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RESEARCH ARTICLE

Preoperative anemia and malnutrition predict postoperative complications in stage III colorectal cancer: a cross-sectional study

Vito Mahendra Ekasaputra[1,2], Naufal Aditya Ramadhan[3*], Mohammad Dhanny Akbar[3], Abdullah Rizky[3], Chodidjah[2,4]

[1] Department of Surgery, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[2] Department of Doctoral Biomedical Science, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[3] Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[4] Department of Anatomy, Faculty of Medicine, Universitas Islam Sultan Agung, Semarang, Indonesia
[*] Correspondence: Naufal Aditya Ramadhan; Address: Kaligawe Raya Street No. Km. 4, Semarang City (50112), Indonesia
Email address: nauval.aditya16@gmail.com

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ABSTRACT

Colorectal cancer remains a major cause of morbidity and mortality. We conducted a cross-sectional observational study of 65 consecutive stage III colorectal cancer patients from medical records at Sultan Agung Islamic Hospital (data collected 3–27 Dec 2024) to examine associations between treatment, preoperative haemoglobin, BMI-defined nutritional status, CEA, Karnofsky Performance Status, and postoperative complications. Postoperative complications occurred in 11/14 (78.6%) patients with mild malnutrition, 2/6 (33.3%) with moderate malnutrition, and 8/8 (100.0%) with severe malnutrition; malnutrition was significantly associated with complications ($p = 0.016$). Among anaemic patients, 24/26 (92.3%) experienced complications, and Anemia was also significantly associated with complications ($p = 0.020$). CEA and Karnofsky Index were not significantly associated with postoperative complications. These findings indicate that preoperative Anemia and malnutrition are important predictors of postoperative morbidity in stage III colorectal cancer and support routine preoperative screening and timely correction of haemoglobin and nutritional deficits to improve surgical readiness and perioperative outcomes.

1. Introduction

Colorectal cancer is the third most common cancer worldwide and the second leading cause of cancer-related death. In 2020, more than 1.9 million new cases and about 930,000 deaths were estimated globally, accounting for roughly one in ten cancer diagnoses and cancer deaths (Morgan *et al.*, 2023). This burden is substantial in Indonesia, where Globocan data have shown colorectal cancer to be a major contributor to national cancer incidence and mortality (Labeda *et al.*, 2022).

The management of colorectal cancer includes surgery, chemotherapy, and radiotherapy, with surgical resection remaining the main curative treatment for patients with stage I–III disease (Kemkes-RI, 2018; Sanjaya *et al.*, 2023). Surgical resection remains the primary treatment for stage I-III colorectal cancer. Despite advances in perioperative care, postoperative complications remain common after colorectal cancer surgery and include anastomotic leakage, infection, bleeding, bowel obstruction, and other systemic complications. These adverse events are clinically important because they worsen short-term recovery

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and can compromise longer-term outcomes (Pak *et al.*, 2020; Vacante *et al.*, 2019).

Anemia and malnutrition are frequent comorbid conditions in patients with colorectal cancer. Anemia in this population commonly arises from chronic tumour-associated bleeding, iron deficiency, systemic inflammation, and inadequate nutritional intake, and can compromise tissue oxygenation and wound healing, thereby increasing postoperative morbidity (Făgărășan *et al.*, 2022; Ristescu *et al.*, 2019). Malnutrition adversely affects immune competence, tissue repair, and resilience to surgical stress, and has been linked to prolonged hospitalisation, higher rates of postoperative complications, and increased mortality after colorectal cancer surgery (Daniele *et al.*, 2017; Sandrucci *et al.*, 2018; Seretis *et al.*, 2018).

Early detection and correction of Anemia and malnutrition represent potentially modifiable perioperative risk-management strategies (Muñoz *et al.*, 2017; Song *et al.*, 2022). Although prior studies have reported associations between these conditions and poorer postoperative outcomes, many investigations have combined heterogeneous cancer stages or assessed Anemia and nutritional status separately, limiting inference about their concurrent impact (Liu *et al.*, 2018; Song *et al.*, 2022). Data specific to Indonesian patients with stage III colorectal cancer are scarce, yet this group is clinically important because standard care typically involves definitive surgery followed by systemic therapy, underscoring the need for optimised perioperative preparation (Lieu *et al.*, 2019; Scott *et al.*, 2024).

Accordingly, this study aimed to evaluate the associations of preoperative Anemia and malnutrition with postoperative complications among patients with stage III colorectal cancer treated at Sultan Agung Islamic Hospital, Semarang, Central Java, Indonesia. Generating local evidence may inform implementation of structured preoperative haemoglobin and nutritional assessment and optimisation in this population.

2. Materials and Methods

2.1. Study design and setting

This retrospective cross-sectional study reviewed medical records of patients with stage III colorectal cancer treated at Sultan Agung Islamic Hospital, Semarang, Indonesia. Records for patients treated between 2018 and 2024 were retrieved and reviewed from December 3 to December 27, 2024.

2.2. Participants and sampling

Eligible patients were adults aged 19–64 years with a histologically confirmed diagnosis of stage III colorectal cancer who underwent curative-intent surgery and had complete documentation of preoperative haemoglobin, anthropometric data, treatment history, and postoperative outcomes. Consecutive sampling was used to include all eligible cases during the study period. Exclusion criteria were history of another primary malignancy, evidence of distant metastases on computed tomography, incomplete surgical or oncologic treatment, or missing key study data.

2.3. Variables and operational definitions

The primary independent variables were preoperative Anemia and nutritional status. Anemia was defined as haemoglobin <13.0 g/dL in men and <12.0 g/dL in women. Nutritional status was assessed using body mass index (BMI) calculated as weight in kilograms divided by height in meters squared and categorised according to WHO/Asian BMI criteria (specify if specific categories used). The primary outcome was any postoperative complication documented in the medical record after the index surgery (including but not limited to anastomotic leakage, surgical-site infection, haemorrhage, bowel obstruction, and systemic complications). Additional variables extracted included treatment modality (surgical procedure type), receipt of neoadjuvant or adjuvant chemotherapy, radiotherapy, preoperative serum carcinoembryonic antigen (CEA) level, and Karnofsky Performance Status (KPS). Serum CEA was classified as normal (0–5 ng/mL) or elevated (>5 ng/mL).

2.4. Data collection

Data were abstracted from electronic and paper medical records using a standardised data extraction form. Extracted items included demographics, comorbidities, tumour location and stage (pathologic stage III), perioperative laboratory values (including haemoglobin and CEA), anthropometrics, details of surgical and oncologic treatment, KPS, and documented postoperative complications. Records with missing values for key variables were excluded from analysis.

2.5. Statistical analysis

Data were analysed using IBM SPSS Statistics version 26. Categorical variables are reported as frequencies and percentages. Continuous variables that were not normally distributed (CEA) are presented as medians and ranges; normality was assessed with the Shapiro–Wilk test. Between-group comparisons of CEA for two independent groups were performed with the Mann–Whitney U test. Associations between categorical variables (Anemia, nutritional status,

Table 1. Comparison of CEA levels by treatment

CEA Level (ng/mL)	Surgery+ Chemotherapy (n, %)	Surgery+ Chemotherapy + Radiotherapy (n, (%)
Normal (0-5)	12 (36.4)	9 (39.1)
Abnormal (>5)	21 (63.6)	14 (60.9)

Table 2. Comparison of CEA levels in patients with and without neoadjuvant chemotherapy

Chemotherapy administration *neoadjuvant*	n (%)	CEA level (ng/mL) Median (Min - Max)
Yes	27 (51,9)	2,6 (1-6,3)
No	25 (48,1)	7,5(1,2-48,5)

Table 3. Anemia and postoperative complications (n = 30)

Variable	n	%
Anemia		
• Yes	26	86,7
• No	4	13,3
Complications		
• Yes	26	86,7
• No	4	13,3
Total	30	100,0

Table 4. Adjuvant chemotherapy and Karnofsky index

Adjuvant Chemotherapy	Karnofsky Index		Total
	Poor	Good	
• Yes	12 (34.3%)	23 (65.7%)	35 (100.0%)
• No	11 (36.7%)	19 (63.3%)	30 (100.0%)
Total	23 (35.4%)	42 (64.6%)	65 (100.0%)

adjuvant chemotherapy, KPS, and postoperative complications) were evaluated using the chi-square test; Fisher's exact test was used when expected cell counts were insufficient. All statistical tests were two-tailed, and $p < 0.05$ was considered statistically significant.

3. Results

Table 1 summarises carcinoembryonic antigen (CEA) distributions by treatment group for 56 stage III rectal cancer patients. The proportion with elevated CEA (>5 ng/mL) was 63.6% in the surgery + chemotherapy group and 60.9% in the surgery + chemotherapy + radiotherapy group. Median CEA values were similar between groups, and the Mann–Whitney U test showed no significant difference ($p = 0.405$).

In the subset of 52 patients who received surgery and chemotherapy, median preoperative CEA was lower among those who received neoadjuvant chemotherapy (median 2.6 ng/mL, range 1.0–6.3) than among those who did not (median 7.5 ng/mL, range 1.2–48.5). This difference was statistically significant by the Mann–Whitney U test ($p < 0.001$) (Table 2).

Table 3 shows the distribution of Anemia and complications in patients at the Sultan Agung Islamic Hospital Semarang. Patients who experienced Anemia were 26 (86.7%) respondents, while 4 13.3% respondents did not experience Anemia. Based on postoperative complications of stage III colorectal cancer, 21 (75.0%) Anemia patients experienced complications, while 7 (25.0%) respondents did not experience postoperative complications of stage III colorectal cancer. The total respondents in this study were 30 respondents. The results of the Chi-square test obtained $p = 0.020$ ($p <0.05$), which shows that there is a significant relationship between Anemia and postoperative complications of stage III colorectal cancer.

Table 4 shows Karnofsky Performance Status (KPS) by receipt of adjuvant chemotherapy. Among patients who received adjuvant chemotherapy (n = 35), 23 (65.7%) had a good KPS and 12 (34.3%) had a poor KPS. Among patients who did not receive adjuvant chemotherapy (n = 30), 19 (63.3%) had a good KPS and 11 (36.7%) had a poor KPS. There was no significant association between adjuvant chemotherapy and KPS ($p = 0.841$).

3. Disscussion

Colorectal cancer treatment typically combines surgery, chemotherapy, and radiotherapy, with surgery remaining the central curative modality in resectable disease (Kim *et al.*, 2021; Hu *et al.*, 2018). The lower postoperative CEA levels observed in this study, particularly among patients who also received neoadjuvant chemotherapy, are consistent with evidence that changes in CEA after curative surgery are associated with prognosis and survival. In patients with abnormal preoperative CEA levels, a persistently high postoperative-to-preoperative CEA ratio has been associated with very poor prognosis, supporting the interpretation of postoperative CEA decline as a favourable treatment signal (Kim *et al.*, 2021). The greater reduction in CEA among patients receiving neoadjuvant chemotherapy may reflect earlier suppression of tumour activity before surgery. That interpretation aligns with evidence that serial

CEA measurements correlate with the effectiveness of chemotherapy and tend to fall in treatment responders. Neoadjuvant and combination systemic therapy have also been linked to improved survival in colorectal cancer.

Radiotherapy also has an established role in colorectal cancer management, particularly for symptom control and selected advanced settings. In the present study, patients treated with surgery, chemotherapy, and radiotherapy had a higher proportion of underweight status, suggesting a greater nutritional burden in those receiving more intensive multimodal therapy. That pattern is biologically plausible because gastrointestinal cancer treatment can aggravate nutritional decline, and postoperative severe malnutrition rises substantially after surgery. Patients undergoing surgery and chemotherapy commonly experience diarrhoea, nausea, anorexia, and weight loss, all of which can worsen nutritional status during treatment (Lee *et al.*, 2023; Yamano *et al.*, 2020). More intensive treatment may also reduce quality of life through cumulative adverse effects. Although the present study did not directly measure neuropathy, the higher pain burden in patients receiving adjuvant therapy is consistent with treatment-related toxicity and symptom accumulation over time (Munawaroh, 2018).

Adjuvant chemotherapy also affects the Karnofsky index, which reflects patients' level of independence and functional ability. The toxic effects of chemotherapy, such as fatigue, peripheral neuropathy, and myopathy, can reduce patients' ability to perform daily activities (Chowdhury *et al.*, 2020). In addition, chemotherapy-induced damage to normal cells can slow tissue healing and regeneration, leading to decreased physical tolerance and quality of life. Chronic inflammation caused by chemotherapy also contributes to muscle weakness and fatigue, which directly decreases the Karnofsky index score (Huot *et al.*, 2021). Therefore, a decrease in the Karnofsky index can be an important indicator for evaluating the impact of therapy and the need for rehabilitative interventions in patients.

At the same time, the absence of a significant association between adjuvant chemotherapy and Karnofsky score in this study should be interpreted cautiously rather than as evidence of no functional effect. Patients selected to receive adjuvant therapy often have better postoperative recovery and baseline performance, which can mask treatment-related decrements in cross-sectional analyses. The maintenance of a normal Karnofsky index in this cohort may therefore reflect selection effects, postoperative recovery, and supportive care rather than complete absence of chemotherapy-related burden.

Nutritional status strongly influences treatment tolerance and outcomes in colorectal cancer. In our study, underweight status was more common among patients receiving combined surgery, chemotherapy, and radiotherapy, a pattern that may increase the risk of post-treatment complications and reduce therapeutic effectiveness. Low body mass index (BMI) has been associated with higher mortality compared with normal nutritional status (Daniele *et al.*, 2017).

Targeted nutritional interventions, including high-protein, energy-dense diets and micronutrient supplementation, alongside regular screening (for example, with the Patient-Generated Subjective Global Assessment, PG-SGA) enable early detection and management of malnutrition and may improve tolerance to treatment-related toxicities such as nausea, vomiting, and fatigue (Burden *et al.*, 2017; Muscaritoli *et al.*, 2021; Ravasco *et al.*, 2012). Because radiotherapy and multimodal regimens commonly impair intake and absorption, proactive nutritional care should be integrated into perioperative and oncologic pathways.

Carcinoembryonic antigen (CEA) remains a useful biomarker for monitoring therapeutic response and disease status. In this cohort, neoadjuvant chemotherapy was associated with a significant decrease in CEA, which is consistent with improved tumour control and, in other studies, with longer survival (Kim *et al.*, 2021; Li *et al.*, 2021). Persistent elevation of CEA after treatment may indicate residual disease or metastasis requiring further evaluation. However, single CEA measurements are limited by variability in tumour burden, sampling timing, and tumour biology; serial measurements before and after treatment provide a more reliable assessment of response and recurrence risk (Kim *et al.*, 2021; Li *et al.*, 2021). Repeated declines in CEA over successive chemotherapy cycles have been correlated with therapeutic success in prior reports (Hu *et al.*, 2018; Shen *et al.*, 2022), and routine CEA monitoring can facilitate earlier detection of recurrence.

Advanced colorectal cancer negatively affects physical, psychological, and social functioning and predisposes patients to malnutrition, which in turn impairs immune competence and increases susceptibility to postoperative infections and mortality (Kemkes-RI, 2018). Preoperative malnutrition is consistently linked to prolonged hospitalisation, higher complication and readmission rates, and increased postoperative mortality. Contributing factors include tumour location and stage, tumour biology, and prior or planned neoadjuvant radiotherapy or chemotherapy (Sandrucci *et al.*, 2018; Seretis *et al.*, 2018). Given these associations, comprehensive nutritional assessment and early intervention should be standard components of multidisciplinary care for colorectal cancer patients.

Anemia is a common and clinically significant problem in patients with colorectal cancer. Even mild Anemia has been associated with increased risk of postoperative complications and prolonged hospitalisation. While red blood cell transfusion is frequently used for moderate to severe Anemia, preoperative transfusion has been linked to higher all-cause and cancer-specific mortality, increased recurrence/metastasis rates, postoperative infections, and additional surgical interventions in colorectal cancer populations (Ristescu *et al.*, 2019; Yan *et al.*, 2023).

Pathophysiologically, colorectal cancer–related Anemia often reflects chronic occult tumour bleeding, impaired luminal iron absorption, and inflammation-driven alterations in iron metabolism, leading to absolute iron deficiency in many patients (Făgărăşan *et al.*, 2022). Anemia reduces tissue oxygen delivery, which can impair collagen synthesis, immune function, and wound healing, mechanisms that plausibly increase susceptibility to infection and delay postoperative recovery. Our finding of an association between preoperative Anemia and postoperative complications aligns with prior reports linking perioperative Anemia to poorer short-term surgical outcomes (Ristescu *et al.*, 2019; Yan *et al.*, 2023).

Given these risks and the limitations of transfusion, emphasis should be placed on early identification and targeted correction of iron deficiency (for example, with intravenous iron when indicated) and optimisation of haemoglobin prior to elective surgery. Randomised and prospective studies are needed to clarify the causal impact of preoperative Anemia correction strategies on postoperative morbidity and long-term oncologic outcomes.

Malnutrition is a major determinant of postoperative morbidity and mortality across surgical specialities and is strongly implicated in adverse outcomes after colorectal cancer surgery, including reduced survival (Riad *et al.*, 2023; Seretis *et al.*, 2018). It affects roughly one-third of colorectal cancer patients and arises from tumor-driven metabolic changes, reduced oral intake due to obstruction, and other gastrointestinal dysfunctions (Daniele *et al.*, 2017). Advanced disease further compromises physical, psychological, and social functioning and predisposes to malnutrition, which impairs immune competence and increases susceptibility to postoperative infections and mortality (Huot *et al.*, 2021; Kemkes-RI, 2018). Preoperative malnutrition is associated with longer hospital stays, higher complication and readmission rates, and increased postoperative mortality; contributing factors include tumour location, histology and stage, and receipt of neoadjuvant radiotherapy or chemotherapy (Sandrucci *et al.*, 2018).

This study's reliance on BMI as the primary nutritional measure is an important limitation, since BMI does not capture recent weight loss, reduced intake, sarcopenia, or inflammatory status, features with independent prognostic value. Additional limitations include the retrospective, cross-sectional design, potential documentation gaps in medical records, single-centre setting, modest sample size, and lack of multivariable adjustment for confounders, all of which constrain causal inference and generalisability. Future studies should employ comprehensive nutritional assessment (e.g., PG-SGA, body composition analysis), prospective designs, and adjusted analyses to better define the impact of malnutrition and the benefit of targeted nutritional interventions.

4. Conclusions

Preoperative Anemia and poor nutritional status were significantly associated with increased postoperative complications among patients with stage III colorectal cancer at Sultan Agung Islamic Hospital, Semarang. Adjuvant chemotherapy was not associated with BMI-defined nutritional status or Karnofsky Performance Status, and overall CEA levels did not differ between major treatment groups; however, patients receiving radiotherapy in addition to surgery and chemotherapy showed a higher prevalence of underweight status. These results support routine preoperative screening and optimisation of haemoglobin and nutritional status as part of perioperative care. Prospective, multicentre studies with larger samples, standardised timing of assessments, comprehensive nutritional measures (including weight loss, muscle mass, and validated screening tools), and multivariable adjustment are warranted to confirm these findings and to test targeted prehabilitation interventions.

Conflict of interest

All authors have no conflicts of interest in this article.

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