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Prognostic scoring system to predict mortality after surgery in resectable colorectal cancer

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ABSTRACT

Background: Colorectal cancer remains as the major problem worldwide. Numerous studies have investigated factors associated with mortality and recurrence rates in colorectal cancer. To facilitate the everyday use of mortality predictors, they should be incorporated into a prognostic scoring system. This study aimed to identify factors affecting mortality in resectable colorectal cancer patients after surgery and to develop a prognostic scoring system capable of predicting mortality in these patients.

Methods: This retrospective cohort study involved colorectal cancer patients at Cipto Mangunkusumo Hospital, Indonesia, from January 2016 – April 2020 diagnosed with resectable colorectal cancer. Data were collected from medical records, operation reports, histopathology reports, and laboratory test results. Mortality was assessed three years after curative surgery.

Result: A total of 214 resectable colorectal cancer patients were included in the study. Tumor size ≥ 5 cm, T3/T4 staging, absence of adjuvant chemotherapy, unachieved free circumferential margin, and CEA levels > 11.4 ng/mL were significantly associated with increased three-year mortality. The constructed three-year mortality prognostic scoring system was able to predict outcomes with a sensitivity of 91.3% and a specificity of 67.6%.

Conclusion: The prognostic scoring system, consisting of five variables, is significantly capable of predicting three-year mortality rates with high sensitivity

Keywords: colorectal cancer, mortality, scoring system, prognosis
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INTRODUCTION

Colorectal cancer is a significant issue as the second leading cause of death among all malignancies on a global scale. Data from the Global Cancer Observatory (GLOBOCAN) in 2018 shows that the prevalence of colorectal cancer worldwide accounts for 11% of total cancer cases and ranks as the fourth most common cancer type. The same year reported 1,096,000 new cases of colon cancer with 551,269 deaths and 704,376 new cases of rectal cancer with 310,394 deaths[1] Data from the Surveillance, Epidemiology, and End Results Program (SEER) indicate that the survival rate for colon cancer is 91% for localized tumors, 72% for regional tumors, and drops to only 14% for tumors with distant metastasis. The overall survival rate for this cancer is 67%.[2] Gan et al. (2007) demonstrated that 30-50% of colorectal cancer patients experience recurrence and die after relapse.[3]

Numerous studies have investigated factors associated with mortality and recurrence rates in colorectal cancer. Retrospective cohort studies reveal that advanced age above 70 years, primary tumor location in the rectum, and T3-4 and N1-2 tumor staging increase the 5-year recurrence and mortality rates for colorectal cancer.[4] Regarding mortality, a study by Miyoshi found that carcinoembryonic antigen (CEA) levels above 40 ng/mL, primary tumor location in the rectum, T4a-b tumor staging, and N2 tumors increase the likelihood of mortality.[5] Valentini et al also demonstrated that the need for adjuvant chemotherapy regimens, radiotherapy, lymphocyte profiles, neutrophil levels, and albumin levels could serve as mortality predictors.[6] To facilitate the everyday use of mortality predictors, they should be incorporated into a prognostic scoring system. In several countries, colorectal cancer mortality predictors have been utilized to create a prognostic score, particularly for resectable cases.[5,7] Similar research has not yet been conducted in the Indonesian population. Therefore, this study aimed to identify factors influencing postoperative mortality in patients with resectable colorectal cancer within the Indonesian population represented as patients from Cipto Mangunkusumo National Hospital (RSCM) and develop a prognostic scoring system capable of predicting patient mortality.

MATERIAL AND METHODS

Patient Selection

This study employed a retrospective cohort design and was conducted at Cipto Mangunkusumo Hospital (RSCM) from November 2022 to May 2023.

The research population consisted of postoperative resectable colorectal cancer patients treated at RSCM with medical records from January 2016 to April 2020. Inclusion criteria for this study were patients aged 18 years and older, colorectal cancer patients managed curatively with primary resection, colorectal cancer stages I-III, stage IV colorectal cancer patients with resectable primary tumor and metastasis, and patients recorded in RSCM medical records. This study excluded patients with stage IV colorectal cancer with unresectable metastasis, residual colorectal cancer, and incomplete patient medical record data.

Research Ethics

This study was conducted after obtaining an ethical clearance certificate from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia / Cipto Mangunkusumo National General Hospital (RSCM) with certificate number KET-165/UN2.F1/ETIK/PPM.00.02/2023.

Data Collection

Data collection was performed by searching RSCM medical records from January 2016 to April 2020. Colorectal cancer patient medical records at RSCM were selected and screened based on the research inclusion-exclusion criteria. Basic clinical characteristics, independent variables, and dependent variables were collected from medical record data. If data were incomplete, particularly concerning colorectal cancer diagnosis, the patient would be excluded from the study. Patient follow-up was conducted retrospectively to observe 3-years mortality incidence, with the latest follow-up in April 2023.

The dependent variable examined was three-year mortality, defined as mortality events within three years after primary resection at RSCM. Independent variables in this study included age, sex, body mass index (BMI), tumor differentiation, primary tumor location, tumor size, TNM staging, nerve fiber invasion, free circumferential margin, CEA levels, albumin, neutrophils, lymphocytes, lymphocyte-albumin-neutrophil ratio (LANR), and adjuvant chemotherapy administration.

Tumor differentiation was determined based on findings in the histopathology report evaluated by RSCM anatomical pathology specialists and divided into three categories: well-differentiated, moderately differentiated, and poorly differentiated. Tumor location was determined based on findings during resection surgery and divided into three categories: rectum, left colon, and right colon. Tumor size was divided into two categories using a 5 cm cutoff value. T staging was divided into three categories: T1-T2, T3, and T4. N staging was divided into two categories: N0 and N1-N2. M staging was also divided into two categories: M0 and M1. Nerve fiber invasion was determined based on the evaluation of RSCM anatomical pathology specialists reported in the histopathology report. Free circumferential margin was determined during resection surgery and defined as the shortest distance between the radial resection margin and tumor tissue dissemination, nerve/blood vessel invasion, or the shortest distance to the involved lymphatic gland > 1 mm. Adjuvant chemotherapy administration was considered valid if the patient underwent a complete regimen of 6-8 cycles in the postoperative period at RSCM.

Statistical Analysis

All statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS) version 20 software. For proportion analysis, numeric data were tested using the Kolmogorov-Smirnov or Shapiro-Wilk distribution tests to determine if the data were normally distributed or not. Normally distributed numeric data were presented as mean values and standard deviations, while non-normally distributed numeric data were presented as median values and interquartile ranges. Categorical data were presented in the form of proportions.

The chi-square test was used to analyze differences in proportions between variables and mortality rates. For numeric variables, conversion to categorical variables was performed by determining cutoff values. Cutoff values for numeric variables, such as age, leukocytes, lymphocyte count, neutrophils, albumin, CEA, and LANR, were determined based on receiver operating characteristics (ROC) curve analysis. The prognostic prediction ability of each variable was assessed by examining the area under the curve (AUC), specificity, and sensitivity. After converting all variables to categorical variables, risk score compilation, discrimination testing, and calibration were performed. Prognostic score compilation was done by determining each variable's prognostic score.

Variables included in the scoring system were determined using logistic regression analysis with the stepwise forward method to calculate the adjusted odds ratio (OR) using a multivariate test. Variables included in the multivariate logistic regression analysis were those with a p-value <0.25 in the bivariate proportion test. After performing multivariate logistic regression analysis, unstandardized coefficients (B) for each variable were obtained, indicating the relative strength of each variable in the created regression model.

Conversion from the regression model to the scoring system was done by dividing a variable's B coefficient by the smallest B coefficient of the variable with a significant effect on the outcome, then rounding the decimal result upwards. Variables included in the model but without a significant effect on the outcome were not included in the scoring system. The discrimination ability of the scoring system in predicting three-year mortality was assessed using ROC curve analysis to obtain AUC, cutoff score values for dividing the prognostic score into two categories, and sensitivity-specificity of the scoring system when using the specified cutoff values. Calibration of the scoring system was performed using the Hosmer-Lemeshow test, with a p-value above 0.05 indicating that the compiled scoring system did not overestimate or underestimate the desired outcome (three-year mortality).

RESULTS

Sample Characteristics

In this study, a total of 222 resectable colorectal cancer patients were identified based on the medical records of patients treated at Cipto Mangunkusumo Hospital from January 2016 to April 2020. A total of 8 patients were excluded from the sample due to incomplete data, leaving 214 patients

Table 1. Sample characteristics

Variables	All subjects (n = 214)
Age, Median	59.0 (21.0)
Gender, n (%)	
Female	93 (43.5)
Male	121 (56.5)
Diagnosis, n (%)	
Adenocarcinoma	208 (97.20)
Spindle cell cancer	1 (0.5)
Signet ring cell carcinoma	3 (1.8)
Lymphoma non-Hodgkin	1 (0.5)
GIST	1 (0.5)
Body Mass Index, median (IQR)	21.63 (6.0)
Body Mass Index, n (%)	
Normal	113 (52.8)
Underweight	54 (25.2)
Obesity	47 (22.0)
Tumor Differentiation, n (%)	
Well-differentiated	154 (72.0)
Moderately differentiated	38 (17.8)
Poorly differentiated	22 (10.3)
Tumor Location, n (%)	
Right Colon	50 (23.4)
Left Colon	45 (21.0)
Rectum	119 (55.6)
Tumor Size. n (%)	
<5 cm	184 (86.0)
≥5 cm	30 (14.0)
Staging T, n (%)	
T1/T2	27 (12.6)
T3	117 (54.7)
T4	70 (32.7)
Staging N, n (%)	
N0	96 (44.9)
N1/N2	118 (55.1)
Staging M, n (%)	
M0	174 (81.3)
M1	40 (18.7)
Adjuvant Chemotherapy, n (%)	156 (72.9)
Nerve Fiber Invasion, n (%)	44 (20.6)
Free circumferential margin, n (%)	169 (79.0)
Lymphocyte, median (IQR)	1.31 (0.85)
Neutrophil, median (IQR)	7.99 (5.71)
Leukocyte, median (IQR)	10.66 (5.64)
Albumin, median (IQR)	31.55 (9.65)
LANR, median (IQR)	4.52 (5.07)
CEA, median (IQR)	5.5 (44.19)
3-years mortality rate, n (%)	111 (51.9)

CEA: carcinoembryonic antigen; IQR: interquartile range; LANR: Lymphocytes, Albumin, and Neutrophils Ratio

for analysis. The sample characteristics are presented in Table 1. The 3-year mortality rate of this study sample was 51.9%. Almost all patients (97.2%) were diagnosed with adenocarcinoma.

Determination of cutoff points for numeric variables

The calculation of cutoff values for numeric variables was performed for the compilation of the three-year mortality scoring system (Table 2). The cutoff values for each variable in the scoring system were obtained, with AUC values ranging between 0.50 and 0.64.

Bivariate Proportion Difference Analysis

The bivariate proportion difference analysis for the three-year mortality scoring system compilation (Table 3) found that moderate/poor tumor differentiation, tumor location, tumor size, T3/T4 staging, N1/N2 staging, M1 staging, not receiving adjuvant chemotherapy, not achieving free circumferential margin, decrease in albumin level below the cutoff value, LANR below the cutoff value, and CEA above the cutoff value increased the incidence of three-year mortality.

Multivariate Analysis

Multivariate analysis was performed using the forward stepwise regression method based on the likelihood ratio (LR), including all variables with a p-value <0.25 in the bivariate proportion test. The results of the multivariate logistic regression analysis using the forward stepwise method based on LR for the three-year mortality outcome are presented in Table 4. Based on the multivariate analysis, tumor differentiation, tumor location, N staging, M staging, leukocytes, albumin, and LANR were excluded. The model was well-calibrated, with a Hosmer-Lemeshow test p-value of 0.604.

Prognostic Score Construction

Weighting variables into scores in this scoring system was done by dividing the unstandardized coefficient (B) value of a variable by the smallest B value. Weighting scores for the three-year mortality outcome are shown in Table 5.

The probability of three-year mortality occurrence for each additional score value

Table 2. Cutoff Points for Numeric Variables for 3-years mortality

Variable	3-years mortality			
	AUC	Cutoff	Se (%)	Sp (%)
Age (years)	0.533	≥ 56.5	59.5	47.6
Lymphocyte (x10^9 cells/L)	0.500	≥ 1.265	55.0	52.4
Neutrophil (x10^9 cells/L)	0.537	≥ 7.175	59.5	45.6
Leukocyte (x10^9 cells/L)	0.537	≥ 12.145	43.2	67.0
Albumin (g/L)	0.579	≤ 34.05	73.0	39.8
LANR	0.541	≤ 5.12	65.8	48.5
CEA (ng/mL)	0.635	≥ 11.4	52.3	69.9

AUC: area under curve; CEA: carcinoembryonic antigen; LANR: Lymphocytes, Albumin, and Neutrophils Ratio; Se: sensitivity; Sp: specificity

when using the scoring system is presented in Table 6. Based on the probability of three-year mortality, the scoring system can be divided into two risk categories: low risk for scores <4 and high risk for scores >4. The multivariate model analysis showed an increase in high mortality risk (more than 50-55%) between patients with a total score of 4 and a total score of 5, so the cutoff value used was 4. In addition, at a cutoff value of 4, the highest LR + / LR - ratio was obtained, which is considered to have the best consistency and validity. Based on the cutoff value, patients can be categorized into two risk degrees: low and high risk.

Discrimination Test for Prognostic Score

The diagnostic ability of the scoring system to predict three-year mortality was tested using ROC analysis (Table 7).

Using data from this study, dividing patients into low and high-risk categories with a cutoff score of 4 for predicting three-year mortality resulted in proportions of patients in the study sample as shown in Table 8. Based on the 2x2 table, the predictive ability of the scoring system has a sensitivity of 91.3%, specificity of 67.6%, negative predictive value (NPV) of 89.3%, and positive predictive value (PPV) of 72.3%. The recommended prognosis scoring system were given in Table 9.

DISCUSSION

In this study, a total of 111 patients (51.9%) experienced death within three years after undergoing curative surgery, with primary tumor resection and combined resection for liver metastasis tumors. The patients in this study were dominated by adenocarcinoma patients (97.20%) located in the rectum (55.6%) with T3 staging (54.7%), N1/N2 staging (55.1%), and M0 staging (81.3%) which are stage II to stage III colorectal cancer patients based on the classification by The American Joint Committee on Cancer (AJCC).[8] The three-year mortality rate of 51.9% obtained in this study is not much different from the findings of epidemiological studies in the United States. Data from the Surveillance, Epidemiology, and End Results (SEER) show that the five-year survival rate in stage IIIB colorectal cancer patients is slightly higher than the findings in this study, at 72%, with similar findings for five-year survival rates in stage IIIC patients, at 58%.[9] The mortality rate found in this study is slightly higher than a similar study conducted in Indonesia. Labeda, et al. (2022) in their study using patient samples in Makassar, eastern Indonesia, showed a five-year mortality rate of 33.3%. This finding may be due to different sample conditions. A study by Labeda et al study has a fairly even distribution of colorectal cancer staging with stages II, III, and IV covering one-third of the total sample.[10]

This study was conducted at RS Cipto Mangunkusumo, which is a national referral hospital, so the samples obtained in this study can represent the Indonesian population. The ROC curve analysis also shows that this scoring system has a relatively very good predictive ability with an area under the curve (AUC) value of 0.880.[11] The reverse analysis, categorizing the research sample into low and high risk, shows that this scoring system has a high sensitivity of 91.3%, making it suitable for use as a screening tool because it has a low false-negative value.[12]

The mortality prognosis scoring system generated in this study consists of several components, such as tumor size >5 cm, T3/T4 staging, not receiving adjuvant chemotherapy, tumor resection not achieving free circumferential margin, and CEA levels >11.4 ng/mL. Tumor size is one variable that has been frequently associated with increased mortality in colorectal cancer patients. Similar findings were also described by Alese et al using data from The National Cancer Database (NCDB) involving a total of 61,000 patients. In this study, it was reported that compared to patients with tumor size <2cm, patients with tumors 2-5 cm (hazard ratio (HR) 1.33; 95% CI 1.19-1.49; p<0.001), 5-10 cm (HR 1.51 (1.34-1.70; p<0.001), and above 10 cm (HR 1.95 (1.65-2.31; p<0.001) had worse survival rates.[13] This study found that T3 and T4 staging were associated with increased three-year mortality, with higher scores given to T4 patients compared to T3. Similar findings were also reported by Valentini et al, showing a significant decrease in the 5-year overall survival rates in patients with T3 and T4 tumors compared to those with T2 tumors.[6] In addition, Lim et al in their retrospective cohort study reported worse cancer-specific survival (CSS) rates for patients with T4a (HR 2.27; p<0.001) and T4b (HR 3.53, p<0.001) compared to T3 patients.[14] Free circumferential margin in this study was defined as the circumferential resection margin (CRM) exceeding the outer limit, which is >1 mm from the tumor tissue based on the outer limit of tumor infiltration, the area with nerve/blood vessel invasion, or the presence of involved lymph nodes. These findings are in line with previous studies. A study by Birbeck et al of proportion analysis showed a significant increase in the proportion of patients with poor prognosis in the group with tumor tissue at the resection margin with CRM 0-1.0 mm (54.5% vs. 27.8%; p<0.001). The poor prognosis rate also significantly decreased if the CRM value was >1.0 mm (10%).[15] A retrospective study by Liu et al showed that a CRM value of <1.0 mm was the margin threshold that determined the prognosis of colorectal cancer patients. In Liu et al.'s study, patients with CRM values between 2.0 and 10.0 mm did not have significantly

Table 3. Proportion analysis of variables with 3-years mortality.

Variables	3-years mortality		*p*-value
	No (n = 103)	Yes (n = 111)	
Age (years), n (%)			0.30
< 56.5	49 (52.1)	45 (47.8)	
≥ 56.5	54 (45.0)	66 (55.0)	
Gender, n (%)			0.733
Female	46 (49.5)	47 (50.5)	
Male	57 (47.1)	64 (52.9)	
Body Mass Index, n (%)			0.768
Normal	54 (47.8)	59 (52.2)	
Underweight	28 (51.8)	26 (49.2)	
Obesity	21 (44.7)	26 (55.3)	
Tumor Differentiation, n (%)			0.020*
Well-differentiated	83 (53.8)	71 (46.2)	
Moderately differentiated	14 (36.8)	24 (63.2)	
Poorly differentiated	6 (27.2)	16 (72.8)	
Tumor Location, n (%)			0.004*
Right Colon	29 (58.0)	21 (42.0)	
Left Colon	12 (26.7)	33 (73.3)	
Rectum	62 (52.1)	57 (47.9)	
Tumor Size. n (%)			0.032*
<5 cm	94 (51.1)	90 (48.9)	
≥5 cm	9 (30.0)	21 (70.0)	
Staging T, n (%)			0.000*
T1/T2	23 (85.1)	4 (14.9)	
T3	67 (57.3)	50 (42.7)	
T4	13 (18.6)	57 (81.4)	
Staging N, n (%)			0.000*
N0	61 (63.5)	35 (36.5)	
N1/N2	42 (35.6)	76 (64.4)	
Staging M, n (%)			0.000*
M0	97 (55.7)	77 (44.3)	
M1	6 (15.0)	34 (85.0)	
Adjuvant Chemotherapy, n (%)	98 (62.8)	58 (37.2)	0.000*
Nerve Fiber Invasion, n (%)	17 (38.6)	27 (61.4)	0.157
Free circumferential margin, n (%)	101 (59.7)	68 (40.3)	0.000*
Lymphocyte, n (%)			0.426
< 1.265	52 (50.9)	50 (49.5)	
≥ 1.265	51 (45.5)	61 (54.5)	
Neutrophil, n (%)			0.452
< 7.175	47 (51.1)	45 (48.9)	
≥ 7.175	56 (45.9)	66 (54.1)	
Leukocyte, n (%)			0.124
< 12.145	69 (52.3)	63 (47.7)	
≥ 12.145	34 (41.5)	48 (58.5)	
Albumin, n (%)			0.047*
> 34.05	41 (57.7)	30 (42.3)	
≤ 34.05	62 (43.4)	81 (56.6)	
LANR, n (%)			0.034*
> 5.12	50 (56.8)	38 (43.2)	
≤ 5.12	53 (42.1)	73 (57.9)	
CEA, n (%)			0.001*
< 11.4	72 (57.6)	53 (42.4)	
≥ 11.4	31 (34.8)	58 (65.2)	

LANR: *Lymphocytes, Albumin, and Neutrophils Ratio*

different survival rates compared to those with CRM 1.1-2.0 mm, so the 1.0 mm threshold was used to determine patient prognosis.[16] CEA levels have been found to affect patient prognosis, but the cutoff values used vary greatly. In this study, ROC curve analysis showed that the best CEA cutoff value for predicting three-year mortality was 11.4 ng/mL. Lakemeyer et al. (2021) divided patients into three categories using CEA cutoff values of 5 ng/mL and ≥200 ng/mL. In this study, Kaplan-Meier curve analysis showed a significant worsening of survival in patients with CEA levels of 5-200 ng/mL and ≥200 ng/mL.[17] Miyoshi et al in a retrospective cohort study involving stage IV cancer patients used a CEA cutoff value of 40 ng/mL and successfully demonstrated a significant relationship between CEA levels above the cutoff value and mortality in colorectal cancer patients.[5]

The multivariate model used as the basis for creating the scoring system in this study involved all variables with a p-value <0.25 in the bivariate proportion test using the chi-square test. In the multivariate model development process using the stepwise forward LR method, some variables were found to be insignificant and were not included in the model, such as leukocyte levels, albumin, and LANR values calculated by multiplying lymphocyte levels by the ratio of albumin to neutrophils. Although significant in the proportion test, these three variables were relatively less significant compared to other variables, such as free circumferential margin and not receiving adjuvant chemotherapy. The ROC curve analysis performed to determine the cutoff values for these three variables also showed a poorer ability to predict three-year mortality with an AUC value <0.60. Leukocyte and LANR values represent the patient's inflammatory status. Previous studies have shown a relationship between inflammation and malignancy. Leukocyte infiltration is known to negatively correlate with T lymphocyte infiltration and is associated with a worse prognosis in colorectal cancer.[18] Liang et al in their retrospective cohort study showed that high LANR, leukocyte, and lymphocyte levels, as well as low albumin, were associated with worsening patient survival

Table 4. Multivariate analysis for 3-years mortality

Variable	3-years mortality			
	B	SE	Nilai p	OR (95%CI)
Tumor Differentiation, n (%)				
Well-differentiated	(-)			
Moderately differentiated	(-)			
Poorly differentiated	(-)			
Tumor Location, n (%)				
Right Colon	(-)			
Left Colon	(-)			
Rectum	(-)			
Tumor Size. n (%)				
<5 cm	Ref			
≥5 cm	1.536	0.578	0.008*	4.645 (1.49 – 14.43)
Staging T				
T1/T2	Ref			
T3	1.527	0.673	0.023*	4.603 (1.23 – 17.22)
T4	2.434	0.750	0.001*	11.404 (2.62 – 49.56)
Staging N				
N0	(-)			
N1/N2	(-)			
Staging M				
M0	(-)			
M1	(-)			
Adjuvant Chemotherapy, n (%)	2.833	0.555	0.000*	17.001 (5.73 – 50.41)
Nerve Fiber Invasion, n (%)	(-)			
Free circumferential margin, n (%)	2.655	0.814	0.001*	14.219 (2.88 – 70.11)
Leukocyte				
< 12.145	(-)			
≥ 12.145	(-)			
Albumin				
> 34.05	(-)			
≤ 34.05	(-)			
LANR				
> 5.12	(-)			
≤ 5.12	(-)			
CEA				
< 11.4	Ref			
≥ 11.4	0.894	0.386	0.021*	2.446 (1.15 – 5.21)

B: unstandardized coefficient; SE: standard error; OR: odds ratio; 95% CI: 95% confidence interval; (-): excluded during logistic model construction

Table 5. Scoring system for 3-years mortality

Variable	B	Smallest B value	Division result	Score
Tumor location ≥5cm	1.536	0.894	1.718	2
Staging T				
Staging T3	1.527	0.894	1.708	2
Staging T4	2.434	0.894	2.723	3
Not receiving adjuvant chemotherapy	2.833	0.894	3.169	4
Unachieved *Free circumferential margin*	2.655	0.894	2.970	3
CEA ≥11.4	0.894	0.894	1.000	1
TOTAL SCORE				13

B: unstandardized coefficient

based on multivariate Cox regression analysis.[19] The use of albumin also has been evaluated by another study.[20]

Previous studies have examined scoring systems to predict mortality in colorectal cancer patients with varying populations. Achilonu et al conducted a study to create a mortality prognosis scoring system for South African patients. In this study, the variables included in the scoring components based on the multivariate regression model were stage III cancer, chemotherapy history, adenocarcinoma histology, age at first hospital admission, and previous surgery history. The scoring system obtained from this study had an AUC value of 0.820.[21] A retrospective cohort study by Miyoshi et al also aimed to create a mortality prognosis scoring system for the Japanese population. Unlike this study, Miyoshi et al used survival analysis and Cox regression models in the development of their scoring system. The scoring system obtained by Miyoshi et al consisted of components such as T3/T4 staging, N2 staging, CEA levels ≥40 ng/mL, rectal tumor location, and the presence of metastases.[5] This study has fundamental differences from study by Miyoshi et al. This study used a categorical outcome with a clear time limit for mortality, which was three years after the intervention, and did not use survival analysis like Miyoshi et al. The use of survival analysis and Cox regression in a study by Miyoshi et al may provide a better representation of survival and a more accurate model compared to this study. However, the use of logistic regression models and clear mortality limits in this study aimed to create a prediction model that is easy to use in daily practice, especially as a reference for educating patients and their families. The accuracy of mortality prediction obtained in this study was also relatively excellent, with an AUC value of 0.880, although external validation using a different cohort is still needed to measure the reliability of this scoring system.[11,22,23]

Limitations of this study include the fact that medical records older than five years were not available, so the chosen mortality prediction was set at three years. The adjuvant chemotherapy regimen used primarily m-Folfox 6, but the doses were not well documented, making it impossible to analyze whether the regimen and doses also affected the three-year mortality rate. Future research should evaluate the long-term mortality and consider the effect of chemotherapy regimen and dosage.

Table 6. Probability of 3-years mortality for each score.

Score	Probability of 3-years mortality incidence (%)	Risk category
0	4.719	
1	10.804	
2	18.563	Low risk
3	35.796	
4	51.427	
5	76.422	
6	86.516	
7	90.457	
8	97.389	
9	98.916	High risk
10	99.273	
11	99.701	
12	99.843	
13	99.936	

Table 7. Discrimination test for prognostic score

Outcome	Cutoff	AUC	Se (%)	Sp (%)
3-years mortality	3.5	0.880	74.8	83.5

AUC: area under curve; Se: sensitivity; Sp: specificity

Table 8. Sensitivity and specificity test for prognostic score using the study sample.

	3-years mortality (-)	3-years mortality (+)	p-value
Risk category, n (%)			0.000
Low risk	94 (72.3)	36 (27.7)	
High risk	9 (10.7)	75 (89.3)	

Table 9. The recommendation prognosis scoring system to predict three-year mortality.

Variable	Yes/No	Score
Tumor location ≥5cm	Yes	2
Staging T		
Staging T3	Yes	2
Staging T4	Yes	3
Adjuvant Chemotherapy	No	4
Free circumferential margin	No	3
CEA ≥11,4	No	1
TOTAL SCORE		**13**

Total Score	3 year-mortality (%)
0-4	≤ 51.42 % (Low risk)
5-13	≥ 76.42 % (High risk)

CONCLUSION

This retrospective cohort study successfully identified the mortality rate

and influencing factors on three-year mortality in resectable colorectal cancer patients undergoing curative surgery at Cipto Mangunkusumo Hospital. The three-year mortality rate obtained was 51.9%. Meanwhile, the factors affecting and becoming the variables of the three-year mortality prognosis scoring system established in this study include tumor size > 5 cm, T3/T4 staging, not receiving adjuvant chemotherapy, failure to achieve a free circumferential margin, and CEA levels > 11.4 ng/mL. This prognosis scoring system has excellent predictive ability with a very high sensitivity of 91.3%, specificity of 67.6%, negative predictive value (NPV) of 89.3%, and positive predictive value (PPV) of 72.3%. The sample size is quite large, but it is recommended to conduct further studies using a prospective cohort design and a multicenter approach with a longer duration so that the population characteristics in Indonesia are more representative, confounding variables that will become research biases can be detected and minimized effectively, and the predicted mortality rate can be extended up to five years.

ETHICAL CONSIDERATION

This study was conducted after obtaining an ethical clearance certificate from the Health Research Ethics Committee of the Faculty of Medicine, Universitas Indonesia / Cipto Mangunkusumo National General Hospital (RSCM) with certificate number KET-165/UN2.F1/ETIK/PPM.00.02/2023.

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CONFLICT OF INTEREST

The author reports no conflicts of interest in this work.

AUTHOR'S CONTRIBUTION

AHPS responsible for study's conception and design, data analysis, statistical analysis, manuscript preparation, manuscript editing. ASP responsible for study's conception and design, manuscript review, final approval of the manuscript. LAN responsible for data acquisition, statistical analysis, manuscript editing.

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