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

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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 50,017 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 25.63–35.09), 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

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.3 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.

| Stage | Description |
|-------|-------------|
| T1    | No sign of a primary tumor |
| T2    | Tumor invasion of propria muscularis |
| T3    | Tumor invasion into subserosa |
| T4    | Tumor invasion through propria muscularis to the subserosa or to non-peritoneal tissue or perirectal tissue |
| N1    | Regional lymph node cannot be assessed |
| N2    | Regional lymph node cannot be assessed |
| N3    | There is no metastasis to regional lymph |
| M1    | Metastasis is far away |
| M0    | No distant metastasis |
| M1    | Distant metastasis |

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Subjects’ characteristics, including age, gender, body mass index (BMI), were taken from the cancer registration system in Indonesia, is 8.6% (GLOBOCAN, 2018). The incidence in dr. Cipto Mangunkusumo General Hospital (RSCM), as a referral center, is 0.66% in male and 0.44% in a female, with a five-year survival rate in those aged <45 years (73.2%), and of metastasis, 15.5%.

The Kaplan Meier showing up to 50% of those aged ≥45 years died 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 IIa and IIb 87%, 65%, stage IIIa, and IIIb 90% and 72%, and stage IIIc 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.

| Variable                  | Non survive (n = 81) | Survive (n = 61) | p     |
|---------------------------|----------------------|------------------|-------|
| Age                       |                      |                  |       |
| <45 years                 | 20(52.6%)            | 18(47.4%)        | 0.463 |
| ≥45 years                 | 61(58.7%)            | 43(41.3%)        |       |
| Stage                     |                      |                  |       |
| Stage II                  | 6(27.3%)             | 16(72.7%)        | 0.001 |
| Stage III                 | 23(28.4%)            | 23(50.0%)        |       |
| Stage IV                  | 52(64.2%)            | 22(29.7%)        |       |
| Definitive Surgery        |                      |                  |       |
| Yes                       | 38(40.4%)            | 56(59.6%)        | 0.000 |
| No                        | 43(89.6%)            | 5(10.4%)         |       |
| Adjuvant therapy          |                      |                  |       |
| Without adjuvant therapy  | 31(63.3%)            | 18(36.7%)        | 0.703 |
| Chemotherapy              | 41(52.6%)            | 37(47.4%)        |       |
| Chemotherapy and radiotherapy | 7(58.3%)          | 5(41.7%)         |       |
| Radiotherapy              | 2(66.7%)             | 1(33.3%)         |       |

In this study, the group of those aged ≥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 32.0-45.75) with a median of 36 months.

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).

The five-year survival rate ranges between 72.7% in stage II and 29.7% in stage IV.

This study's overall survival rate was 36.17 months (95% CI 35.5-39.75) with a median of 25 months. The survival rate of subjects receiving chemotherapy was 38.28 months (95% CI 33.4-43.11). The group's survival rate not receiving adjuvant therapy was 33.71 months (95% CI 27.8-39.63). 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%.

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

The survival rate of subjects receiving definitive surgery was 44.39 months (95% CI 40.3-48.4), while subjects receiving no definitive surgery was 20.08 months (95% CI 15.8-24.36).
with a 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     | CI95%   | p     |
|---------------------------|----------------------|------------------|--------|---------|-------|
| Age                       | 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   | (1.00-10.35) | 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   | (0.113-17.147) | 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 (95% CI)   | 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 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.

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