12-18-2020

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Recommended Citation

Jeo, Wifanto S. and Subrata, Feyona H. (2020) "The Survival Rate of Colorectal Cancer in dr. Cipto Mangunkusumo Hospital," *The New Ropanasuri Journal of Surgery*. Vol. 5 : No. 2 , Article 4.

DOI: 10.7454/nrjs.v5i2.1081

Available at: <https://scholarhub.ui.ac.id/nrjs/vol5/iss2/4>

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The Survival Rate of Colorectal Cancer in dr. Cipto Mangunkusumo Hospital

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Corresponding author: drfeyona@gmail.com Received: 11/Jul/2020 Accepted: 15/Dec/2020 Published: 18/Dec/2020
Website: <https://scholarhub.ui.ac.id/nrjs/> DOI:10.7454/nrjs.v5i2.1081

Abstract

Introduction. Colorectal cancer (CC) is a malignancy with the third highest incidence and the second cause of death. 1.4 million new cases of colorectal cancer occurred in 2012, increasing to 1.8 million new cases in 2019, with almost 900,000 deaths caused by CC in the world. In Indonesia, there were 30,017 new cases of CC in 2019, with fatalities reaching nearly 16,000 cases. There are differences in the survival rates of the CC between developed countries and Indonesia. This study aims to determine the survival rate of CC patients in Indonesia.

Method. A retrospective cohort study design with survival analysis. The study was conducted at the Department of Surgery, Faculty of Medicine, University of Indonesia, RSCM, from January 2014 to December 2016. 316 samples were obtained from the registration of the RSC M CC with the CC who had received therapy according to the stage of cancer they suffered during the period January 2014 to December 2016.

Results. The overall five-year survival rate in this study was 43%. The survival rate of colorectal cancer patients aged ≥ 45 years reached 50% at observation 20 months. Age group (95% CI 44.03-57.32) months, stage III was 38.59 months (95% CI 32.20-44.97), 30.36 months in stage IV subjects (95% CI 25.638-35.09). the average survival of subjects who received chemotherapy was 38.28 months (95% CI 33.44-43.11). not receiving adjuvant therapy was 33.71 months (95% CI 27.79-39.63). Mean survival of subjects who received definitive surgery (44.39 months; 95% CI 40.35-48.43) and who did not get definitive surgery (20.08 months; 95% CI 15.82-24.36).

Conclusion: The overall survival rate of the CC within five years at the RSCM was 43%. Factors that influence patient survival are clinical stage and definitive surgery in primary tumor mass resection

Keywords: colorectal cancer, survival rate

Introduction

Colorectal cancer (CC) consisted of colon cancer and rectal cancer, depending on where the tumor is found.¹ The primary etiology of these tumors was a combination of genetic and environmental factors. Most CC spreads sporadically. About three-quarters of patients have no previous family history. However, those with a family history and diagnosed at age 50-70 are likely to risk developing cancer two folds. Whereas when diagnosed at age <50 years, the first-degree family members' risk increases to three folds. Such a risk increase for individuals having more than a family member with CC.^{2,3}

The classification is based on the stage, which is essential to determine the treatment and prognosis. There are classification systems: the TNM system, the most used classification in daily clinical practice, and the Surveillance, Epidemiology, and End Results (SEER) systems. The SEER classification is used for descriptive and statistical analysis for the benefit of patient registration data.⁴ Another classification is the Duke classification. According to Duke, CC commencing with epithelial proliferation resulting in an adenoma. Cancer cells remain confined to the rectal wall classified as Duke A. Should these cells progressed beyond the rectum, classified as Duke B, and if metastasis occurred, then classified as Duke C.

Table 1. Classification of tumors, nodes, and metastases in CC:⁵

T- Primary tumor
T _x The primary tumor cannot be assessed
T ₀ no sign of a primary tumor
T _{is} carcinoma in situ: intraepithelial tumor invasion or lamina propria
T ₁ tumor invasion into submucosa
T ₂ tumor invasion of propria muscularis
T ₃ tumor invasion through propria muscularis to the subserosa or to non-peritoneal tissue or perirectal tissue
T ₄ tumors directly invade other organs or structures and penetrate the visceral peritoneum
N- Regional lymph nodes
N _x Regional lymph node cannot be assessed
N ₀ there is no metastasis to regional lymph
N ₁ metastasis in 1 to 3 regional lymph nodes
N ₂ metastasis in 4 or more regional lymph nodes
M-metastasis is far away
M _x distant metastases cannot be assessed
M ₀ there is no distant metastasis
M ₁ is distant metastasis

Table 2. Classification of tumors according to TNM, Dukes, and MAC

Stage	T	N	M	Duke	MAC
0	T _{is}	N ₀	M ₀	-	-
I	T ₁	N ₀	M ₀	A	A
	T ₂	N ₀	M ₀	A	B ₁
II _A	T ₃	N ₀	M ₀	B	B ₂
II _B	T ₄	N ₀	M ₀	B	B ₃
III _A	T ₁ , T ₂	N ₁	M ₀	C	C ₁
III _B	T ₃ , T ₄	N ₁	M ₀	C	C ₂ /C ₃
III _C	T _{Any}	N ₂	M ₀	C	C ₁ /C ₂ /C ₃
IV	T _{Any}	N _{Any}	M ₁	D	D

Table 3. Duke classification and five-year survival

Stage classification based on Duke criteria	Description	Five year survival rate (%)
A (stage I)	Localized to the mucosa and sub-mucosa	93%
B (stage II _A and II _B)	Extends to the muscular layer without lymph node involvement	72%-85%
C (stage III _{A-C})	Lymph node involvement	44%-83%
D (s stage IV)	Distant metastasis	8%

Surgery is the primary treatment for CC with no metastasis. The outcome depends on the quality of surgery, the stage, and further therapy. In more severe cases, neoadjuvant therapy (such as perioperative chemotherapy for T₄ cancer lesions and [chemo] radiotherapy for local lesions) may reduce tumor stage and increase resection success.³

According to GLOBOCAN data in 2019, CC is the third most deadly cancer and places the fourth rank as the most commonly diagnosed cancer worldwide. There are two million new cases, and one million patients died due to CC in 2019. The incidence of CC continually increases every year, especially in developing countries. The reason why developing countries because adopting the "western lifestyle." Obesity, lack of physical activity, red meat consumption, alcohol, and tobacco are risk factors for CC. Cumulative death risk of CC at the age of 0-74 years is 0.66% in male and 0.44% in a female, with a mortality rate of 8.9 per 100,000 cases.² The survival rate is the proportion of cancer patients who can survive within a certain period after a cancer diagnosis is made. In well-developed countries, the five-year life expectancy is more than 60%, but lower at <50% in Iran. In the United States, five-year life expectancy for stage I is 92%, stage II_A and II_B 87%, 65%, stage III_A, and III_B 90% and 72%, and stage III_C 53%. In contrast, for metastasis, only 12%.⁶

Most Indonesian come in an advanced stage; for many reasons such as ignorance, cultural, social, and economic ones. The incidence in dr. Cipto Mangunkusumo General Hospital (RSCM), as a referral center, with a reasonably high as in Indonesia, is 8.6% (GLOBOCAN, 2018). So far, the survival rate in the hospital remain unclear. Thus, we run a study focus on this survival

Method

This study was a retrospective cohort design with survival rate analysis, enrolling subjects diagnosed as CC managed in RSCM from January 2014 to December 2016. Data were taken from the cancer registration in RSCM. Inclusion were those diagnosed and managed in the hospital. Subjects' characteristics, including age, gender, body mass index (BMI), comorbid, family history, clinical stage, and therapy, were the focus of interests subjected to analysis. Outcomes, particularly mortality within five years, was the dependent variable. Survival analysis was carried out using the log-rank test and Kaplan Meier curve showing the probability

of an event. The committee of ethic Faculty of Medicine, Universitas Indonesia, approved the study.

Results

Out of 316 patients recorded from January 2014 to December 2016, 142 enrolled in the study.

Table 4. Subjects characteristics with colorectal cancer in RSCM 2014-2016

Clinical	n	%
Age		
<45 years	38	26.8
≥45 years	104	73.2
Gender		
Male	79	55.6
Female	63	44.4
Stage		
II	22	15.5
III	46	32.4
IV	74	52.1
Surgery		
Yes	94	66.2
No	48	33.8
Adjuvant Therapy		
Without adjuvant therapy	49	34.5
Chemotherapy	78	54.9
Radiotherapy	3	2.1
Chemotherapy and radiotherapy	12	8.5
Five years survival rate		
Survive	61	43.0
Non survive	81	57.0

Subjects predominated by males (55.6%) with the most age more than 45 years (73.2%), and of stage IV (52.1%). Out of these, 66.2% underwent definitive surgery followed by adjuvant therapy, namely chemotherapy (54.9%). Overall five-year survival in this study was 43%.

Table. 5 Log-rank tests and prognostic factors influencing the five-year survival

Variable	Non survive (n = 81)	Survive (n = 61)	P
Age			
<45 years	20(24.6%)	18(29.5%)	0.463
≥45 years	61(75.4%)	43(70.5%)	
Stage			
Stage II	6(7.4%)	16(26.2%)	0.001
Stage III	23(28.4%)	23(37.7%)	
Stage IV	52(64.2%)	22(36.1%)	
Definitive Surgery			
Yes	38(47.0%)	56(91.3%)	0.000
No	43(53.0%)	5(8.2%)	
Adjuvant therapy			
Without adjuvant	31(38.3%)	18(29.5%)	0.703
Chemotherapy	41(50.6%)	37(60.7%)	
Chemotherapy and radiotherapy	7(8.6%)	5(8.2%)	
Radiotherapy	2(2.5%)	1(1.6%)	

In this study, the group of those of age ≥45 years, showing the most group with high mortality with a five-year survival of 41.3%. However, age was not significantly associated with survival (p = 0.521).

The Kaplan Meier showing up to 50% of those aged ≥45 years died with 20 months. In contrast, those aged <45 years remained during period observation of five years. The survival rate in those aged <45

years was 38.9 months (95% CI 32.08-45.75) with a median of 36 months.

Figure 1. Kaplan-Meier survival curve for the variable of age

Figure 2. Kaplan-Meier survival curve for variable of cancer stage

There was a significant association between stage and mortality ($p = 0.001$). The five-year survival rate ranges between 72.7% in stage II and 29.7% in stage IV.

Figure 3. Kaplan-Meier survival curve by stadium

Overall survival in this study was 36.17 months (95% CI 32.59-39.75), for stage II 50.68 months (95% CI 44.03-57.32), stage III 38.59 months (95% CI 32.20-44.97), and stage IV 30.36 months (95% CI 25.638-35.09).

Subjects receiving chemotherapy showed a survival rate of 47.4% among the other adjuvant therapy groups and those whose not receiving adjuvant therapy. Compared with the group not receiving adjuvant therapy (36.7%), those receiving radiotherapy showed a survival rate of 33.3%.

However, no significant difference between the group of adjuvant therapy (both those receiving and not receiving adjuvant therapy) with survival ($p = 0.674$).

Figure 4. Kaplan Meier survival curve based on adjuvant therapy

This study's overall survival rate was 36.17 months (95% CI 35.596-39.756) with a median of 25 months. The survival rate of subjects receiving chemotherapy was 38.28 months (95% CI 33.44-43.11). The group's survival rate not receiving adjuvant therapy was 33.71 months (95% CI 27.79-39.63). There was no significant association between adjuvant therapy and survival ($p = 0.703$). Subjects receiving definitive surgery showed the five-year survival rate of 59.6%.

Further, a significant differences showed between subjects receiving definitive surgery compared to those not ($p = 0.000$) in the outcome.

Figure 5. Kaplan Meier survival curves based on definitive surgery

The survival rate of subjects receiving definitive surgery was 44.39 months (95% CI 40.35-48.43), while subjects receiving no definitive surgery was 20.08 months (95% CI 15.82-24.36).

On bivariate analysis, we found a significant association between stage II ($p = 0.002$), stage IV ($p = 0.001$) and definitive treatment ($p < 0.001$)

with s mortality. In contrast, stage III no significant association ($p = 0.241$). Stage II showed a 23% likelihood of death than stage III and IV ($p = 0.002$; CI 0.082-0.617). Subjects with stage IV showed a likelihood of 3.2 times to death rather than other stages. Compared with subjects not receiving definitive surgery, those receiving showed a reduced likelihood of death by 79%.

Table 6. The survival rate

Variable	Non survive (n = 81)	Survive (n = 61)	HR	CI 95%	p
Age					
<45 years	20	18	1.27	(0.61-2.69)	0.521
≥45 years	61	43			
Stage					
Stage II	6	16	0.23	(0.08-0.62)	0.002
Stage III	23	23	0.66	(0.32-1.33)	0.241
Stage IV	52	22	3.18	(1.60-6.35)	0.001
Definitive surgery					
Yes	38	56	0.79	(0.029-0.22)	0.000
No	43	5			
Adjuvant Therapy					
Without adjuvant	31	18	1.48	(0.728-3.011)	0.277
Chemotherapy	41	37	0.67	(0.339-1.303)	0.234
Chemotherapy and radiotherapy	7	5	1.52	(0.135- 17.147)	1.000
radiotherapy	2	1	1.06	(0.319-3.514)	0.925

HR: Hazard Ratio; CI: Confidence Interval

A multivariate analysis with logistic regression was carried out to find the probability of survival in subjects exposed to all risk factors, including those with p values <0.25 in bivariate analysis.

Table 7 Multivariate analysis of the five-year survival of the CRC.

Variable	HR	CI 95%	p
Stage II	5.19	(1.524-17.692)	0.008
Stage III	3.72	(1.446-9.574)	0.006
Definitive surgery	11.70	(3.961-34.519)	0.000

It was found that only stage II, III, and those receiving definitive therapy showed a significant association with the five-year survival. Furthermore, we found stage II showing a 5.2-fold to live ($p = 0.008$; CI 1.524-17.692) compared to other stages, Subjects receiving definitive surgery showing 11.7 times to live ($p < 0.001$; CI 3.961-34.519) compared to other variables.

Discussion

Of the 142 colorectal cancer patients included in this study, 43% of patients survived until the observation period (5 years). Four main factors were analyzed to find its effect on colorectal cancer survival, namely age, clinical stage, definitive therapy, and adjuvant therapy. Based on the analysis, subjects aged <45 years showed better five-year survival (47.4% vs. 41.3%). However, we found no significant difference between age and survival. Our findings differ from the study by Chao-Hsien et al., which shows age is a predictor of survival and prognosis in colorectal cancer.⁷

The subjects were mostly of stage IV (52.8%), whereas Chao-Hsien et al., showing the majority were stage II and III. In this study, we noted there were nine (6.3%) subjects aged under 30 years. It should be noted that colorectal cancer is now found in the younger population and those who may have symptoms but not included in the qualification screening based on the American Cancer Society (ACS) to worsen the prognosis. For this reason, targeting the screening to a younger population may improve outcomes.⁷

In the present study, the higher stage, the higher the mortality found. The five-year survival in stage II up to 72.7%; and dramatically fall to 29.7% in stage IV. This study's finding consistent with the study by Joachim et al., the more advanced when diagnosed, the higher mortality shown.⁸ Early-stage showed a better prognosis; in those with advanced stages, cancer develops very progressively and aggressively, reducing survival.⁹ Similar findings were reported by Ghazali et al. that showing liver metastasis was a significant prognostic factor for survival ($p < 0.001$). Subjects with stage IV showing a risk of 6.7-times to death compared with stage II, and those with liver metastasis showing a risk of 3.8-times to death than those without liver metastasis.¹⁰

The overall five-year survival rate in the present study was 43%, and almost similar to other Southeast Asian countries, such as Malaysia (45.4%), Thailand (42.45%), and the Philippines (44%).¹¹ However, Australia, Taiwan, and The United States of America showed a better survival rate of 63%, 68.66%, and 64.9%, respectively.^{12,13} Most of the population in Southeast Asian countries came in an advanced stage, as reported by Phimha et al. in Thailand where 71.81% of patients admitted were found in an advanced stage with insufficient screening programs and awareness for early detection. The screening program in the United States screening program commenced in 1960, and in Taiwan, the program launched in 2004, reducing mortality in the first decade after the program launched.¹⁴

Cox regression analysis showed that definitive surgery, which is tumor resection significantly associated with better survival. Those receiving resection showed a five-year survival of 59.6%, and those not were 10.4%. However, the overall survival rate in those receiving resection was 44.39 months. This finding is similar to the study by Duraker et al. showing a better survival rate in those receiving tumor resection.¹⁵ When we focused on the tumor staging, the analysis showed the risk of mortality for stage IV 3.2 times to stage II and III. Those with stage II and III showed a risk of 5.2 and 3.7 times, respectively, compared to those with stage IV. Circulating tumor cells that are difficult to treat may be responsible as the causal, even though radical dissection has been carried out to control the tumor invasion locally. Thus, distant metastasis (namely, stage IV) was the most risk of death.¹⁶

Comparing the prognosis of those receiving resection and not receiving may lead to a bias in patient selection. Non-resection applied to those with poor conditions in a more advanced case.¹⁷⁻¹⁹ A meta-analysis shows that palliative tumor resection in asymptomatic and/or mild symptomatic colorectal cancer patients with stage IV showed a better survival as it reduces the risk of intestinal complications.²⁰ Survival has not been associated with adjuvant therapy. The analysis showed that those receiving adjuvant therapy were found to have better survival (382 months; 95% CI 33.48-43.11). Papamichael et al. showed that 5-Fluorouracil (5-FU)/Leucovorin (LV) intravenous leading to 29% five-year mortality risk.³⁸ Different regimens may responsible for the different findings. Different characteristics, particularly those predominated with stage IV (52.1%) in RSCM, may have a poor prognosis.²¹

The consensus recommends surgical resection on those with locally advanced completed with adequate lymphadenectomy followed by adjuvant chemotherapy in those at risk of recurrence. The treatment including local resection through transanal approach, plus total mesorectal excision completed with neoadjuvant chemoradiotherapy in locally advanced when diagnosed.²¹

Conclusion

The overall five-year survival of colorectal cancer was 43%. Influencing factors are clinical stage and definitive surgery, namely tumor resection

Disclosure

The authors disclose no conflict of interest

References

1. Araghi M, Soerjomataram I, Jenkins M, Brierly J, Morris E, et al. Global trends in colorectal cancer mortality: projections to the year 2035. *Int J Cancer*. 2019;144(12):2992-3000
2. World Health Organization. World Source: GLOBALCAN 2019, The Global Cancer Observatory: International Agency for Research on Cancer, WHO. 2019
3. Dekker E, Tanis JP, Vleugels JLA, Kasi PM, Wallace MB. Colorectal cancer. *Lancet*. 2019;339:1467-80
4. Puppa G, Sonzogni A, Colombari R, Pelosi G. TNM staging system of colorectal carcinoma. *Arch Patol Lab Med*. 2010;134:837-852
5. Akkoca AN, Yanik S, Ozdemir ZT, Cihan FG, Sayar S, et al. TNM and modified Dukes staging along with the demographic characteristics of patients with colorectal carcinoma. *Int J Clin Exp Med*. 2014;7(9):2828-35
6. Bujanda L, Sarasqueta C, Hijona E, Hijona L, Cosme A, et al. Colorectal prognosis twenty years later. *World J Gastroenterol*. 2010;16(7):862-7
7. Chao-Hsien, Shu-Chen, Hong-Yi, Shih-Chang, Ching-Yun, Wu Shu-Fen. The risk factors affecting survival in colorectal cancer in Taiwan. *Iran J Public health*. 2018;47(4):519-530
8. Joachim C, Macni J, Drame M, Pomier A, Escarmant P, Veronique-Baudin J, Vinh-Hung V. Overall survival of colorectal cancer by stage at diagnosis-Data from Martinique Cancer Registry. *Medicine*. 2019;98(35):1-9
9. Xu B, Yu L, Zhao L. Prognostic factors in the patients with T2N0M0 colorectal cancer. *World J Surg Onc*. 2016;14(76):1-6
10. Ghazali AK, Musa KI, Naing NN, Mahmood Z. Prognostic Factors in Patients with Colorectal Cancer at Hospital Universiti Sains Malaysia. *Asian J Surg* 2010;33(3):127-33.
11. Magaji AB, Moy MF, Roslani AC, Law CW. Survival rates and predictors of survival among colorectal cancer patients in a Malaysian tertiary hospital. *BMC Cancer* 2017;17:339
12. Roder D, et al. Colorectal Cancer Treatment and Survival: the Experience of Major Public Hospitals in South Australia over three decades. *Asian Pac J Cancer Prev* 2015;16(6):2431-40.
13. Lee CH, et al. Comparison of risk factors between colon cancer and rectum cancer in a single medical center hospital, Taiwan. *Arch Med Sci* 2020;16(1):102-111.
14. Phimha S, et al. Health insurance and colorectal cancer survival in Khon Kaen, Thailand. *Asian Pac J Cancer Prev* 2019;20(6):1797-1802.
15. Stelzner S, Hellmich G, Koch R, Ludwig K. Factors predicting survival in stage IV colorectal carcinoma patients after palliative treatment: a multivariate analysis. *J Surg Oncol*. 2005;89:211-217
16. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J. Global cancer statistics, 2012. *CA Cancer J Clin*. 2015;65(2):87-108
17. Kleespies A, Fuessl KE, Seeliger H. Determinants of morbidity and survival after elective non-curative resection of stage IV colon and rectal cancer. *Int J Colorectal Dis*. 2009;24:1097-1109
18. Costi R, Mazzeo A, Mauro D. Palliative resection of colorectal cancer: does it prolong survival? *Ann Surg Oncol*. 2007;14:2567-2576
19. Var der Pool, Damhuis RS, Ijzermans JNM. Trends in incidence treatment and survival of patients with stage IV colorectal cancer: a population-based series. *Colorectal Dis*. 2011;14:56-61
20. Stillwell AP, Buettner YH. Meta-analysis of survival of patients with stage IV colorectal cancer managed with surgical resection versus chemo-therapy alone. *World J Surg*. 2010;34:797-807
21. Papamichael D, Hernandez P, Mistry R, Xonophontos E, Kakani C. Adjuvant chemotherapy in patients with colorectal cancer-Is there a role in the older adult? *Eur J Surg Oncol* 2020;1-5