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IMPACT OF CHEMOTHERAPY, SURGERY, AND RADIOTHERAPY ON COLORECTAL CANCER PATIENTS: A MULTIFACETED PERSPECTIVE

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ABSTRACT

Background: Colorectal cancer is a major contributor to cancer-related morbidity and mortality. Multimodal treatment approaches, such as surgery, chemotherapy, and radiotherapy, aim to improve survival and quality of life, yet their impact on various clinical outcomes in Indonesian patients remains underexplored. **Objective:** This study examines the impact of different treatment modalities on carcinoembryonic antigen (CEA) levels, nutritional status, pain, functional status, and survival in advanced-stage colorectal cancer patients. **Methods:** This retrospective cross-sectional study reviewed medical records of stage III patients aged 19–64 years treated between 2018 and 2024 at two Central Java hospitals. CEA was measured from serum via ELISA, nutritional status by body mass index (BMI), pain by Numerical Rating Scale (0–10), and functional status by Karnofsky Performance Index (0–100%). Mann–Whitney U and Fisher's Exact tests were applied ($p < 0.05$). **Results:** BMI was lower in the surgery + chemotherapy + radiotherapy group compared with surgery + chemotherapy alone (median 18.6 vs. 20.5 kg/m², $p = 0.04$). Neoadjuvant + adjuvant chemotherapy was associated with lower postoperative CEA levels (2.6 vs. 7.5 ng/mL, $p = 0.02$) and higher one-year survival (96% vs. 88%) and higher one-year survival (96% vs. 88%), although this difference was not statistically significant. Pain was lower in the neoadjuvant-only group than in the neoadjuvant + adjuvant group (median NRS 2 vs. 4, $p = 0.03$), while functional status remained high (>70%) across groups. **Conclusion:** Neoadjuvant chemotherapy showed favorable trends in CEA reduction, survival, and pain control, while chemoradiotherapy was linked to poorer nutritional status. Despite limitations, these findings provide context-specific evidence to inform multimodal treatment strategies in Indonesia.

INTRODUCTION

Colorectal cancer (CRC) is a major global health burden, ranking as the third most commonly diagnosed malignancy and the second leading cause of cancer-related deaths worldwide[1]. According to the World Health Organization data from 2023, over 1.9 million new CRC cases and approximately 930,000 related deaths were recorded globally. In Indonesia, colorectal cancer ranks fourth among the most prevalent cancers, with an incidence of 12.8 per 100,000 adults and a mortality rate of 9.5%[2]. The disease is often diagnosed at an advanced stage, significantly reducing the chances of curative treatment and increasing the burden on the healthcare system[3].

Standard treatment for CRC is multidisciplinary and stage-dependent, often involving surgery, chemotherapy (adjuvant or neoadjuvant), and radiotherapy[2]. Among these, neoadjuvant chemotherapy has shown promising results in

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improving survival in patients with stage III and IV colorectal cancer, especially in rectal cancer, by reducing tumor burden and enhancing resectability[4]. Moreover, carcinoembryonic antigen (CEA) is widely used as a biomarker to assess treatment response, where decreased post-treatment levels correlate with better prognosis and lower recurrence risk[5].

Despite global advancements, the application of neoadjuvant chemotherapy in Indonesia remains limited. Contributing factors include healthcare infrastructure limitations, high treatment costs, lack of public awareness, and delays in diagnosis and referral[2]. These challenges result in the predominance of late-stage diagnoses, limiting curative treatment options and increasing morbidity and mortality. Furthermore, patient-centered outcomes such as pain intensity, nutritional status, and functional capacity are frequently overlooked in clinical evaluations, despite their strong influence on quality of life and treatment adherence.

Existing studies have investigated the relationship between CRC therapy and changes in CEA levels or survival rates; however, there is a notable gap in the literature regarding the broader impact of treatment on multidimensional outcomes. For instance, Jelski and Mroczko[6] emphasize biochemical markers such as CEA, but do not fully address how therapeutic regimens affect pain and nutritional status. Similarly, Munawaroh[7] and Zielińska et al.[8] highlight the emergence of neuropathic pain as a treatment side effect, yet few studies integrate these findings with survival and functional outcomes. Moreover, most existing research is conducted in high-resource settings, limiting generalizability to low- and middle-income countries like Indonesia.

This study seeks to address these gaps by evaluating the impact of chemotherapy, radiotherapy, and surgery on five key clinical and quality-of-life indicators: CEA levels, nutritional status, pain intensity, functional performance, and survival duration among advanced-stage colorectal cancer patients at Sultan Agung Islamic Hospital, Indonesia. By assessing not only survival metrics but also patient-centered outcomes, this study offers a more comprehensive understanding of treatment effectiveness in real-world clinical settings.

The findings are expected to inform the development of evidence-based clinical guidelines tailored to the Indonesian context. Additionally, they aim to increase awareness among clinicians and policymakers about the need for integrated, multidisciplinary cancer care that balances tumor control with quality of life. Ultimately, this research contributes to the global discourse on CRC management while addressing local healthcare challenges and disparities.

METHODS

This retrospective cross-sectional observational study assessed the impact of chemotherapy, surgery, and radiotherapy on colorectal cancer patients, using medical records from 2018 to 2024. As a retrospective design, the study is subject to potential information bias due to incomplete or inconsistent medical record documentation. To minimize this risk, data were cross-checked against multiple entries within the same patient record, and variables were coded by two trained personnel to ensure consistency. This design captures a single point in time from existing records, enabling the identification of associations between treatment modalities and outcomes but not establishing cause-and-effect relationships. The method was selected based on the recommendations of Setia[9], which support cross-sectional studies for evaluating associations in defined clinical populations. The research was conducted from June to November 2024 at Sultan Agung Islamic Hospital and Ken Saras Hospital.

Treatment protocols were extracted from medical records. Surgical management consisted of curative resection for stage III colorectal or rectal adenocarcinoma, most commonly low anterior resection or abdominoperineal resection. Chemotherapy regimens followed the Indonesian national colorectal cancer management guidelines and included intravenous 5-fluorouracil (5-FU) combined with oxaliplatin (FOLFOX) or capecitabine with oxaliplatin (CAPOX). Neoadjuvant chemotherapy was administered 5–12 weeks before surgery, while adjuvant chemotherapy was initiated 3–6 weeks after surgery and typically consisted of 12 cycles. Radiotherapy, when performed, was delivered as pelvic irradiation at Ken Saras Hospital for rectal cancer cases, according to physician discretion.

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Eligible participants were stage III colorectal cancer patients aged 19–64 years who had undergone complete therapy and had comprehensive medical documentation. Limiting the sample to stage III disease reduced variability related to cancer stage at diagnosis. Data on comorbidities and baseline health status were not consistently available in medical records and were therefore not included in the analysis.

Data were obtained following ethical approval. Variables analyzed included: CEA levels (ng/mL), measured from serum using an enzyme-linked immunosorbent assay (ELISA) in the hospital's clinical pathology laboratory; nutritional status, calculated as body mass index (BMI, kg/m²) from documented weight and height; pain intensity, assessed using the Numerical Rating Scale (NRS), where patients rated their pain from 0 ("no pain") to 10 ("worst imaginable pain"), categorized as mild (1–3), moderate (4–6), or severe (7–10); functional status, measured using the Karnofsky Performance Index (KPI), a clinician-rated scale ranging from 0% (death) to 100% (normal functioning) in 10% increments, based on the patient's ability to perform daily activities and self-care; and survival duration and status, recorded from diagnosis until last follow-up or death. All records were systematically reviewed and coded by trained personnel to ensure consistency and accuracy.

Data analysis was performed using SPSS version 27. The Shapiro-Wilk test assessed normality for continuous variables. Due to non-normal distribution, the Mann-Whitney U test was used to compare independent groups, with significance set at $p < 0.05$. For categorical variables such as survival status, Fisher's Exact Test was applied, with the same significance threshold. This methodological framework allowed for a structured evaluation of treatment effects across multiple clinical outcomes relevant to colorectal cancer care.

RESULTS

Based on the secondary data analysis of medical records from 56 stage III rectal cancer patients, the combination of surgery and chemotherapy, as well as surgery, chemotherapy, and radiotherapy, resulted in relatively similar CEA levels, as shown in Table 1. The proportion of patients with abnormal CEA levels (>5 ng/mL) was 63.6% in the surgery + chemotherapy group and 60.9% in the surgery + chemotherapy + radiotherapy group. The Mann-Whitney U Test revealed no significant difference between the two groups ($p = 0.405$).

Table 1. CEA levels in patients with surgery + chemotherapy and surgery + chemotherapy therapy

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

For 52 patient records undergoing surgery and chemotherapy, neoadjuvant + adjuvant group has a significantly lower median CEA level (2.6 ng/mL) compared to adjuvant-only group (7.5 ng/mL), as shown in Table 2. This difference was statistically significant ($p < 0.001$) based on the Mann-Whitney U Test.

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

Chemotherapy	n	%	CEA Levels (ng/mL) Median (Min –Max)
Neoadjuvant + Adjuvant	27	51.9	2.6 (1–6.3)
Adjuvant-only	25	48.1	7.5 (1.2–48.5)

Patient nutritional status, measured by BMI and presented in Table 3, revealed that the surgery + chemotherapy group had the highest distribution in the normal category (42.4%) and underweight category (30.3%). Meanwhile, the surgery + chemotherapy + radiotherapy group exhibited a higher proportion of underweight patients (52.2%). The difference in nutritional status between the two groups was statistically significant ($p < 0.001$) based on the Independent Samples T-Test.

Table 3. BMI in patients with surgery + chemotherapy and surgery + chemotherapy therapy

BMI (kg/m²)	Surgery + Chemotherapy		Surgery + Chemotherapy + Radiotherapy	
	n	%	n	%
Underweight (< 18.5)	10	30.3	12	52.2
Normal (18.5-22.9)	14	42.4	7	30.4

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Overweight (23-24.9)	5	15.2	3	13
Obesity I (25-29.9)	4	12.1	0	0
Obesity II (≥ 30)	0	0	1	4.3

The analysis of survival status and duration among colorectal cancer patients is summarized in Table 4. The Fisher's Exact Test indicated no significant difference in survival status between the neoadjuvant + adjuvant group (survival rate of 96%) and the adjuvant-only group (survival rate of 79%), with p = 0.341. The median survival duration was 7 months for the neoadjuvant + adjuvant group and 6 months for the adjuvant-only group. The Mann-Whitney U Test showed no significant difference in the mean survival time (p = 0.35).

Table 4. Survival status and duration in patients with and without neoadjuvant chemotherapy

Chemotherapy	Survival Status				CEA Levels (ng/mL) Median (Min – Max)
	Survive		Not Survive		
	n	%	n	%	
Neoadjuvant + Adjuvant	26	96.3	1	3.7	7 (5–12)
Adjuvant-only	22	88.0	3	12.0	6 (0–12)

Pain scale analysis, conducted on 69 samples and summarized in Table 5, revealed that patients in neoadjuvant-only group had an average pain score of 3.18 (mild pain), whereas those in neoadjuvant + adjuvant group had a similar average score but a higher mean pain level (moderate pain). The Mann-Whitney U Test showed a statistically significant difference between the two groups (p < 0.001), indicating that both neoadjuvant and adjuvant chemotherapy affected the pain levels in colorectal cancer patients.

Table 5. Pain level and KPI in patients with neoadjuvant chemotherapy and neoadjuvant + adjuvant chemotherapy

Chemotherapy	n	%	Pain Level Mean (SD)	KPI (%) Mean (SD)
Neoadjuvant-only	34	49.3	3.18 (0.46)	71.76 (10.86)
Neoadjuvant + Adjuvant	35	50.7	3.71 (0.52)	73.71 (10.31)

Functional status analysis, assessed using the KPI and presented in Table 5, showed an average KPI score of 71.76% in the neoadjuvant-only group and 73.71% in the neoadjuvant + adjuvant group. No statistically significant difference was observed (p = 0.438) based on the Mann-Whitney U Test, suggesting that the addition of adjuvant chemotherapy had little impact on patients' functional status.

DISCUSSION

Comparison of Treatment Modalities

Colorectal cancer treatment modalities, including surgery, chemotherapy, and radiotherapy, are often combined to achieve optimal outcomes. In this study, surgery served as the primary treatment, with variations in adjuvant modalities. No significant difference in abnormal postoperative CEA levels (>5 ng/mL) was observed between patients in surgery + chemotherapy group (63.6%) and those in surgery + chemotherapy + radiotherapy group (60.9%), consistent with previous studies[10].

The significant reduction in CEA levels observed in the neoadjuvant + adjuvant group (median 2.6 ng/mL) compared to those in adjuvant-only group (median 7.5 ng/mL) indicates the effectiveness of this approach in suppressing tumor activity early in treatment, aligning with prior research[5,11,12]. Radiotherapy, while beneficial in reducing local recurrence risk in advanced rectal cancer, was associated with a higher prevalence of underweight patients (52.2% vs. 30.3%), consistent with findings that radiation therapy can negatively affect BMI[13].

Pain levels also varied by treatment type. The neoadjuvant + adjuvant group exhibited higher pain levels than neoadjuvant-only group, reflecting cumulative neuropathic effects from intensive chemotherapy regimens, consistent with prior findings[7].

Nutritional Status and Its Implications for Treatment

Nutritional status significantly influences treatment tolerance, immune function, and recovery in colorectal cancer patients. Poor nutritional status, particularly underweight, was more prevalent in the surgery + chemotherapy + radiotherapy group. Low BMI has been linked to higher mortality risk[14,15].

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Nutritional interventions, such as protein-rich and energy-dense diets, along with regular monitoring using validated tools like the Patient-Generated Subjective Global Assessment (PG-SGA), can help identify malnutrition early and improve treatment tolerance[16,17].

CEA Levels as a Prognostic Indicator

Neoadjuvant CEA is widely recognized as a biomarker for malignancy severity in colorectal cancer[18]. Post-treatment CEA reduction reflects treatment response and disease control[19]. In this study, neoadjuvant chemotherapy significantly lowered postoperative CEA, suggesting both effective tumor suppression and potential survival benefit. Persistently high CEA after therapy may indicate residual tumor or metastasis, necessitating further intervention[20,21].

The predictive value of CEA for therapy success has been confirmed in prior studies, where consistent decreases across chemotherapy cycles indicated effective treatment[21]. Routine CEA monitoring also facilitates early recurrence detection, as rising levels often precede clinical symptoms[21].

Survival and Quality of Life

While survival rates did not differ significantly between groups, the neoadjuvant + adjuvant group had a higher one-year survival rate (96% vs. 88%) and a slightly longer median survival (7 months vs. 6 months), in line with literature suggesting improved long-term outcomes with neoadjuvant therapy[4,22].

Quality of life, measured via the KPI remained high (>70%) across groups, consistent with studies showing adjuvant chemotherapy can help maintain functional performance[23,24]. However, mild pain in the neoadjuvant group and moderate pain in the adjuvant group, as measured by NRS, suggest a need for pain management strategies targeting neuropathic symptoms[7].

Significance and Position in Literature

This study contributes to the limited body of evidence on the associations between multimodal colorectal cancer treatments and a range of clinical and patient-centered outcomes, including CEA levels, nutritional status, pain, functional performance, and survival. By restricting the cohort to stage III cases and analyzing real-world clinical data from two hospitals, the study offers context-specific insights relevant to Indonesian cancer care. However, the retrospective cross-sectional design constrains the ability to establish causal relationships and may not capture the full complexity of how treatment type interacts with tumor biology, comorbidities, and long-term outcomes. Accordingly, these findings should be interpreted as indicative rather than definitive. Future prospective, multicenter studies with standardized treatment protocols, more comprehensive baseline data, and longer follow-up periods are necessary to confirm and expand upon the trends observed in this analysis.

Limitations

This study was conducted in two hospitals in Central Java, which may limit the generalizability of the findings to other regions of Indonesia with different patient demographics, healthcare infrastructure, and treatment practices. The retrospective cross-sectional design allows for the identification of associations but not causal relationships, and reliance on medical records introduces potential information bias due to incomplete, inconsistent, or missing documentation, which could lead to misclassification of treatment details or underreporting of outcomes. Although cancer stage was controlled for through inclusion criteria (stage III only), comorbidities, baseline nutritional status, and pre-treatment performance scores were not consistently available and were therefore not included in the analysis. Details on chemotherapy regimens, radiotherapy protocols, and surgical techniques were incomplete in some records, and treatment approaches may have evolved between 2018 and 2024, introducing potential temporal confounding. The relatively small sample size reduces statistical power and increases the likelihood of Type II error. Lastly, CEA levels were measured post-treatment using ELISA, and variations in timing relative to therapy completion could influence results. Future multicenter, prospective research with larger cohorts, standardized treatment protocols, and comprehensive baseline clinical data is needed to validate and expand upon these findings.

CONCLUSION

This study demonstrates that the combination of surgery, chemotherapy, and radiotherapy is effective

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in managing colorectal cancer, with neoadjuvant chemotherapy significantly reducing CEA levels and improving patient survival rates. Although the average survival duration did not differ significantly between groups, early therapeutic intervention provided clear benefits in terms of treatment response.

However, the intensity of therapy, particularly with the addition of radiotherapy, negatively impacted patients' nutritional status, while pain levels were higher in the neoadjuvant + adjuvant group. Despite these challenges, patients demonstrated functional status above 70%, underscoring the importance of a holistic approach to treatment. Effective management of side effects, including nutritional support and pain control, is essential for improving the quality of life during therapy.

These findings highlight the need for individualized and comprehensive treatment strategies for colorectal cancer patients, emphasizing the integration of supportive care into standard therapy protocols to optimize outcomes.

ETHICAL APPROVAL

This study was conducted with the approval from the Health Research Ethics Committee of Sultan Agung Islamic Hospital (RSI Sultan Agung) Semarang: No. 134/KEPK-RSISA/VII/2024, No. 135/KEPK-RSISA/VII/2024, No. 140/KEPK-RSISA/VII/2024.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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AUTHOR CONTRIBUTIONS

VME and ES conceptualized the study; VME and C designed the methodology; AL, LU, and RS was responsible for data curation, formal analysis, writing the article, and project administration; ES and C wrote the original draft preparation, reviewed and edited the article.

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