**Original Research Report**

# PROGNOSTIC NUTRITIONAL INDEX WITH WOUND COMPLICATION AFTER LAPAROTOMY IN COLORECTAL CANCER PATIENTS AT DR. ZAINOEL ABIDIN GENERAL HOSPITAL BANDA ACEH

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## ABSTRACT

Colorectal cancer patients generally undergo laparotomy as a part of disease management. The earliest complications of laparotomy include bleeding, surgical wound infection, and anastomotic dehiscence. Albumin-lymphocytes are indicators of nutritional status and inflammation as measured by the Prognostic Nutritional Index (PNI). However, the evaluation of PNI related to the degree of post-laparotomy wounds has not been widely explained. This study aimed to determine the correlation between PNI and laparotomy wound complications in colorectal cancer patients at dr. Zainoel Abidin Regional General Hospital, Banda Aceh, Indonesia. This cross-sectional study assessed the correlation between PNI and postoperative wound degree, which was assessed using the Southampton wound scale. The PNI values were determined by albumin and lymphocyte measurements. The subjects comprised 30 colorectal cancer patients, who were 18 years old or above and underwent laparotomy. The assessment was carried out on the seventh day post-laparotomy. The Spearman test was performed to determine the correlation between variables ($p<0.05$). The colorectal cancer patients had an average age of 49.43 years (±11.06), were predominantly male (56.7%), with moderately differentiated adenocarcinoma (46.7%), an average albumin level of 3.08 (±0.47), and an average lymphocyte count of 13.93 (±8.22). After the evaluation, we found that patients with normal PNI values exhibited Southampton grade 1 wounds (23.3%), whereas those with mild malnutrition were categorized in grades 1 (6.7%) and 2 (6.7%). Patients with moderate malnutrition were categorized in grades 3 (23.3%) and 4 (16.7%), while those with severe malnutrition were assigned to grades 4 (16.7%) and 5 (13.3%). There was a significant correlation ($p=0.00$) between nutritional status and wound degree, as measured by the PNI and Southampton score, respectively, with a very strong inverse correlation ($R=-0.938$) after laparotomy for colorectal cancer. In conclusion, PNI exhibits a robust correlation with postoperative wound complications in colorectal cancer patients following laparotomy.

**Keywords:** Prognostic Nutritional Index (PNI); Southampton wound scale; colorectal cancer; laparotomy

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**Highlights:**
1. This study evaluated nutritional status and inflammation as indicated by the Prognostic Nutritional Index (PNI), since comprehensive reports regarding laparotomy are limited.
2. The findings provide crucial information that early management of unfavorable nutritional status and inflammation can improve surgical outcomes related to laparotomy wounds.
3. This research report may guide digestive surgeons to achieve a favorable prognosis for colorectal cancer patients after laparotomy by preventing postoperative wound complications and ensuring good nutritional status.

## INTRODUCTION

Colorectal cancer is a malignancy originating from the epithelial cells of the colon and rectum. This disease has become the third most common cancer and the fourth leading cause of death worldwide. In 2020, there were around 1.9 million new cases of colorectal cancer and 930,000 deaths caused by this disease. The incidence of colorectal cancer is estimated to increase by 63%, reaching 3.2 million new cases and 1.6 million deaths by 2040. According to the World Health Organization reports, the incidence of colorectal cancer has decreased due to effective screening programs in developed countries (Arnold et al. 2017, Sung et al. 2021).

In Asia, the risk of colorectal cancer was higher in Japan, China, and Korea compared to India and Malaysia. The Global Cancer Observatory (GLOBOCAN) 2020 data indicated that the incidence of colorectal cancer per 100,000 population was 48.1 for men and 23.5 for women in Hong Kong, 58.7 for men and 23.5 for women in Japan, and 40.1 for men and 28 for women in South Korea. In Indonesia, the number of colorectal cancer cases was 12.8 per 100,000 adults, with a mortality rate of 9.5% among all cancer cases. This number is increasing along with changes in the lifestyle of the Indonesian population (Ng & Wong 2013, Ferlay et al. 2013, Ministry of Health of the Republic of Indonesia 2018).

Colorectal cancer management includes surgery, chemotherapy, and radiotherapy. Laparotomy is an approach used for the treatment of colorectal cancer. However, postoperative complications have been a major problem in colorectal cancer patients. In addition, postoperative complications of colorectal cancer are not only associated with poor short-term outcomes but also with diminished long-term outcomes. Complications that can occur after surgery are bleeding, nonspecific infections, wound dehiscence, postoperative ileus, fascial dehiscence, and anastomotic leakage (Debas 2006, Ge et al. 2017).

The prognosis of colorectal cancer depends on various factors, including tumor stage, biological factors, and patient-specific variables. Nutritional and immunological status are among the most important factors affecting the prognosis of colorectal cancer (Mohil et al. 2008). The evaluation of nutritional status can be determined by calculating the Prognostic Nutritional Index (PNI), also known as Onodera's Prognostic Nutritional Index. This index was first proposed in the study of gastrointestinal surgery for malnourished cancer patients, demonstrating that PNI was a significant indicator of postoperative outcomes. PNI is assessed by serum albumin concentration and peripheral blood lymphocyte count. Because it is easier to apply, PNI is more frequently utilized compared to other predictors. Preoperative PNI values serve as useful predictive indicators for postoperative complications and survival in abdominal surgery (Schmoll et al. 2012, Mohri et al. 2013, Keung & Raut 2017). However, studies have not widely reported the application of PNI in assessing post-laparotomy surgical wound complications, especially in colorectal cancer cases. Against this background, we were interested in exploring the correlation between PNI and post-laparotomy surgical wound complications in colorectal cancer patients at dr. Zainoel Abidin Regional General Hospital, Banda Aceh, Indonesia.

## MATERIALS AND METHODS

This correlational study used an observational analytical research methodology with a cross-sectional design. The research was conducted in the surgical ward and operating room of dr. Zainoel Abidin Regional General Hospital, Banda Aceh, Indonesia, from February to July 2024. The study sample consisted of colorectal cancer patients aged 18 years or older who were diagnosed with histopathological evidence and had not undergone chemotherapy or laparotomy procedures previously. Patients with diabetes mellitus, coagulation disorders, and peritonitis were excluded from this study (Ismael & Satroasmoro 2008, Wang & Cheng 2020).

Patients who met the inclusion criteria were selected as subjects and subsequently assessed for their Prognostic Nutrition Index (PNI) using the following formula: serum albumin (gr/dL) + 0.005 × lymphocytes ($mm^3$). The albumin levels and lymphocyte count were measured using routine blood tests prior to the laparotomy surgery. The PNI values were divided into four categories: normal (≥55), mild malnutrition (50–54), moderate malnutrition (46–50), and severe malnutrition (≤45). Seven days after laparotomy, the degree of surgical wounds was assessed using the Southampton wound scale, consisting of grade 0 for normal healing, grade 1 for mild erythema, grade 2 for erythema accompanied by inflammatory signs, grade 3 for the presence of clear or haemoserous discharge along the wound, grade 4 for pus ranging from a localized point to the entire wound length, and grade 5 for severe infection, tissue damage, and hematoma requiring aspiration. The correlation between PNI and wound degree was analyzed using the Spearman test through IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA), with a value of $p<0.05$ considered statistically significant (Sedgwick 2014).

## RESULTS

Within six months, this study gathered 30 colorectal cancer patients who fulfilled the inclusion criteria and served as the research subjects. The characteristics of the research subjects can be seen in Table 1.

Table 1. Characteristics of the colorectal cancer patients.

| Characteristics | n (%) | Mean±SD (min–max) |
|---|---|---|
| Age (y.o.) | | 49.43±11.06 (27–63) |
| Sex | | |
| Male | 17 (56.7) | |
| Female | 13 (43.4) | |
| Histopathology | | |
| Moderately differentiated adenocarcinoma | 14 (46.7) | |
| Well-differentiated adenocarcinoma | 11 (36.7) | |
| Poorly differentiated adenocarcinoma | 5 (16.7) | |
| Albumin (gr/dL) | | 3.08±0.47 (2.47–4.15) |
| Lymphocytes (%) | | 13.93±8.22 (2.00–28.00) |

Legends: SD=standard deviation; y.o.=years old.

The characteristic data showed that the colorectal cancer patients had an average age of 49.43±11.06 years, with a minimum age of 27 years and a maximum age of 63 years. The majority of the colorectal cancer patients were male, with 17 patients (56.7%). The remaining patients were female, with 13 individuals (43.4%). The results of postoperative histopathology indicated that moderately differentiated adenocarcinoma (46.7%) was the most common type of malignancy, followed by well-differentiated adenocarcinoma (36.7%) and poorly differentiated adenocarcinoma (16.7%). Furthermore, the blood evaluation showed that the average albumin level in the colorectal cancer patients was 3.08±0.47 gr/dL, with a minimum of 2.47 gr/dL and a maximum of 4.15 gr/dL. The colorectal cancer patients exhibited an average lymphocyte count percentage of 13.93±8.22, with a minimum of 2% and a maximum of 28%.

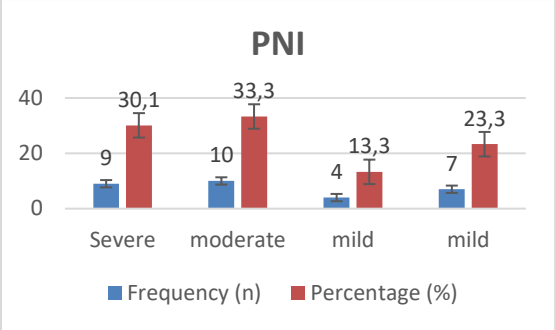


Figure 1. Distribution of Prognostic Nutrition Index in the colorectal cancer patients.

Figure 1 shows the distribution of nutritional status as assessed using the Prognostic Nutrition Index (PNI). The analysis revealed that 33.3% of the colorectal cancer patients exhibited moderate malnutrition, while severe malnutrition was observed in 30.1% of the patients. Figure 2 displays the distribution of wound degree according to the evaluation using the Southampton wound scale. The most prevalent degrees of the wounds were grade 1 (30%) and grade 4 (26.7%).

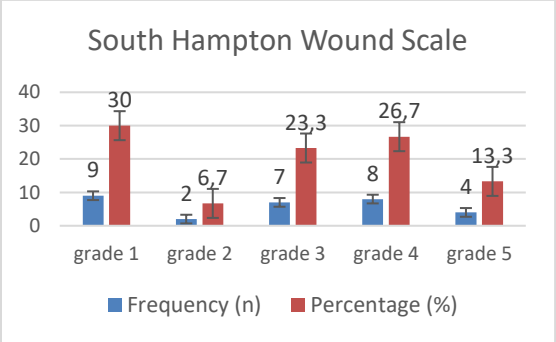


Figure 2. Distribution of wound degrees according to the Southampton wound scale.

This study included an analysis of the correlation between colorectal cancer patients' nutritional status, as measured by the Prognostic Nutrition Index, and the degree of their wounds, as indicated by the Southampton wound scale post-laparotomy. Table 2 presents the results of the analysis, demonstrating that PNI was correlated with the degree of wound, particularly during the healing process after the procedure.

The correlation between PNI and the Southampton wound scale was predominantly observed in patients with normal nutritional status and grade 1 wounds (23.3%). However, it was absent in post-laparotomy colorectal cancer patients with higher wound degrees. Concurrently, patients with mild malnutrition mostly exhibited grade 1 (6.7%) and grade 2 (6.7%) wounds. Colorectal cancer patients

with moderate malnutrition predominantly presented with grade 3 wounds (23.3%), whereas those with severe malnutrition primarily exhibited grade 4 (16.7%) and grade 5 (13.3%) wounds. Patients with severe malnutrition exhibited more severe wounds compared to those with more desirable nutritional status. There was a significant correlation between nutritional status and the degree of wound (p=0.00), indicating a very strong correlation with an opposite direction (R=-0.938) after laparotomy for colorectal cancer.

Table 2. Correlation between prognostic nutrition index and southampton wound scale post-laparotomy.

| PNI | Wound scale (n, %) | | | | | p | R |
|---|---|---|---|---|---|---|---|
| | Grade 1 | Grade 2 | Grade 3 | Grade 4 | Grade 5 | | |
| Severe malnutrition | 0 0.0 | 0 0.0 | 0 0.0 | 5 16.7 | 4 13.3 | 0.000 | -0.938 |
| Moderate malnutrition | 0 0.0 | 0 0.0 | 7 23.3 | 3 10.0 | 0 0.0 | | |
| Mild malnutrition | 2 6.7 | 2 6.7 | 0 0.0 | 0 0.0 | 0 0.0 | | |
| Normal | 7 23.3 | 0 0.0 | 0 0.0 | 0 0.0 | 0 0.0 | | |
| Total | 9 30.0 | 2 6.7 | 7 23.3 | 8 26.7 | 4 13.3 | | |

Legends: PNI=Prognostic Nutrition Index.

## DISCUSSION

### Characteristics of colorectal cancer patients

In this study, most of the colorectal cancer patients were male (56%), with an average age of 49.43 years. According to the histopathological evaluation, the most common type of malignancy among the patients was moderately differentiated adenocarcinoma. Colorectal cancer ranks as the third most prevalent malignancy in the general population. It is estimated that by 2035, the total number of deaths from rectal and colon cancer will increase by 60% and 71.5%, respectively. These figures may vary from country to country depending on the level of economic development. The risk of developing the disease ecalates with increased consumption of red meat and alcohol. In 2018, there were approximately 1.8 million new cases and 881,000 deaths globally. The incidence of colorectal cancer-associated deaths in individuals aged 50 and over has continued to decline, with the latest trend indicating an average annual percentage change of -0.7 for those aged 50–65 from 2007 to 2016 and -4.0 for those aged 65 and over (Baidoun et al. 2021).

The postoperative histopathology showed that moderately differentiated adenocarcinoma was the predominant malignancy at 46.7%, followed by well-differentiated adenocarcinoma (36.7%) and poorly differentiated adenocarcinoma (16.7%). The recent World Health Organization (WHO) classification for malignant epithelial colorectal tumors includes four main categories: adenocarcinoma, neuroendocrine tumor, mixed neuroendocrine carcinoma, and other types. Adenocarcinoma (90%) was the most common type compared to the other categories. Colorectal adenocarcinoma has several histopathological subtypes, with specific morphological, clinical, and molecular characteristics. These subtypes include serrated adenocarcinoma, micropapillary adenoma-like adenocarcinoma, mucinous adenocarcinoma, cohesive carcinoma, ring cell carcinoma, medullary adenocarcinoma, adenosquamous carcinoma, undifferentiated carcinoma, and carcinoma with sarcomatoid components (Venugopal & Carethers 2022).

### Correlation between Prognostic Nutrition Index and the degree of wounds post-laparotomy

This study found that the mean albumin level of the colorectal cancer patients was 3.08±0.47 gr/dL, with a minimum of 2.47 gr/dL and a maximum of 4.15 gr/dL. Serum albumin has traditionally been used as a quantitative indicator of patient nutritional status due to the availability and affordability of the test. Preoperative albumin levels are the best predictor of mortality after colorectal cancer surgery. Hypoalbuminemia significantly prolongs the length of hospitalization, elevates the incidence of surgical site infections, heightens the risk of enterocutaneous fistula, and enhances the likelihood of deep vein thrombosis (Truong et al. 2016, Chiang et al. 2017). The postponement of surgical procedures to allow for preoperative correction of albumin levels in hypoalbuminemia patients has demonstrated an increase in morbidity and mortality in patients with severe nutritional risk.

Wierdak et al. (2018) conducted a prospective analysis involving 105 consecutive patients who underwent laparoscopic colorectal cancer resection between August 2014 and September 2016. The 105 subjects comprised 82 patients without complications in group 1 and 23 patients with at least one infectious complication in group 2. Preoperatively, the two groups showed no significant difference in serum albumin levels, measuring 38.7±4.9 g/L for group 1 and 37.7±5.0 g/L for group 2. Conversely, a decrease was observed in both groups during the postoperative

evaluations. The serum albumin levels in the first postoperative evaluation were 36.5±4.2 g/L for group 1 and 34.7±4.2 g/L for group 2 (p=0.07). In the second postoperative evaluation, the albumin levels were 36.2±4.1 g/L for group 1 and 32.6±5.6 g/L for group 2 (p=0.01) In the third postoperative evaluation, groups 1 and 2 exhibited serum albumin levels of 36.0±4.4 g/L and 30.9±3.5 g/L, respectively (p=0.01). The decrease was significantly greater in group 2 during the second and third postoperative evaluations, which demonstrated lower mean albumin levels.

Ge et al. (2017) elucidated that a cutoff value of a 15% decrease in serum albumin within two days after surgery can help identify patients at elevated risk for postoperative complications, thereby indicating the requirement for safe and quick discharge after colorectal surgery. The cutoff value was obtained from all of the patients, who exhibited a median postoperative albumin of 15%. Therefore, albumin was deemed an independent risk factor for overall complications (p<0.01). Patients exhibiting a delta albumin difference of ≥15% experienced an increase in the risk of major postoperative complications, the comprehensive complication index, extended postoperative hospitalization, and surgical site infections (p<0.05) (Ministry of Health of the Republic of Indonesia 2018, Wierdak et al. 2018).

In this study, we obtained an average lymphocyte count percentage of 13.93±8.22 from the colorectal cancer patients, with a minimum of 2% and a maximum of 28%. Lymphocytes have been used as a biomarker for colorectal cancer outcomes. The neutrophil-lymphocyte ratio serves as a simple index of systemic inflammatory response. This ratio is correlated with medium-term survival in colorectal cancer patients. Mohri et al. (2013) reported that the five-year recurrence-free survival rate in the group with a high lymphocyte count was generally superior to that in the group with a low lymphocyte count. The five-year overall survival rate in the group with a high lymphocyte count was significantly higher compared to the group with a low lymphocyte count. The multivariate analysis indicated that the lymphocyte percentage is independently associated with patient survival. The findings suggest that lymphocyte percentage is a more reliable predictor of survival than the absolute lymphocyte count in colorectal cancer patients. The combination of preoperative and postoperative lymphocyte count may operate as a prognostic indicator in colorectal cancer patients (Iseki et al. 2017, Yamamoto et al. 2019).

This study indicated a significant correlation between PNI and the degree of wound as measured by the Southampton wound scale. Patients with moderate, mild, or severe malnutrition typically exhibit a more severe degree of wound. Patients with moderate malnutrition presented with wounds classified as grades 3 and 4, whereas those with severe malnutrition exhibited grades 4 and 5 wounds. The Prognostic Nutritional Index, determined using serum albumin levels and lymphocyte counts to indicate nutritional status, has been reported to correlate with survival and perioperative complications in various types of cancer (Katundu 2018). A low PNI has recently been found to be associated with poor prognosis in malignant colorectal cancer. Mohri et al. (2013) evaluated PNI in relation to postoperative outcomes of colorectal cancer and determined that it can predict short-term and long-term outcomes. In addition, 365 patients undergoing cancer resection exhibited low PNI values, which were significantly associated with poor survival (p<0.0001) and correlated with the incidence of postoperative complications. PNI has also been utilized to observe tumor, node, and metastasis (TNM) stages I or IV. The low PNI group had a significantly increased incidence of total and severe postoperative complications (Zhou et al. 2017, Sun et al. 2019).

Bailón-Cuadrado et al. (2019) found that PNI is correlated with clinical wound infection and severe wounds after colorectal cancer surgery. PNI emerged as a great predictive and protective factor for overall complications (RR=0.279, 95% CI=0.141–0.552). It can also serve as a predictor for severe complications (RR=0.355, 95% CI=0.130–0.965), infectious complications (RR=0.220, 95% CI=0.099–0.489), and anastomotic leak (RR=0.151, 95% CI=0.036–0.640) (Baidoun et al. 2021). Correlations among nutritional status, inflammation, and cancer have been identified. The interaction induced by tumors triggers a systemic inflammatory reaction in which several cytokines are released. In addition, several neuroendocrine changes trigger hormonal imbalances, resulting in a tendency for anorexia and catabolism (increased proteolysis and lipolysis). Nutritional status and inflammation in colorectal cancer patients are significantly correlated, as indicated by PNI, leading to increased morbidity following curative surgery. From another perspective, PNI has been associated with the emergence of severe overall surgical wound complications during the first 30 days post-surgery, such as anastomotic leak (Mohri et al. 2013, Iseki et al. 2017, Bailón-Cuadrado et al. 2019).

**Strength and limitations**

This study provides an overview indicating that nutritional status, albumin levels, and inflammatory response can serve as prognostic indicators for colorectal cancer patients undergoing surgery.

Enhanced evaluation and preparation are essential to ensure favorable postoperative outcomes for colorectal cancer patients. Postoperative outcomes extend beyond wound assessments. Therefore, it is important to follow up on other factors, such as length of stay, pain levels, complication risk, and stoma status. This may warrant consideration in further research to address the limitation of this study. Other nutritional indicators besides albumin, such as liver function, intestinal absorption, and other biomarkers, need to be considered to help evaluate the prognosis of colorectal cancer patients.

## CONCLUSION

A very strong correlation exists between the Prognostic Nutritional Index (PNI) and the occurrence of post-laparotomy surgical wound complications in colorectal cancer patients. A diminished PNI value leads to an increasingly severe degree of wound in colorectal cancer patients following laparotomy.

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### Conflict of interest

None.

### Ethical consideration

This research had obtained ethical permission from the Research and Development Division/ LITBANG dr. Zainoel Abdinin Hospital with letter number 630/LITBANG/154/PPDSBEDAH/IX/2024.

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None.

### Author contribution

AH, MY, IN, IM, and SR contributed to the conception and design of the study, drafted the manuscript, and collected, assembled, and analyzed the data. AH, MY, and SR contributed to the final approval of the article. All authors also contributed to the critical revisions of the article for important intellectual content.

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