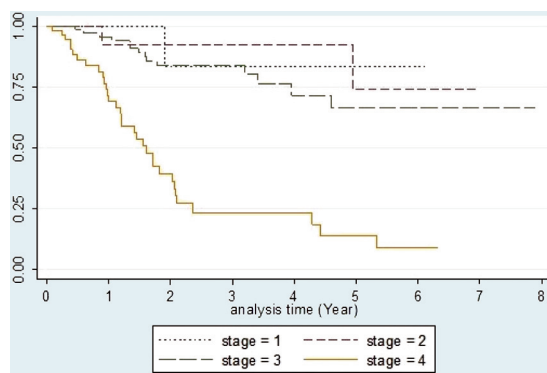
of patients in both healthcare coverage schemes were comparable.

The overall median survival period for all stages of rectal cancer patients was 5.33 years. The survival curve for overall mortality is shown in Figure 1. The overall 1-year, 3-year, and 5-year survival time for all rectal cancer were 87.03%, 64.94%, and 50.21%, respectively. The overall 1-year, 3-year, and 5-year survival time for each stage are shown in Figure 2.

There was no incidence of recurrence in patients with stage I or stage II in the present study. For



**Figure 1.** The overall survival for all stage of cancer patients.



**Figure 2.** The patient survival for each stage of rectal cancer.

stage III rectal cancer patients, 1-year, 3-year, and 5-year disease-free survival were 94.17%, 86.81%, and 83.19%, respectively. The median survival time for stage IV was 1.60 years (95% CI 1.19 to 2.06). The median survival time for stage IV patients with lung, lymph node, multiple sites, and liver metastasis were 5.33, 2.03, 1.41, and 0.98 years, respectively. The survival curves for stage IV patients with different sites of metastasis are also shown in Figure 3. By applying univariate analysis, only the staging of disease and the site of metastasis were found to be statistically significant factors that affected the survival of rectal cancer patients, as shown in Table 4.

To compare the effect of health care coverage scheme on patient survival, survival analysis for patients covered under the Universal Healthcare Coverage scheme and for those under the Government Medical Benefit scheme were performed, as shown in Figure 4. Although the overall patient survival was higher in Government Medical Benefit scheme

**Table 4.** Univariate analysis for factors affecting survival in rectal cancer

Variables	HR	95% CI	p-value
<b>Sex</b>			
Female	1		
Male	1.14	0.62 to 2.09	0.671
<b>Stage</b>			
I	1		
II	1.15	0.10 to 12.72	
III	2.04	0.27 to 15.52	
IV	12.11	1.65 to 88.78	<0.001
<b>Healthcare coverage scheme</b>			
Government medical benefit	1		
Universal healthcare coverage	1.27	0.72 to 2.25	0.411
<b>Metastatic sites*</b>			
None	1		
Lung	2.43	0.71 to 8.31	
Lymph node	6.28	1.80 to 21.90	<0.001
Multiple site	8.75	4.16 to 18.42	<0.001
Liver	8.48	4.03 to 17.83	<0.001

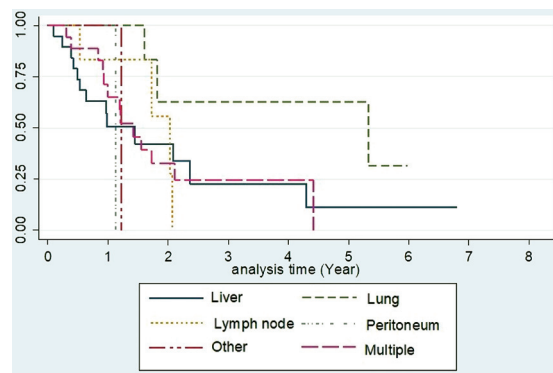
HR=hazard ratio; CI=confidence interval

\* Peritoneal and other site of metastasis were not included in the univariate analysis due to the insufficient number of patients for meaningful analysis

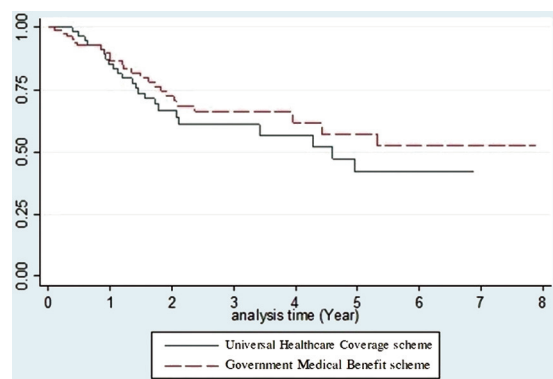
than in Universal Healthcare Coverage scheme, the difference was not statistically significant. To exclude the potential confounding effect of having more stage I cancer patients under the Universal Healthcare Coverage scheme than in Government Medical Benefit scheme, a subgroup analysis was conducted with the exclusion of patients in stage I. The difference in patient survival between both groups was still insignificant,  $p>0.05$ . The patient survival under both schemes after the exclusion of stage I patients are shown in Figure 4.

## Discussion

In the present study, most patients were in their late 50s to early 60s, most commonly males, and mostly in stages III and IV. There was no recurrence of rectal cancer in patients with stage I and stage II. The overall 5-year disease free survival of rectal cancer in stage III was 83.19%. The overall 1-year, 3-year, and 5-year survival time for all rectal cancer patients was 87.03%, 64.94%, and 50.21%, respectively. The



**Figure 3.** The survival time of rectal cancer patients for each metastatic location.



**Figure 4.** Patient survival for universal healthcare coverage scheme and government medical benefit scheme ( $p>0.05$ ).

most common site of metastasis was liver. Both the stage of disease and the site of metastasis were the factors affecting patient survival, similar to other studies<sup>(3-5)</sup>.

The present study was based on the population of the lower northern region of Thailand, which is geographically and ethnically close to the population in the north eastern region. The authors, therefore, compared the present study with the study from Srinagarind Hospital<sup>(3)</sup>, a university hospital in the north eastern region of Thailand. The presentation of rectal cancer patients in the present study is comparable to those reported from Srinagarind Hospital and Phramongkutklao Hospital in many aspects<sup>(3,5)</sup>. In Srinagarind Hospital<sup>(3)</sup>, the mean age of the patients was 57.56 years and they commonly presented in advanced stage, 15.23% in stage III and 24.73% in IV. These findings, where both of the studies presented a predominant number of patients with advanced stage of rectal cancer, may be caused by the lack

of awareness, absence of national cancer screening policy, and limited access to healthcare services. Delay in referral system might be an additional cause for such outcome. In the present study, as well as in Srinagarind Hospital and SEER-based studies<sup>(6)</sup>, the most common site for distant metastasis in stage IV patients was liver. However, the 1-year (75%), 3-year (43%), and 5-year survival periods in the study conducted at Srinagarind Hospital were lesser than those recorded in the Naresuan Cancer Program. The lower rate of survival in Srinagarind Hospital might be influenced primarily by the period when both studies were conducted. The study from Srinagarind Hospital was conducted by collecting data between 2000 and 2010, while the present study was between 2010 and 2018. According to Zaheer et al, surgical technique played an important role in the management of rectal cancer<sup>(7)</sup>. Surgical technique and care have improved dramatically over the past 10 years.

Currently, there are three healthcare schemes in Thailand, Government Medical Benefit Healthcare scheme, Social Security Healthcare scheme, and Universal Healthcare Coverage scheme. Unfortunately, there were insufficient number of patients in Social Security scheme for analysis in the present study. Therefore, the present analysis was limited to the other two healthcare schemes. There is a public concern that the Government Medical Benefit scheme provides better treatment and patient support than the Universal Healthcare Coverage scheme. Due to the different policies among the two healthcare coverage schemes, stages III and IV rectal cancer patients received different chemotherapy regimens, FOLFOX regimen (folinic acid, fluorouracil, and oxaliplatin) for Government Medical Benefit scheme, whereas de Gramont or Mayo regimen (folinic acid and fluorouracil) for Universal Healthcare Coverage scheme. On the average FOLFOX (based on body surface area [BSA] 1.5 m<sup>2</sup>) costs 6,000 baht whereas de Gramont or Mayo costs 400 to 700 baht. Therefore, the authors conducted the comparison of patient survival between both schemes. Although there was a higher number of patients diagnosed with advanced stage of rectal cancer in the Government Medical Benefit scheme than in the Universal Healthcare Coverage scheme, survival time was remarkably higher in patients covered under the former than the latter scheme. This might be a result from a more effective chemotherapy, FOLFOX, and better care included in the Government Medical Benefit scheme, however, the difference was not statistically significant. To eliminate the negative impact of

advanced stage on patient survival in Government Medical Benefit scheme, the authors conducted a subgroup analysis by excluding patients with stage I cancer. However, the subsequent analysis was still unable to demonstrate statistical difference between the survival periods in both schemes. The failure to reach statistical significance may be due to the relatively small sample size in the present study. Unfortunately, no further studies are available regarding the comparison of the outcomes of both regimens in Thai patients diagnosed with rectal cancer. It is still uncertain whether the Government Medical Benefit scheme provides a better outcome in the treatment of rectal cancer than the Universal Healthcare Coverage scheme. Nonetheless, it should be noted that there were more patients diagnosed with stage I cancer who were covered under the Universal Healthcare Coverage scheme than in the Government Medical Benefit scheme. This observation suggests that patients under the former have a lesser opportunity to access healthcare services than those covered under the latter. Based on the current findings, both schemes provide comparable outcomes for rectal cancer patients. It is important to note that some patients in the present studies were referred from other hospitals and had limited information of mortality and complication from overall treatment. Further studies with higher number of subjects and more particulars are required to ensure the comparable results and services of both schemes.

## Conclusion

Rectal cancer patients are commonly between late 50s and early 60s, and in advanced stages. The stage of disease and site of metastasis are the factors that significantly affect patient survival. Liver is the most common site of single organ metastasis and associated with the worst prognosis. The outcomes of rectal cancer treatment are comparable in both the Government Medical Benefit and the Universal Healthcare Coverage schemes. Further studies with higher number of patients should be performed to evaluate the outcomes of rectal cancer treatments in the different healthcare coverage schemes.

## What is already known on this topic?

The chemotherapy regimens for advanced stage rectal cancer are different in each healthcare scheme. However, the outcome of rectal cancer treatment in Naresuan University Cancer Program for these healthcare coverage schemes has never been systematically evaluated.

## What this study adds?

The outcomes of rectal cancer treatment are comparable in both Government Medical Benefit and Universal Healthcare Coverage schemes. Further studies with larger number of subjects and more particulars are required to ensure the comparable results and services of both schemes.

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## Conflicts of interest

The authors declare no conflict of interest.

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