THE EFFECT OF ORAL ALBUMIN ADMINISTRATION [EGG WHITE EXTRACT (37%) AND *OPHIOCEPHALUS STRIATUS* EXTRACT (1%)] ON THE MODIFIED GLASGOW PROGNOSTIC SCORE IN PATIENTS WITH STAGE I TO STAGE III COLORECTAL CANCER WHO UNDERWENT COLORECTAL CANCER SURGERY AT DR. SAIFUL ANWAR REGIONAL GENERAL HOSPITAL, EAST JAVA

Aries Budianto[1*], Sinung Wikanadi[1], Bramantya Andyatma[1], Heru Sulistyo[1], Achmad Efendi[1]

[1]Universitas Brawijaya, Malang, East Java, Indonesia

***Corresponding Author:** Aries Budianto, Universitas Brawijaya, Malang, East Java, Indonesia | Email: bramandyatma@gmail.com

ABSTRACT

Background: *Colorectal cancer (CRC) is the third most common cancer worldwide, and hypoalbuminemia and systemic inflammation, captured by the modified Glasgow Prognostic Score (mGPS), are associated with poor prognosis in CRC. Oral albumin is a more cost-effective alternative to intravenous albumin.* ***Objective:*** *To determine the effect of oral albumin [egg white extract (37%) and* Ophiocephalus striatus *extract (1%)] on the mGPS in patients with stage I–III CRC undergoing surgery at Dr. Saiful Anwar Regional General Hospital, East Java.* ***Methods:*** *Thirty patients with stage I–III CRC who underwent surgery were divided into an Albumed/egg white extract group, an* Ophiocephalus striatus *extract group and a control group receiving a standard diet (n = 10 each). Oral albumin was given in addition to the standard diet for 14 days, and serum albumin and C-reactive protein were measured on days 0 and 14. Changes in mGPS were analysed using the Wilcoxon signed-rank, Kruskal–Wallis and Mann–Whitney U tests with Bonferroni correction.* ***Results:*** *Before the intervention, 50.0% of patients had a moderate and 50.0% a high mGPS; after the intervention, 16.7% had a low, 53.3% a moderate and 30.0% a high mGPS. The mGPS improved in 60.0% of the egg white extract group (p = 0.014) and in 50.0% of the* Ophiocephalus striatus *extract group (p = 0.025), whereas all control patients remained unchanged (p = 1.000). Changes differed significantly among groups (H = 8.603; p = 0.014); both intervention groups differed from the control group (p = 0.004 and p = 0.012) but not from each other (p = 0.661).* ***Conclusion:*** *Oral albumin administration improved the mGPS in patients with CRC undergoing surgery, with no significant difference between egg white extract and* Ophiocephalus striatus *extract; the egg white extract was more cost-effective and more convenient to consume.*

Keywords: *Colorectal Cancer, Oral Albumin, Modified Glasgow Prognostic Score, Egg White Extract,* Ophiocephalus striatus

How to cite this article: Budianto A, Wikanadi S, Andyatma B, Sulistyo H, Efendi A., The Effect of Oral Albumin Administration [Egg White Extract (37%) and Ophiocephalus striatus Extract (1%)] on the Modified Glasgow Prognostic Score in Patients with Stage I to Stage III Colorectal Cancer Who Underwent Colorectal Cancer Surgery at Dr. Saiful Anwar Regional General Hospital, East Java. Int J Drug Deliv Technol. 2026;16(89s): 2072-2091; DOI: 10.25258/ijddt.16.89s.195

INTRODUCTION

Colorectal cancer (CRC) is the third most common type of cancer worldwide, with more than 1.9 million diagnosed cases. It is the second leading cause of cancer-related deaths. In Indonesia, the incidence of colorectal cancer in 2020 reached 4,189 (8.6%) cases.[1,2]

Serum albumin is a prognostic factor for patients with CRC. This is supported by a retrospective cohort study of CRC patients in Taiwan, which showed that high serum albumin levels are associated with improved survival in CRC patients (HR 1.45, 95% CI 1.09–1.92). A study in Japan demonstrated that serum albumin is an independent prognostic factor for overall survival (HR 0.85, 95% CI 0.73–0.99). A study in the United States showed that increased albumin levels are associated with decreased serum C-reactive protein (CRP) levels.[3,4]

Albumin can bind to endogenous ligands of the pro-inflammatory molecule interleukin-6 (IL-6). Interleukin-6 is a cytokine that activates signal transducer and activator of transcription 3 (STAT-3), which increases the production of C-reactive protein (CRP) in the liver, thereby raising serum CRP levels.[5,6]

Hypoalbuminemia occurs due to the leakage of albumin through the capillary walls into the extravascular compartment caused by the release of tumor necrosis factors, thereby increasing microvascular permeability. A 2020 study in the United Kingdom found 147,950 cases of colorectal cancer, with approximately 20%–37% of patients experiencing hypoalbuminemia. Among colorectal cancer patients in the UK who underwent surgery, approximately 30% had hypoalbuminemia, and 25% showed evidence of a systemic inflammatory response.[7–9]

The Modified Glasgow Prognostic Score (mGPS) is a prognostic tool used in Korea; studies have reported that a high mGPS is associated with poor prognostic outcomes in various types of cancer, including colorectal cancer (CRC). The National Cancer Center Hospital Singapore demonstrated that the mGPS, as a prognostic factor, improves the survival rate of stage IV CRC patients who did not undergo surgery (HR 2.32, 95% CI 1.38–3.90).[10,11]

Albumin infusion is a treatment option for patients with hypoalbuminemia; patients with albumin deficiency may benefit from this therapy, especially if they are unconscious, vomiting frequently, or having difficulty swallowing. However, this therapy has drawbacks due to its high cost and limited availability. Low albumin levels can alternatively be treated with oral albumin, which offers similar potential benefits while being more cost-effective.[12]

Oral albumin supplementation has long been used. Syamsiatun found that administering egg white juice three times a day—containing 144.8 kcal and 8.3 grams of protein per serving—can effectively increase albumin levels. Boiled or blended egg white preparations are the most economical,

but they have limitations due to their unpleasant taste and odor, especially when consumed in large quantities; furthermore, neither form can be stored for long and must be consumed immediately. Another form is ready-to-drink (RTD) preparations, which are convenient to consume. Egg white supplements in powder form are more suitable for use in hospitals. The powder form is considered more practical, more flexible (it can be used on its own or as an addition to meals), and has a longer shelf life. A study conducted at Dr. Saiful Anwar Hospital in East Java found a significant difference in albumin levels between sepsis patients in the ICU who were given powdered albumin (egg white extract) and sepsis patients in the ICU who were given only a standard diet without powdered albumin (egg white extract).[13–15]

Elderly patients with hypoalbuminemia who were given *Ophiocephalus striatus* extract showed an increase in albumin levels. The high dose of albumin found in the ready-to-drink *Ophiocephalus striatus* extract serves as a source of the amino acids needed for albumin synthesis in the body. An increase in albumin levels (≥3.5 g/dL) following administration of the *Ophiocephalus striatus* extract indicates a favorable prognosis.[16,17]

Based on the above findings, the researchers were interested in investigating the administration of oral albumin (egg white extract and *Ophiocephalus striatus* extract), particularly in patients with CRC at Dr. Saiful Anwar Regional General Hospital in East Java.

A. Research Questions

General research question. How does oral albumin administration affect the Modified Glasgow Prognostic Score in colorectal cancer patients treated at Dr. Saiful Anwar Regional General Hospital in East Java?

Specific research questions. The specific research questions were as follows:

1. Is there a correlation between albumin levels and the administration of oral albumin (egg white extract) in colorectal cancer patients?
2. Is there a correlation between albumin levels and the administration of oral albumin (*Ophiocephalus striatus* extract) in colorectal cancer patients?
3. Is there a correlation between blood CRP levels and oral albumin administration (*Ophiocephalus striatus* extract) in colorectal cancer patients?
4. Is there a correlation between blood CRP levels and oral albumin administration (egg white extract) in colorectal cancer patients?
5. Is there a prognostic impact on colorectal cancer patients treated at Dr. Saiful Anwar Regional General Hospital in East Java as assessed by the Modified Glasgow Prognostic Score?

B. Objectives of the Study

General objective. To determine the relationship between oral albumin administration and the Modified Glasgow Prognostic Score in colorectal cancer patients treated at Dr. Saiful Anwar Regional General Hospital in East Java.

Specific objectives. The specific objectives were as follows:

1. To determine the relationship between albumin levels after oral albumin administration (egg white extract) compared to patients who did not receive an oral albumin diet in colorectal cancer patients.
2. To determine the relationship between albumin levels after oral albumin administration (*Ophiocephalus striatus* extract) compared to patients who did not receive an oral albumin diet in colorectal cancer patients.
3. To determine the relationship between blood CRP levels after oral albumin administration (*Ophiocephalus striatus* extract) compared to patients who did not receive an oral albumin diet in colorectal cancer patients.
4. To determine the relationship between blood CRP levels after oral albumin administration (egg white extract) compared to patients who did not receive an oral albumin diet in colorectal cancer patients.
5. To determine the prognosis of colorectal cancer patients treated at Dr. Saiful Anwar Regional General Hospital in East Java using the Modified Glasgow Prognostic Score.

C. Research Hypothesis

The administration of oral albumin (egg white extract and *Ophiocephalus striatus* extract) as a nutritional supplement will increase albumin levels and lower serum CRP, resulting in a low mGPS score in colorectal cancer patients treated at Dr. Saiful Anwar Regional General Hospital in East Java.

D. Significance of the Study

Academic benefits. The academic benefits of this study were as follows:

1. To contribute to the literature on the benefits of oral albumin on the prognosis of colorectal cancer as assessed by the Modified Glasgow Prognostic Score in colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital, East Java.
2. To determine the effect of oral albumin administration on the Modified Glasgow Prognostic Score in colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital, East Java.
3. To determine the effect of oral albumin administration on albumin levels in colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital, East Java.
4. To determine the effect of oral albumin administration on CRP levels in colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital, East Java.

Practical benefits. The practical benefits of this study were as follows:

1. Reducing the cost of care for colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital in East Java.

2. Identifying alternatives to provide a favorable prognosis for colorectal cancer patients at Dr. Saiful Anwar Regional General Hospital in East Java.

LITERATURE REVIEW

A. Colorectal Cancer

Definition and epidemiology

Malignancy is a disease characterized by uncontrolled abnormal cell division. Colorectal cancer occurs when uncontrolled cell division takes place in the colon or rectum. Colorectal cancer can be divided into three anatomical locations: proximal colorectal cancer, which generally includes cancer of the cecum, ascending colon, hepatic flexure, and transverse colon; distal colorectal cancer, which includes the descending colon and sigmoid colon; and rectal cancer, in which the splenic flexure is classified based on its proximal or distal location.[18,19]

In 2020, an estimated 104,610 new cases of colon cancer and 43,340 cases of rectal cancer were diagnosed in the United States. Although most colorectal cancers occur in adults aged 50 and older, 17,930 (12%) were diagnosed in individuals under the age of 50, equivalent to 49 new cases per day. An estimated 53,200 people will die from colorectal cancer in 2020, including 3,640 men and women under the age of 50. The high rate of misclassification is partly due to a misconception among some people that the terms "colon cancer" and "colorectal cancer" mean the same thing, stemming from the widespread use of "colon cancer" to refer to both colon and rectal cancers. In Indonesia, the incidence of colorectal cancer was recorded at 396,914 new cases with 234,511 deaths, ranking as the fourth most common type of cancer in the country.[18,20]

Risk factors

In the United States, more than half (55%) of all colorectal cancers are caused by lifestyle factors, including an unhealthy diet, lack of physical activity, high alcohol consumption, and smoking. These behaviors are typically associated with high-income countries, where colorectal cancer incidence rates are the highest. Globally, the rise in colorectal cancer incidence is considered a marker of economic transition. Importantly, however, several studies show that people with healthy lifestyle behaviors have a 27% to 52% lower risk of colorectal cancer compared to individuals with unhealthy lifestyles. Colorectal cancer risk factors can be classified into modifiable and non-modifiable risk factors.[18,21,22]

Non-modifiable risk factors: hereditary and family history. Up to 30% of colorectal cancer patients have a family history of the disease, making it one of the most important and investigable risk factors. Individuals with a first-degree relative (parent, sibling, or child) who has been diagnosed with colorectal cancer have a 2- to 4-fold higher risk of developing the disease compared to those without such a family history, with a higher likelihood of being diagnosed before the age of 50. However, a history of colorectal cancer in distant relatives also increases the risk, as does a family history (first- or second-degree relatives) of adenomas. Most cases of colorectal cancer that run in families are thought to reflect an interaction between lifestyle factors and the cumulative effects of relatively common genetic variations that increase the risk of the disease.[18,23]

The most common hereditary risk factor for colorectal cancer is Lynch syndrome, which accounts for about 3% of all colorectal cancers. Individuals with Lynch syndrome are also at higher risk for other cancers, including endometrial, ovarian, small intestine, stomach, and bladder cancers, among others. These individuals have mutations in specific genes that impair the cells' ability to repair errors that occur during DNA replication. These errors result in additional mutations that can ultimately lead to cancer, the likelihood of which depends on which genes are affected. Among the 80% of Lynch syndrome patients with high-risk gene mutations (MLH1 or MSH2), 19% to 25% will develop colorectal cancer by age 50, and 40% will develop the disease by age 70. The average age at diagnosis of colorectal cancer in patients with Lynch syndrome is 61 years, and 8% of colorectal cancers occurring in adults under the age of 50 are caused by Lynch syndrome. About 1% of colorectal cancer patients have inherited mutations in the breast cancer susceptibility genes BRCA1 and/or BRCA2, which are among the most extensively studied cancer predisposition genes. A study of colorectal cancer patients under the age of 50 also found a prevalence of 1%. In addition to breast cancer, these mutations increase the risk of ovarian, prostate, and pancreatic cancers. Although their effect on colorectal cancer risk is not significant, it has been well studied; a recent review reported a limited association among BRCA1 mutation carriers, who have a 50% increased risk of the disease compared to individuals without the mutation.[18,24–26]

Polyposis syndromes are another type of hereditary condition associated with an increased risk of colorectal cancer; the most common is familial adenomatous polyposis (FAP), which accounts for about 1% of all colorectal cancer cases. FAP is characterized by the development of up to thousands of polyps during the second and third decades of life. This is typically caused by a mutation in the adenomatous polyposis coli (APC) gene, which normally prevents uncontrolled cell growth and division. These mutations are usually inherited, but occur spontaneously in 10% to 25% of affected individuals, so the condition does not always run in families. The severity of the disease ranges from severe (classic FAP) to mild (attenuated FAP); the latter is associated with a later age of onset and fewer polyps (<100), yet it still carries a high lifetime risk of colorectal cancer.[18,27]

Non-modifiable risk factors: past medical history. People with a history of colorectal cancer are more likely to develop colon or rectal cancer, especially when the initial diagnosis was made at a young age. A history of adenomatous polyps also increases the risk of colorectal cancer, particularly multiple polyps or large polyps. The risk of colorectal cancer is also elevated among individuals with a history of other types of cancer due to the carcinogenic effects of certain treatments. Examples include childhood cancer survivors, particularly those who received radiation therapy to the pelvic or

abdominal area or to the whole body, or certain medications (e.g., cisplatin, procarbazine); men who received radiation therapy for prostate cancer; and men who underwent platinum-based chemotherapy for testicular cancer.[18,28,29]

Inflammatory bowel disease (IBD) is a lifelong condition, typically diagnosed in early adulthood, in which the digestive tract experiences long-term inflammation. People with IBD have twice the risk of developing colorectal cancer compared to the general population. The most common forms of IBD are ulcerative colitis and Crohn's disease. The risk of cancer increases with the extent, duration, and severity of the disease, but decreases over time, most likely due to the increased use of medications to treat inflammation. Two recent meta-analyses reported a 33% to 50% reduction in colorectal cancer risk among individuals with ulcerative colitis, but no such effect was observed in those with Crohn's disease. IBD has been diagnosed in approximately 3.1 million Americans and is most common among non-Hispanic whites, women, and those with the lowest levels of education. Although surveillance data in the U.S. are limited, the prevalence appears to have increased in recent years.[18,30,31]

Modifiable risk factors: physical activity. Physical activity is strongly associated with a reduced risk of colon cancer, but not with rectal cancer. Studies consistently show that people who are most physically active have a 25% lower risk of developing proximal and distal colon cancer compared to individuals who are less physically active. Sedentary individuals (for example, those who spend most of their time watching TV) have a 25% to 50% increased risk of colon cancer compared to individuals who rarely exercise. However, sedentary individuals who become active later in life can reduce this risk. Additionally, people who were more physically active before a colorectal cancer diagnosis are less likely to die from the disease than less active individuals. Based on these findings, as well as the many other health benefits of regular physical activity, the American Cancer Society and the Centers for Disease Control and Prevention (CDC) recommend that adults engage in at least 150 to 300 minutes of moderate-intensity activity or 75 to 150 minutes of vigorous-intensity activity each week (or a combination of both), preferably spread throughout the week, and limit the time spent on sedentary activities such as watching television.[18]

Modifiable risk factors: obesity. Excess body weight increases the risk of colorectal cancer, even among those who are physically active. Compared to people of normal weight, obese men have a 50% higher risk of colon cancer and a 25% higher risk of rectal cancer, while obese women have a 10% increased risk of colon cancer and no increased risk of rectal cancer. This increased risk is also associated with higher levels of abdominal fat, as measured by waist circumference or waist-to-hip ratio, and fat stored in the abdomen is independent of body mass index and waist circumference. Thus, abdominal fat specifically may be more important than overall body weight in influencing the risk of colorectal cancer. Higher body weight, even within the normal range, appears to increase the risk of early-onset colorectal cancer (before age 50), at least in women.[18,32,33]

Modifiable risk factors: diet. Most studies have found that calcium intake from dairy products and/or supplements is associated with a reduced risk of developing adenomas and colorectal cancer, although the mechanism remains unclear. Adequate calcium intake (approximately 700–1,000 mg/day) appears to provide protection, with limited additional benefits from higher intakes. Folate intake, whether from food or supplements, appears to have a complex relationship with colorectal cancer risk, potentially inhibiting the formation of new tumors in healthy tissue.[18,34]

Pathophysiology

A relevant concept that has emerged in recent years is the key role of the inflammatory process in the tumorigenesis, progression, and metastasis of colorectal cancer. The induction of an inflammatory state in the colorectal mucosa is influenced by environmental factors or dietary patterns that can trigger colorectal carcinogenesis. High consumption of alcohol or red meat can alter the composition of the gut microbiota—a condition known as dysbiosis—characterized by a decrease in commensal bacterial species (i.e., butyrate-producing bacteria) and an increase in harmful bacterial strains (i.e., pro-inflammatory opportunistic pathogens). In addition to playing a role in the initiation of colorectal cancer, dysbiosis also appears to be involved in resistance to certain chemotherapy agents, due to its ability to modulate the immune response, and is associated with shorter cancer-specific survival. Therefore, probiotics, prebiotics, or antibiotics capable of restoring the normal balance of the gut microbiota (eubiosis) may offer a pathway for the prevention or management of colorectal cancer.[35,36]

The potential role of inflammation in the development of colorectal cancer is also indicated by the prognostic significance of blood neutrophil counts in patients with neoplasms. A high neutrophil-to-lymphocyte ratio (H-NLR) was found to be significantly associated with shorter overall survival in patients with non-metastatic colorectal cancer at the time of diagnosis (pathological TNM Stages I and II). The mechanism by which a high H-NLR may influence disease progression requires further investigation; however, its association with histopathological features related to tumor dedifferentiation (e.g., poorly differentiated tumors) suggests that an inflammatory state may induce the activation of pathways linked to the epithelial-mesenchymal transition in colorectal cancer.[37]

Mutations in certain genes can lead to the development of colorectal cancer, as is the case with other types of cancer. These mutations can occur in oncogenes, tumor suppressor genes, and genes associated with DNA repair mechanisms. Depending on the origin of the mutation, colorectal carcinoma can be classified as sporadic, hereditary, or familial. Cancers arising from point mutations are called sporadic cancers and account for 70% of all colorectal cancers. The molecular pathogenesis of sporadic cancer is heterogeneous because mutations can target different genes. However, about 70% of colorectal cancer cases follow a specific sequence of

mutations that translates into a specific morphological progression, beginning with the formation of an adenoma and ending in carcinoma. The first mutation occurs in the adenomatous polyposis coli (APC) gene, a tumor suppressor gene that triggers the formation of non-malignant adenomas, also known as polyps. It is estimated that about 15% of these adenomas will progress to carcinoma within ten years. This APC mutation is followed by mutations in KRAS, TP53, and DCC. The majority of sporadic colorectal cancers (nearly 85%) arise from adenomas characterized by chromosomal instability (CIN), a negative CpG island methylation phenotype (CIMP), microsatellite stability (MSS), and KRAS mutations with BRAF wild-type (wt). The remaining 15% of colorectal cancers originate from serrated adenomas and are characterized by high CIMP, microsatellite instability (MSI), and BRAF mutations (Figure 1).[38,39]

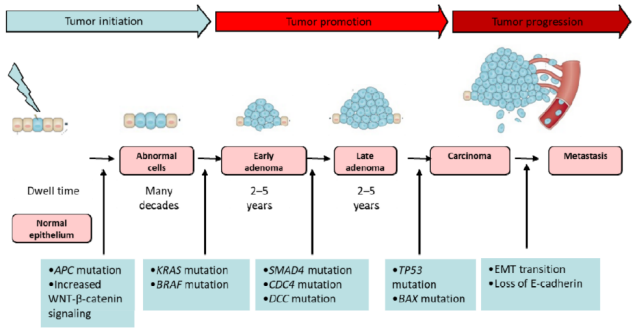


Figure 1: Mechanism of colorectal cancer carcinogenesis. APC, adenomatous polyposis coli; EMT, epithelial–mesenchymal transition.[39]

Hereditary cancers account for only 5% of all colorectal cancer cases. These cancers are caused by inherited mutations that affect one allele of a mutated gene, meaning that a point mutation in the other allele will trigger the emergence of tumor cells and, subsequently, carcinoma. Hereditary colorectal cancer is classified into two groups: polyposis and non-polyposis. The polyposis variant primarily involves familial adenomatous polyposis (FAP), which is characterized by the formation of multiple potentially malignant polyps in the colon. In contrast, hereditary non-polyposis colorectal cancer (HNPCC) is associated with mutations in DNA repair mechanisms. The primary cause of HNPCC is Lynch syndrome, which is caused by an inherited mutation in one of the alleles encoding DNA repair proteins such as MSH2, MLH1, MLH6, PMS1, and PMS2. Lynch syndrome accounts for 2%–3% of all colorectal cancer cases and is therefore the most common syndrome within the HNPCC group. Familial colorectal cancer accounts for approximately 25% of all cases and is also caused by inherited mutations, although it is not classified as a hereditary cancer because it does not fit into any of the categories of hereditary cancers.[38]

Diagnosis

Almost all colorectal cancers are diagnosed using colonoscopy, even in asymptomatic patients. Patients diagnosed through routine cancer screening are often at an earlier stage compared to those with advanced disease discovered incidentally during surgery. Diagnostic colonoscopy is usually performed when patients present with rectal bleeding (37%), abdominal pain (34%), and anemia (23%). The most common indications for emergency surgery are obstruction (57%), peritonitis (25%), and perforation (18%). The location of the tumor in the clinical presentation can be roughly distinguished as being on the left side—with more complaints related to changes in bowel habits and hematochezia—and suspected to be on the right side when accompanied by anemia with an unclear source of bleeding. CRC diagnosis is currently performed via colonoscopy, which has been recognized as the "gold standard" due to its potential for diagnosing and removing adenomas. However, colonoscopy is an uncomfortable and invasive diagnostic procedure for patients; it requires advance preparation, and patients are allowed only clear liquids 12 hours before the procedure. Consequently, many patients do not comply with the procedure because it is extremely uncomfortable, and in some cases, patients refuse to undergo it.[40,41]

The current use of molecular biomarkers in the detection of colorectal cancer is very limited. The only serum biomarker for colorectal cancer tested in the United Kingdom is carcinoembryonic antigen (CEA) (UniProtKB ID Q13982). However, CEA is not routinely tested in clinical practice worldwide to aid in the diagnosis of colorectal cancer because its levels can be elevated in various other inflammatory conditions such as diverticulitis and inflammatory bowel disease. CEA levels may also be elevated in other cancers, such as pancreatic cancer. CEA has poor sensitivity but very good specificity. Therefore, CEA is tested in patients known to have colorectal cancer to monitor their response to treatment following chemotherapy or to detect disease recurrence after therapy is completed. One limitation of CEA-based diagnosis is the lack of a direct correlation between the degree of CEA elevation and prognosis or disease spread. Currently, there are no other suitable molecular diagnostic biomarkers used for colorectal cancer screening. Another biomarker, KRAS (UniProtKB ID P01116), is used to guide adjuvant therapy in colorectal cancer.[42–44]

Treatment

Currently, various treatment strategies for colorectal cancer include surgery, chemotherapy, radiation therapy, targeted therapy, immunotherapy, and nutritional therapy. These treatments can be categorized into local therapy, systemic therapy, and combined therapeutic approaches, and their application depends on the tumor stage. Local therapy is treatment that targets only the tumor without affecting the entire body. This approach is more effective for early-stage cancer but may also be used in certain other situations. Types of local therapy used for colorectal cancer include surgery, ablation, embolization, and radiation. The most common surgical procedure is surgical resection, which is effective for removing solid malignant tumors in the early stages and when the tumor is clearly defined, but is not as effective in advanced stages. In colorectal cancer, a portion of the healthy colon or rectum and the surrounding lymph nodes may be removed.[39,45]

Systemic therapy includes chemotherapy, targeted therapy, and immunotherapy. Chemotherapy uses drugs to destroy cancer cells, typically by stopping the cancer cells' ability to

grow and divide. Depending on the type of colorectal cancer, various types of drugs may be used, either orally or injected directly into a blood vessel. Chemotherapy currently includes single-agent therapy, which is largely based on fluoropyrimidine (5-FU), and multi-agent regimens containing one or more drugs, including oxaliplatin (OX), irinotecan (IRI), and capecitabine (CAP or XELODA or XEL). The fluoropyrimidine 5-fluorouracil (5-FU), an analog of thymine and a DNA replication inhibitor, has been widely used in the treatment of colorectal cancer. Currently, 5-FU regimens are classified into three groups: 5-FU prodrugs such as Tegafur and Capecitabine, 5-FU prodrugs combined with dihydropyrimidine dehydrogenase inhibitors, and 5-FU combined with dihydropyrimidine dehydrogenase inhibitors. Since the early 2000s, irinotecan (a topoisomerase I inhibitor) has been introduced into oncological practice, along with oxaliplatin (a DNA cross-linker). On the other hand, cytotoxic drugs kill healthy, rapidly dividing cells such as white blood cells, red blood cells, and platelets. This necessitates the simultaneous administration of leucovorin, a vitamin that boosts blood cell production and enhances treatment efficacy during standard chemotherapy for colorectal cancer.[39,45,46]

Albumin is a water-soluble protein that has been approved by the FDA for use in humans. Albumin is the most abundant protein in the blood and accounts for about half of the total protein in plasma. Because albumin is endogenous, nanoparticles made from albumin exhibit excellent biocompatibility, including non-toxicity, low immunogenicity, and appropriate biodegradation. Because albumin has three homologous domains capable of interacting with various drugs, it is considered to have a high drug-binding capacity. Furthermore, anticancer agents are typically released from albumin nanoparticles with a characteristic sustained-release profile, improving the pharmacokinetics and utilization of the drug. Albumin-based paclitaxel formulations (Abraxane®) have been approved by the FDA for the treatment of metastatic breast cancer, non-small cell lung cancer, and pancreatic adenocarcinoma. In recent years, efforts have been made to utilize albumin-based drugs to treat colon cancer. Thao et al. developed albumin nanoparticles for the delivery of doxorubicin and TRAIL in colon cancer.[47–49]

Prognosis

The prognosis for colorectal cancer is poor, and its mortality rate ranks third among all cancers worldwide. Surgery is the primary treatment for colorectal cancer. Accurate assessment of surgical prognosis plays a crucial role in the management of patients with colorectal cancer. Studies have shown that a high Glasgow Prognostic Score (GPS) in colorectal cancer is more likely to predict a poor prognosis. The findings of Arfa et al. indicate that the tumor-node-metastasis (TNM) stage is associated with the prognosis of colorectal cancer. A study conducted by Kanemitsu et al. has shown that histological type and tumor differentiation grade can influence biological behavior and, consequently, clinical outcomes. In addition, research has found that the in vivo inflammatory response can impact tumor initiation and progression. Serum C-reactive protein, albumin, the C-reactive protein-to-albumin ratio (CAR), and the neutrophil-to-lymphocyte ratio (NLR) are potential indicators of complications related to the inflammatory process and have a negative impact on the prognosis of colorectal cancer patients.[50–54]

B. The Role of CRP in Colorectal Cancer

The systemic inflammatory response (SIRS) plays a complex and multifaceted role in the pathophysiology of cancer. A meta-analysis of several studies indicates that SIRS can be used to predict disease progression and outcomes for various types of malignancies. Recent studies have shown that several systemic inflammatory biomarkers, such as the neutrophil-to-lymphocyte ratio, C-reactive protein (CRP), and the platelet-to-lymphocyte ratio, act as prognostic predictors in several types of malignant tumors, including colorectal cancer. Therefore, given their potential to predict prognosis, combinations of systemic inflammatory biomarkers can be used in disease management and follow-up to improve overall survival (OS) in colorectal cancer patients.[55–57]

CRP is a plasma protein that is highly conserved phylogenetically and plays a crucial role in SIRS. Its levels in peripheral blood rise rapidly during acute inflammation, infection, and tissue damage. In addition, plasma CRP concentrations increase moderately in cancer. Recently, numerous studies have reported that elevated circulating CRP levels are associated with a poorer prognosis in various malignancies, such as colorectal cancer, cervical cancer, renal clear cell carcinoma, bladder cancer, non-small cell lung cancer, and breast cancer. Furthermore, lymphocyte count is considered a prognostic predictor in several malignancies. In addition, lymphopenia is considered to have a significant impact on the survival of patients with metastatic solid tumors. All of the above indicate the prognostic role of CRP and lymphocyte count in malignant tumors. However, it remains unclear how the combination of these two factors can predict prognosis in colorectal cancer. CRP is an acute-phase protein synthesized by the liver. Elevated serum CRP concentrations have been shown to induce the production of cancer-associated inflammatory cytokines. Meanwhile, serum albumin levels are a general marker of nutritional status and are associated with chronic inflammation that activates cytokines such as IL-1 and TNF-α. Thus, the CRP/albumin ratio (CAR) can effectively reflect the potential inflammatory state caused by the expansion or invasion of the tumor microenvironment and is used as a simple and independent prognostic factor.[57–62]

Acute-phase proteins, including CRP, albumin, and the mGPS composite (mGPS0: serum CRP $\leq$ 10 mg/L and serum albumin $\geq$ 35 g/L or < 35 g/L; mGPS1: serum CRP > 10 mg/L and serum albumin $\geq$ 35 g/L; mGPS2: serum CRP > 10 mg/L and serum albumin < 35 g/L), are among the most widely studied prognostic parameters based on systemic inflammation in colorectal cancer. Several studies have reported that high circulating CRP levels, low albumin levels, and high mGPS scores are associated with poor patient outcomes. In addition, the blood differential leukocyte count is a definitive prognostic parameter in colorectal cancer. Myeloid cell proliferation, associated with the systemic response to colorectal cancer, leads to an increase in the

number of circulating neutrophils and monocytes relative to lymphocytes, which is associated with poor outcomes. Indices based on the relative proportions of these cell types represent promising prognostic parameters.[62–65]

C. Modified Glasgow Prognostic Score

The Glasgow Prognostic Score (GPS), a scoring system based on inflammation, has been shown to be an accurate predictor of prognosis in patients with colorectal cancer in several studies. This score is based on a combination of C-reactive protein (CRP) and serum albumin (ALB) levels. The GPS is determined based on the presence of hypoalbuminemia (<35 g/L) and elevated CRP (>10 mg/L): if both are abnormal, the score is 2; if one is abnormal, the score is 1; if neither is abnormal, the score is 0. Furthermore, additional studies have evaluated the prognostic role of the GPS in various types of cancer, such as pancreatic cancer, esophageal cancer, and hepatocellular carcinoma. In addition, some of these centers have implemented a modified Glasgow Prognostic Score (mGPS) to assess the prognosis of colorectal cancer patients.[66]

A recent study that simultaneously analyzed CAR and mGPS in the same cohort showed that both are independent prognostic factors for survival in patients with colorectal cancer. However, there are several systemic inflammatory serum markers, and the mechanisms by which they influence prognosis may differ. Therefore, it may be beneficial to combine nutrition- and inflammation-related prognostic factors to expand independent prognostic capacity and improve the accuracy of prognostic predictions. Laird et al. demonstrated that the combination of mGPS and performance status has higher prognostic accuracy in patients diagnosed with advanced-stage cancer. Inamoto et al. also reported that a combination of GPS and the neutrophil-to-lymphocyte ratio (NLR) can be used to effectively stratify patient outcomes, with patients having an NLR <2.05 and a GPS of 0 having a significantly better prognosis. mGPS is determined based on the presence of hypoalbuminemia (<35 g/L) and elevated CRP (>10 mg/L): if both are abnormal, the score is 2 (high risk); if one is abnormal, the score is 1 (moderate risk); if neither is abnormal, the score is 0 (low risk).[55,66,67]

D. Albumin Therapy in Colorectal Cancer

Albumin

Albumin is a globular protein commonly found in blood plasma, egg whites, milk, and plants. Serum albumin is the most abundant protein in blood plasma in all vertebrates. Albumin is synthesized in the liver as pre-pro-albumin and matures in the endoplasmic reticulum and Golgi apparatus before being secreted from hepatocytes. Human serum albumin (HSA) has a plasma concentration of 35–50 mg/mL with an estimated half-life of 19 days, and is present in both the extravascular and intravascular spaces. Albumin performs various important functions, such as regulating oncotic pressure and blood pH. Albumin also binds to and transports various bioactive molecules, including proteins, peptides, fatty acids, hormones, amino acids, drugs, nutrients, and metal ions. These properties make albumin an excellent candidate for several clinical and biotechnology applications. HSA is clinically used in cases of hemorrhagic shock caused by excessive blood loss, hypovolemia, hypoproteinemia, and fetal erythroblastosis. In addition, purified HSA is commonly used in eukaryotic cell culture. Over the past decade, HSA has been widely used as a nanoparticle for targeted drug delivery, for example, in the administration of doxorubicin to patients with colorectal cancer.[68]

Albumin is widely used as a drug delivery vehicle for various diseases due to its high serum concentration, long half-life, frequent recirculation, extensive accumulation in both benign and malignant tissues, non-toxicity, and lack of stimulation of the immune system. Albumin rapidly diffuses through the leaky blood vessels in tumors, making it ideal for delivering anticancer drugs. A wide variety of large and diverse drug molecules can be effectively bound to albumin-based nanoparticles (NPs). These albumin NPs have been shown to possess high drug entrapment capacity, controlled release, and high biocompatibility. Drug conjugation to albumin can be achieved by covalently linking therapeutic compounds to the N- or C-terminus of the protein or to other albumin amino acids using click chemistry, recombinant DNA technology, chemical cross-linking, or non-covalent interactions.[68,69]

Relationship between CRP and albumin

A study conducted in the United States showed, through multivariate regression analysis, that increased albumin levels are associated with decreased CRP levels. Albumin can bind to endogenous and exogenous ligands. Among other things, it binds to pro-inflammatory molecules. High-dose albumin administration can significantly reduce IL-6 levels in the blood of patients with hepatic cirrhosis. IL-6 is a cytokine that activates the transcription factor STAT3, which modulates CRP expression in the liver.[4–6]

Relationship between albumin and colorectal cancer

Serum albumin is a useful biomarker for many diseases. It has been associated with several acute, chronic, and neoplastic conditions, as well as in healthy populations, serving as a significant prognostic indicator. Many predictive models use baseline serum albumin (BSA) to determine or adjust therapy in specific contexts. In the context of colorectal cancer, BSA has been cited as a prognostic factor associated with survival and a predictor of morbidity and mortality following surgery. Malnutrition in colon cancer patients can result from a disease-induced increase in metabolic rate, reduced food intake, impaired hepatic protein synthesis, blood loss, etc. Serum albumin levels are frequently used, although they cannot comprehensively represent the nutritional status of colorectal cancer patients. It is generally recognized that hypoalbuminemia is a sign of malnutrition. Current research indicates that preoperative hypoalbuminemia is significantly associated with poor postoperative outcomes.[30,70,71]

Several published studies have examined the correlation between comorbidities and hypoalbuminemia. Hospitalized patients with mild hypoalbuminemia (albumin 25–35 g/L) have a lower body mass index, are older, and have higher rates of hypertension, congestive heart failure, and chronic kidney disease compared to patients with normal albumin levels.

Acute kidney injury is strongly associated with severe hypoalbuminemia, which is found in 4% of patients with chronic obstructive pulmonary disease. In individuals with chronic heart failure, the prevalence of hypoalbuminemia ranges from 20% to 25%, rising to 90% in elderly patients with acute heart failure. A study by Christina et al. found that hypoalbuminemia correlates with various comorbidities in patients with colorectal cancer. Early detection of malnutrition in individuals with multiple comorbidities is recommended because even mild hypoalbuminemia is associated with a higher risk of postoperative complications.[71–73]

Hypoalbuminemia is associated with overall survival and cancer-specific survival, which are closely linked to the systemic inflammatory response. Therefore, hypoalbuminemia objectively reflects nutritional and inflammatory status and provides prognostic value in addition to markers of the systemic inflammatory response.[9]

In a recent study of colorectal cancer patients who underwent surgery, approximately 30% had hypoalbuminemia, 25% showed evidence of a systemic inflammatory response, and 50% had a low skeletal muscle index (SMI) prior to surgery. Therefore, even in early-stage cancer, there is evidence of hypoalbuminemia, systemic inflammation, and sarcopenia. Although the relationship between albumin and the systemic inflammatory response has been repeatedly demonstrated in both acute and chronic inflammation, there is limited data regarding the relationship between albumin and body composition. There is a link between chronic activation of the systemic inflammatory response and catabolic loss of muscle protein in patients with colorectal cancer. It is known that proinflammatory cytokines such as interleukin-6 (IL-6), interleukin-1 (IL-1), tumor necrosis factor (TNF), and growth factors (GF) are released as part of a systemic inflammatory response that has a significant catabolic effect on tissue metabolism. For example, IL-6 stimulates the production of CRP and other acute-phase proteins in the liver, thereby increasing the demand for amino acids—the intake of which is often limited in cancer patients. Specifically, low circulating concentrations of glutamine (the most abundant amino acid in plasma) have been reported to be associated with hypoalbuminemia, low SMI (the primary source of glutamine), and poorer survival in patients with colorectal cancer.[9,63,74]

Effect of albumin on the modified Glasgow Prognostic Score in colorectal cancer

The combination of C-reactive protein and albumin, known as the Glasgow Prognostic Score (GPS), has been reported to be useful in assessing the nutritional risk of cancer patients and has been used to predict survival in patients with various diseases. Therefore, overall, the literature indicates a close relationship between nutritional risk and the systemic inflammatory response in cancer patients and suggests that if one is measured, the other should also be measured. There are apparent parallels with studies conducted to examine micronutrient status in health and disease. Indeed, the combination of C-reactive protein and albumin has been used for evaluation in cancer patients. This may point to a fundamental relationship between metabolism and inflammatory processes in cancer patients, as there is a close evolutionary link between immune and metabolic responses in all mammalian cells, known as immunometabolism.[9,55,75]

A study by Liao et al. found that replacing plant-based protein with animal protein—particularly red meat protein—was associated with a lower risk of colorectal cancer. Replacing plant-based protein with red meat protein was associated with an 11% reduction in the risk of colorectal cancer, with a similar reduction observed for distal colon cancer and rectal cancer. When further evaluated by protein source, the statistically significant inverse association with colorectal cancer risk was limited to the substitution of protein from bread, cereals, and pasta with red meat protein, suggesting that the source of protein influences colorectal cancer risk. This inverse association was stronger for distal colon and rectal cancers but was not observed for proximal colon cancer. Hypoalbuminemia is considered an indicator of malnutrition and cachexia. Two studies showed that hypoalbuminemia is associated with a poor prognosis in various types of cancer, including colorectal cancer. The GPS or mGPS scoring system explains that a poor prognosis in colorectal cancer patients is caused by systemic inflammation or malnutrition. Consequently, it is concluded that to prevent a poor prognosis, nutritional interventions are needed to prevent hypoalbuminemia, thereby improving prognosis.[66,76,77]

In hospitals, patients' albumin levels can generally be increased through intravenous administration of albumin solutions and a high-protein diet. Intravenous albumin administration is rarely performed because it is expensive and therefore unaffordable for the lower- and middle-income populations; it is typically administered only when albumin levels fall below 2.0 g/dl. A study by Bektiwibowo and colleagues found that the administration of the Nutren Junior® enteral formula for children, manufactured by PT. Nestlé Indonesia, resulted in an average weight gain of 130 ± 100 g, an increase in the average albumin level of 0.16 ± 0.35 g/dL, and an increase in the average prealbumin level of 2.37 ± 3.88 mg/dL. After 5 days of enteral nutrition, both the well-nourished and malnourished groups showed improvements.[13,78]

Relationship between egg white extract and hypoalbuminemia

Egg whites are a high-quality source of protein that can effectively increase serum albumin levels. Research has shown that egg whites contain high concentrations of albumin, which is the most abundant protein found in blood plasma. When consumed, the amino acids from egg white albumin are easily absorbed and used by the liver to synthesize new albumin.

The mechanism by which egg white protein increases serum albumin involves the digestion and absorption of amino acids. In the stomach, egg white protein is broken down by the enzyme pepsin into smaller peptides and free amino acids. These are then further hydrolyzed by enzymes such as trypsin and chymotrypsin in the small intestine. The free amino acids and small peptides can then be transported across the intestinal

epithelium and into the bloodstream, where they become available for the liver to use in the synthesis of albumin. Egg whites help stimulate the production of new albumin to restore normal serum levels in individuals with hypoalbuminemia.[79]

Relationship between snakehead fish extract and hypoalbuminemia

Snakehead fish (*Channa striata*) effectively increases albumin levels in patients with hypoalbuminemia. The high protein content and amino acid profile of snakehead fish extract provide the building blocks necessary for albumin synthesis in the liver. The extract contains essential amino acids such as leucine, which can activate the mammalian target of rapamycin (mTOR) pathway, ensuring adequate plasma albumin levels. In addition, the mineral content of snakehead fish, including zinc, iron, and copper, supports various enzymatic processes involved in albumin production. The unsaturated fatty acids present in the extract also possess anti-inflammatory properties, which can help reduce the inflammation that often accompanies hypoalbuminemia.

In addition, snakehead fish extract has been shown to modulate the immune system in patients with hypoalbuminemia. The extract can reduce the number of neutrophils—which increase during inflammation—and increase the number of lymphocytes. The albumin, amino acids, and antioxidants in the extract help balance the immune response, reducing inflammation that can contribute to decreased albumin levels. By addressing both the nutritional and inflammatory aspects of hypoalbuminemia, snakehead fish extract offers a comprehensive approach to managing this condition and improving patient outcomes.[80]

Relationship between hypoalbuminemia and CRC

Hypoalbuminemia has been shown to have a significant prognostic impact in colorectal cancer. According to a study by Nazha et al., lower pre-treatment serum albumin levels were associated with poorer overall survival outcomes. A study by Heys et al. showed a 25% increase in the risk of death for every 0.5 g/dL decrease in serum albumin. Preoperative hypoalbuminemia is also associated with higher rates of postoperative complications and mortality in CRC patients undergoing curative surgery.[7]

Research indicates that the association between low albumin levels and a poorer prognosis reflects an underlying systemic inflammatory response rather than merely nutritional deficiency. The association between hypoalbuminemia and poor outcomes becomes more consistent when albumin is considered alongside the inflammatory marker C-reactive protein in the modified Glasgow Prognostic Score. Research also shows that a low albumin-to-globulin ratio, which indicates a pro-inflammatory state, is also associated with poorer survival in colorectal cancer. This study suggests that a systemic inflammatory response, rather than malnutrition, is the primary cause of the poor prognosis observed in CRC patients with low serum albumin levels.[7]

Relationship between CRP and mGPS in CRC patients

Colorectal cancer (CRC) ranks as the third most commonly diagnosed cancer globally, accounting for 11% of all cancer cases. In patients with CRC, systemic inflammation emerges as a significant predictor of survival. Although the exact mechanism remains unclear, increased systemic inflammation correlates with impaired nutritional status, function, and immune function in patients. The Modified Glasgow Prognostic Score (mGPS) stands out as a widely validated tool for prognostic assessment, showing that higher mGPS scores are associated with poor outcomes in various types of cancer, including CRC. Both mGPS and CAR are individual prognostic markers in CRC; however, the prognostic impact of their combination has not yet been clarified.[11]

C-reactive protein (CRP), an acute-phase protein synthesized in the liver along with other inflammatory cytokines, is involved in potential tumor development by stimulating the production of inflammatory cytokines and chemokines. Albumin, which accounts for half of the plasma protein content, reflects nutritional status and the inflammatory response. As an acute-phase protein, its levels or ratios are associated with other inflammatory markers. Thus, these two markers may indicate a balance between inflammation and nutritional status. Consequently, an increased C-reactive protein-to-albumin ratio (CAR) or mGPS often indicates a poorer prognosis. mGPS and CAR are easy to use in combination because they rely on the same laboratory variables.[11]

A recent study that simultaneously analyzed CAR and mGPS in the same cohort showed that they are independent prognostic factors for cancer-specific survival and overall survival in patients with colon cancer. However, there are several serum markers of systemic inflammatory status, and the mechanisms by which they influence prognosis vary. It would be beneficial to combine established nutrition- and inflammation-related prognostic factors to expand their independent prognostic capacity and improve the accuracy of prognostic predictions.[55]

E. Conceptual Framework

The conceptual framework of the present study is presented in Figure 2.

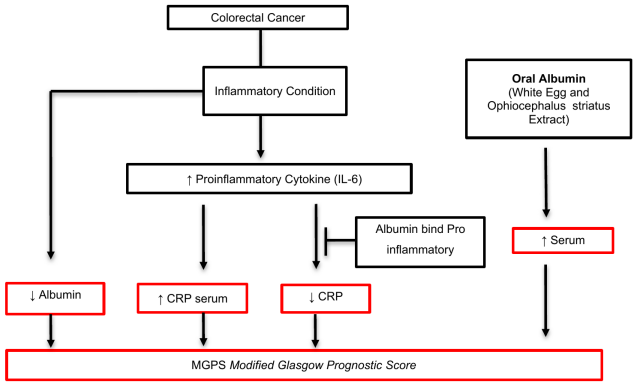


Figure 2: Conceptual framework. Red boxes, variables studied; black boxes, variables not studied. CRP, C-reactive protein; IL-6, interleukin-6; mGPS, modified Glasgow Prognostic Score.

Colorectal cancer patients experience chronic inflammation. Inflammation associated with colorectal cancer leads to

increased production of pro-inflammatory factors, one of which is IL-6, which plays a role in modulating the liver to produce CRP, thereby increasing serum CRP levels. IL-6 is believed to bind to albumin, which can lead to a decrease in serum IL-6 levels and, consequently, a decrease in serum CRP levels. The mGPS (Modified Glasgow Prognostic Score) is used as a prognostic measure for colorectal cancer patients. mGPS is defined as follows: mGPS 0 = CRP ≤ 10 mg/L and albumin ≥ 3.5 g/dL; mGPS 1 = CRP > 10 mg/L and albumin ≥ 3.5 g/dL; and mGPS 2 = CRP > 10 mg/L and albumin < 3.5 g/dL, where a lower mGPS score indicates a better prognosis. The administration of oral albumin, which can increase serum albumin levels and lower serum CRP levels, is expected to improve the prognosis of patients with colorectal cancer.

METHODS

A. Study Design

This study employed a true experimental design, specifically a case-control study, with the study population consisting of patients at Dr. Saiful Anwar Regional General Hospital in Malang.

B. Study Location and Period

The study was conducted in the low-care and high-care wards of Dr. Saiful Anwar Regional General Hospital in Malang, East Java. The study was conducted in August 2024 until the required sample size was reached.

C. Population, Sample and Eligibility Criteria

The population in this study consisted of patients admitted to the inpatient ward at Dr. Saiful Anwar General Hospital in Malang from April 2024 until the sample size was met. The sample comprised members of the population meeting the inclusion criteria.

Inclusion criteria were (1) patients diagnosed with stage I–III colorectal cancer who underwent surgery and had no liver disease, and who were treated at Dr. Saiful Anwar Regional General Hospital in Malang; (2) albumin levels >2.5 and <3.5; and (3) CRP levels <10 and CRP levels >10. Exclusion criteria were (1) the patient or family is unwilling; (2) stage IV colorectal cancer patients; (3) patients with chronic kidney disease; and (4) patients with chronic liver disease. Criteria for discontinuing the trial were (1) death during the study and (2) transfer of the patient to another hospital.

D. Sample Size

The representativeness of a sample relative to the population in a study is an essential requirement for generalization or inference. Essentially, the more homogeneous the values of the variables under study, the smaller the sample size required; conversely, the more heterogeneous the values of the variables under study, the larger the sample size required. In addition to population representativeness, another factor to consider when determining sample size is the requirements of the analysis. Some statistical analyses or tests require a specific minimum sample size for their application.

This paper discusses the determination of sample size with the goal of ensuring that the sample is representative of the population. Several factors to consider when calculating sample size are (1) type and design of the study; (2) purpose of the study/analysis; (3) population size or sample size; (4) population characteristics/sampling method (sampling technique); and (5) type (measurement scale) of data (dependent variable).

Under different conditions, the method for determining sample size also varies. Based on type, research is classified as observational or experimental. Based on the research objective or analysis, it is classified as descriptive or inferential (estimation or hypothesis testing). Based on the number of populations or samples, it is classified as involving a single population/sample or more than one population/sample. This is related to the characteristics of the population or the sampling method, which can be either random or non-random. Random sampling includes simple random, systematic random, stratified random, cluster random, and multistage random sampling. Based on the type of data or variables being analyzed, data can be categorized as categorical or continuous. The factors mentioned above significantly determine how the sample size is calculated. The formula for sample size is as follows:

$$n = N / (1 + N \cdot e^2)$$

where n is the minimum sample size, N is the population size, and e is the percentage margin of error due to sampling error that is still considered acceptable. Thus, the minimum sample size was calculated as $n = 86 / [1 + 86 (0.01)] = 30.22$, rounded to 30. Therefore, the minimum sample size was 30 people.[81]

E. Research Variables and Operational Definitions

The independent variables in this study were the administration of oral albumin (egg white extract and *Ophiocephalus striatus* extract). The dependent variables in this study were serum albumin and CRP levels in patients admitted to the Dr. Saiful Anwar Regional General Hospital in East Java. The operational definitions of the research variables were as follows:

1. Albumin is a protein found in blood plasma that is measured through an albumin test at the Clinical Pathology Laboratory of Dr. Saiful Anwar General Hospital in Malang, with results reported in grams per deciliter (g/dL).
2. C-reactive protein (CRP) is a protein found in blood plasma that is measured through a CRP test at the Clinical Pathology Laboratory of Dr. Saiful Anwar General Hospital in Malang, with results reported in milligrams per liter (mg/L).
3. Albumed Milk is a milk product containing egg white extract, sprouts, and other ingredients, produced by PT Medic Brivit and registered with the Ministry of Industry under Number 7487/SJ-IND.8/TKDN/12/2022, with a net weight of 30 grams per sachet.
4. Colorectal cancer (CRC) is a type of cancer that affects the large intestine (colon) or rectum. It is one of the most common types of cancer worldwide.[82]

5. The Modified Glasgow Prognostic Score (mGPS) is one of the most widely validated prognostic tools, with numerous studies reporting that a high mGPS is associated with poor prognostic outcomes in various types of cancer, including colorectal cancer (CRC). The mGPS is defined as follows: mGPS 0 = CRP ≤ 10 mg/L, mGPS 1 = CRP > 10 mg/L and albumin ≥ 3.5 g/dL, and mGPS 2 = CRP > 10 mg/L and albumin < 3.5 g/dL.[10,11]

F. Equipment and Materials

The equipment used comprised blood reagent chemical tubes and 5-cc syringes. The materials used comprised egg white extract and *Ophiocephalus striatus* extract.

G. Research Procedure

Patients at Dr. Saiful Anwar Regional General Hospital in East Java who met the inclusion criteria underwent measurements of their blood albumin and CRP levels. Patients in the control group were given a standard diet. Patients in the treatment group were given a standard diet and then received additional nutrition in the form of Albumed milk at a dose of 3 × 30 g for 14 days. Serum albumin and CRP levels were measured on day 0 and day 14 in both the control group and the treatment group. The research workflow is shown in Figure 3.

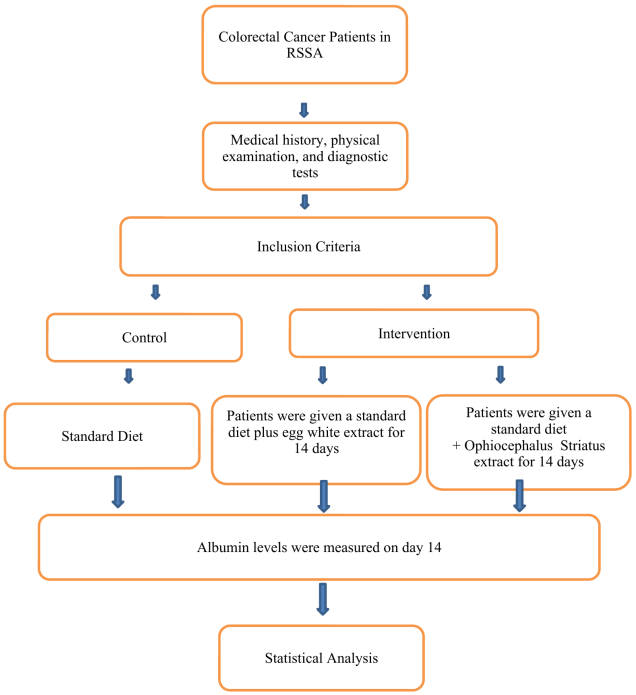


Figure 3: Research workflow. RSSA, Dr. Saiful Anwar Regional General Hospital.

H. Data Analysis

Data obtained from patients' demographic characteristics were analyzed using bivariate analysis (frequency tables, cross-tabulations, graphs, means, standard deviations, etc.) to determine the relationship between Albumed milk and CRP and albumin levels; to assess patients' mGPS, the Pearson correlation test was used. Results were considered statistically significant if the P-value was less than 0.05. To determine the effect of Albumed milk administration on CRP and albumin levels for assessing patients' mGPS, a regression test was used.

RESULTS

This study involved 30 colorectal cancer patients divided into three groups: the Albumed/egg white extract group, the *Ophiocephalus striatus* extract group, and the control group. Each group consisted of 10 patients, or 33.3% of the total study subjects. The variable analyzed was the Modified Glasgow Prognostic Score (mGPS) before and after the intervention.

A. Distribution of the mGPS Before and After the Intervention

The distribution of mGPS scores before the intervention showed that 15 patients (50.0%) were in the moderate category and 15 patients (50.0%) were in the high category. There were no patients in the low mGPS category in the pre-intervention measurement. After the intervention, there were 5 patients (16.7%) in the low mGPS category, 16 patients (53.3%) in the moderate category, and 9 patients (30.0%) in the high category (Table 1).

Table 1. Distribution of the mGPS Before and After the Intervention (n = 30)

mGPS category	Before, n (%)	After, n (%)
Low	0 (0.0)	5 (16.7)
Moderate	15 (50.0)	16 (53.3)
High	15 (50.0)	9 (30.0)
Total	**30 (100.0)**	**30 (100.0)**

mGPS, modified Glasgow Prognostic Score.

At the post-intervention assessment, the number of patients with high mGPS decreased from 15 patients (50.0%) to 9 patients (30.0%). Five patients (16.7%) were found to have low mGPS at the post-intervention assessment.

B. Changes in mGPS by Research Group

Changes in mGPS were categorized as improved, unchanged, and worsened. In the Albumed/egg white extract group, 6 patients (60.0%) showed improvement in mGPS, while 4 patients (40.0%) had unchanged mGPS. In the *Ophiocephalus striatus* extract group, 5 patients (50.0%) showed improvement in mGPS, while 5 patients (50.0%) had stable mGPS. In the control group, all patients had stable mGPS. There were no patients with worsening mGPS in any of the three groups (Table 2).

Table 2. Changes in mGPS by Research Group

Group	Improved, n (%)	Unchanged, n (%)	Worsened, n (%)	Total, n (%)
Albumed/egg white extract	6 (60.0)	4 (40.0)	0 (0.0)	10 (100.0)
Ophiocephalus striatus extract	5 (50.0)	5 (50.0)	0 (0.0)	10 (100.0)
Control	0 (0.0)	10 (100.0)	0 (0.0)	10 (100.0)
Total	**11 (36.7)**	**19 (63.3)**	**0 (0.0)**	**30 (100.0)**

mGPS, modified Glasgow Prognostic Score.

Overall, 11 patients (36.7%) showed improvement in mGPS, while 19 patients (63.3%) had stable mGPS scores. No patients experienced a worsening of mGPS.

C. Changes in mGPS Before and After the Intervention in Each Group

An analysis of changes in mGPS scores before and after the intervention in each group was conducted; the t-test could not be used due to the ordinal distribution of the mGPS data, so the Wilcoxon signed-rank test was used instead. In the Albumed/egg white extract group, there were 6 patients whose mGPS scores after the intervention were lower than before the intervention, 4 patients whose scores remained the same, and no patients whose mGPS scores increased. The analysis results showed a Z-value of −2.449 with a p-value of 0.014.

In the *Ophiocephalus striatus* extract group, there were 5 patients whose mGPS scores after the intervention were lower than before the intervention, 5 patients whose scores remained the same, and no patients whose mGPS scores increased. The analysis results showed a Z-value of −2.236 with a p-value of 0.025 (Table 3).

Table 3. Wilcoxon Signed-Rank Test for Changes in mGPS Before and After the Intervention

Group	Negative ranks	Positive ranks	Ties	Z	p
Albumed/egg white extract	6	0	4	−2.449	0.014
Ophiocephalus striatus extract	5	0	5	−2.236	0.025
Control	0	0	10	0.000	1.000

mGPS, modified Glasgow Prognostic Score.

Based on the results of the Wilcoxon signed-rank test, the p-values for the Albumed/egg white extract group (p = 0.014) and the kutuk fish extract group (p = 0.025) indicated statistically significant differences between mGPS scores before and after the intervention.

D. Comparison of Changes in mGPS Across Groups

Changes in mGPS between groups were analyzed using the Kruskal–Wallis test. The variable used was delta mGPS, which is the difference between mGPS values before and after the intervention. The results of the analysis showed a mean rank of 12.00 in the Albumed/egg white extract group, 13.50 in the kutuk fish extract group, and 21.00 in the control group. The results of the Kruskal–Wallis test showed an H value of 8.603 with a p-value of 0.014 (Table 4).

Table 4. Kruskal–Wallis Test for Changes in mGPS Across Groups

Group	n	Mean rank
Albumed/egg white extract	10	12.00
Ophiocephalus striatus extract	10	13.50
Control	10	21.00
Total	30	–
Kruskal–Wallis H = 8.603; df = 2; p = 0.014		

Delta mGPS = difference between mGPS values before and after the intervention. df, degrees of freedom; mGPS, modified Glasgow Prognostic Score.

Based on the results of the Kruskal–Wallis test, the p-value obtained was 0.014, indicating that there were statistically significant differences in changes in mGPS among the study groups.

E. Post Hoc Analysis Across Groups

Further intergroup analysis was performed using the Mann–Whitney U test. Comparisons were made between the Albumed/egg white extract group and the kutuk fish extract group, the Albumed/egg white extract group and the control group, and the kutuk fish extract group and the control group. Because there were three comparisons, the Bonferroni correction was applied with a significance threshold of $p < 0.0167$.

In the comparison between the Albumed/egg white extract group and the kutuk fish extract group, the values obtained were U = 45.000, Z = −0.438, and p = 0.661. In the comparison between the Albumed/egg white extract group and the control group, the values obtained were U = 20.000, Z = −2.854, and p = 0.004. In the comparison between the kutuk fish extract group and the control group, the values obtained were U = 25.000, Z = −2.517, and p = 0.012 (Table 5).

Table 5. Mann–Whitney U Test for Changes in mGPS Between Groups

Group comparison	U	Z	p	Interpretation
Albumed/egg white extract vs *Ophiocephalus striatus* extract	45.000	−0.438	0.661	Not significant
Albumed/egg white extract vs control	20.000	−2.854	0.004	Significant
Ophiocephalus striatus extract vs control	25.000	−2.517	0.012	Significant

Bonferroni-corrected significance threshold, $p < 0.0167$. mGPS, modified Glasgow Prognostic Score.

Based on the results of the Mann–Whitney U test with Bonferroni correction, the significance threshold for the post-hoc analysis was set at $p < 0.0167$. Based on this threshold, the comparison between the Albumed/egg white extract group and the kutuk fish extract group was not statistically significant (p = 0.661). The comparison between the Albumed/egg white extract group and the control group was statistically significant (p = 0.004), as was the comparison between the kutuk fish extract group and the control group (p = 0.012).

DISCUSSION

Colorectal cancer remains one of the malignancies with a substantial clinical burden. Bray et al. reported that in 2022 there were more than 1.9 million new cases of colorectal cancer and approximately 904,000 deaths worldwide. The magnitude of these figures makes colorectal cancer not only an oncological problem but also a nutritional, inflammatory and perioperative problem, because patients are often in an unstable metabolic condition both before and after cancer therapy.[83]

The discussion of these study results focuses on changes in the Modified Glasgow Prognostic Score (mGPS) following oral

albumin administration. The mGPS is an inflammation- and nutrition-status-based prognostic score that uses two main components: C-reactive protein (CRP) and albumin. A score of 0 indicates relatively favorable CRP and albumin levels; a score of 1 indicates elevated CRP or hypoalbuminemia; and a score of 2 indicates a combination of elevated CRP and hypoalbuminemia. Cotan et al. used a similar classification in patients with metastatic colorectal cancer, namely mGPS 0, 1, and 2 based on the combination of CRP and albumin.[84]

The study results showed a shift in mGPS categories following the intervention. Before the intervention, patients were in the moderate and high categories, with 15 patients (50.0%) in each category. After the intervention, the low category was observed in 5 patients (16.7%), the moderate category increased to 16 patients (53.3%), and the high category decreased to 9 patients (30.0%). These changes align with the biological basis of mGPS, as the score is designed to capture the balance between systemic inflammatory response and body protein status. Son et al. noted that both mGPS and the C-reactive protein/albumin ratio are derived from CRP and albumin components, and both have prognostic significance in colorectal cancer.[11]

In the Albumed/egg white extract group, an improvement in mGPS was observed in 6 out of 10 patients (60.0%), while 4 patients (40.0%) maintained the same score. In the kutuk fish extract group, an improvement was observed in 5 out of 10 patients (50.0%), while 5 patients (50.0%) maintained the same score. In the control group, all patients had unchanged scores. This pattern is quite relevant when considered in relation to the principles of nutritional therapy for cancer patients, as Muscaritoli et al. recommend periodic evaluation of nutritional intake, changes in body weight, body mass index, muscle mass, physical performance, and the degree of systemic inflammation from the time of cancer diagnosis.[85]

Analysis using the Wilcoxon signed-rank test revealed a statistically significant difference in mGPS scores before and after the intervention in the Albumed/egg white extract group ($p = 0.014$). In the kutuk fish extract group, the difference was also statistically significant ($p = 0.025$). In the control group, there was no statistically significant difference ($p = 1.000$). These results indicate that changes in scores were more pronounced in the group receiving oral albumin compared to the control group, although the assessment was limited to changes in mGPS scores.

Conceptually, a lower mGPS score indicates a better nutritional-inflammatory status compared to a higher score. Boukovala et al. noted that an increase in mGPS is associated with reduced cancer-specific survival, regardless of tumor location, tumor stage, performance status, or type of therapy. In the same article, a cited meta-analysis involving 2,227 colorectal cancer patients showed that an mGPS score of ≥1 was associated with worse overall survival, with a hazard ratio of 1.69, a 95% confidence interval of 1.40–2.04, and $p < 0.00001$.[86]

The association between mGPS and outcomes in colorectal cancer patients has also been reported in other analyses. Cotan et al. evaluated 65 patients with stage IV colorectal cancer and reported that mGPS 2 was associated with an increased risk of death, with a hazard ratio of 8.127, a 95% confidence interval of 3.241–12.239, and $p < 0.001$. In the same study, mGPS 2 was also associated with an increased risk of cancer progression, with a hazard ratio of 5.933, a 95% confidence interval of 4.762–10.338, and $p < 0.001$.[84]

Changes in mGPS in the intervention group do not imply that clinical outcomes such as overall survival, progression-free survival, complications, or length of hospital stay have directly changed. This score is more appropriately positioned as an inflammation-nutrition indicator. Yamamoto et al. explain that inflammatory biomarkers available from routine blood tests—including the neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, Glasgow Prognostic Score, and Prognostic Nutritional Index—have been extensively studied to predict the prognosis of colorectal cancer patients.[87]

A comparison of changes in mGPS among the three groups using the Kruskal–Wallis test yielded a p-value of 0.014, indicating a statistically significant difference among the groups at the 5% significance level. The mean rank value for the control group was higher than that of the Albumed/egg white extract and kutuk fish extract groups. For the mGPS delta variable, lower values indicate a decrease in score, while a value of 0 indicates no change in score. These results are consistent with the descriptive pattern, namely that improvement was found only in the intervention groups.

Further analysis using the Mann–Whitney U test with Bonferroni correction showed that the Albumed/egg white extract group differed significantly from the control group, with $p = 0.004$. The kutuk fish extract group also differed significantly from the control group, with $p = 0.012$. The significance threshold after the Bonferroni correction was $p < 0.0167$. The comparison between the Albumed/egg white extract group and the kutuk fish extract group was not significant, with $p = 0.661$. These results indicate that both forms of oral albumin are interventions with relatively similar trends in mGPS changes.

The similarity in the effects of the two interventions is biologically plausible, as both are aimed at improving protein status. Albumed/egg white extract is based on the protein albumin found in egg whites, while kutuk fish extract contains protein, amino acids, and other bioactive components. Muscaritoli et al. recommend a protein intake for cancer patients of more than 1 g/kg/day, and up to 1.5 g/kg/day if possible. This recommendation is based on the view that muscle protein synthesis in cancer patients remains responsive to amino acid supply.[85]

The lack of a statistically significant difference between the two intervention groups should also be interpreted with caution. The absence of a significant difference does not necessarily mean that the two interventions are biologically identical, as several confounding variables—such as effect size, sample size, variations in baseline inflammatory status, adherence to the intervention, daily protein intake, and disease burden—can influence the final results. Comparative studies

on oral nutrition are often influenced by actual consumption and patient tolerance, so larger sample sizes are needed to distinguish the effects between protein-based products. Weimann et al. also emphasized that adherence to oral nutritional supplements plays a role in the benefits of perioperative nutritional therapy.[88]

mGPS combines two markers that represent distinct but interrelated processes. CRP is an acute-phase protein that increases in response to inflammation, whereas albumin levels may decrease in states of inflammation, malnutrition, increased capillary permeability, impaired synthesis, or increased catabolism. Son et al. explain that CRP is synthesized in the liver along with other inflammatory mediators, while albumin reflects nutritional status and the inflammatory response; thus, the combination of the two can illustrate the balance between inflammation and nutritional status.[11]

In colorectal cancer, the systemic inflammatory response is not merely a concomitant phenomenon but is associated with tumor progression, treatment tolerance, and long-term outcomes. Yamamoto et al. identified CRP as a variable that tends to increase with disease progression, whereas albumin is a variable that tends to decrease. This combination of rising and falling variables forms the basis for several inflammatory scores, including the GPS and several other nutrition-inflammation indices.[87]

Liao et al. also support the relevance of the combination of CRP and albumin through a meta-analysis of the C-reactive protein/albumin ratio in colorectal cancer. The meta-analysis included 15 studies involving 6,329 patients and found that a high C-reactive protein/albumin ratio was associated with poorer overall survival, with a hazard ratio of 2.028, a 95% confidence interval of 1.808–2.275, and $p < 0.001$. A high ratio was also associated with poorer disease-free survival or progression-free survival, with a hazard ratio of 1.768, a 95% confidence interval of 1.321–2.365, and $p < 0.001$.[89]

Although mGPS and the C-reactive protein/albumin ratio use the same components, they are not entirely equivalent. mGPS simplifies patient status into categories 0, 1, and 2, whereas the C-reactive protein/albumin ratio retains a continuous ratio form. Son et al. reported that the combination of mGPS and the C-reactive protein/albumin ratio has higher predictive ability than each indicator alone in stage I–III colorectal cancer patients undergoing curative resection.[11]

Oral albumin in this study was administered in two forms, namely Albumed/egg white extract and kutuk fish extract. Egg white is a protein source with a good amino acid composition and is therefore frequently used as an option for oral protein supplementation in hypoalbuminemia. A systematic review and meta-analysis by Gong et al., covering 30 randomized controlled trials with 1,938 subjects, reported that egg white protein supplementation in dialysis patients significantly increased serum albumin, with a mean difference of +0.42 g/dL (95% confidence interval 0.12–0.72; $I^2 = 82.4\%$), based on four randomized controlled trials. However, the quality of evidence was rated as very low, so its application to populations other than dialysis patients should still be interpreted with caution. Detarun et al. also reported that egg white formula supplementation for 2 weeks in bedridden elderly patients increased mean serum albumin from 3.56 ± 0.44 g/dL to 3.72 ± 0.45 g/dL ($p = 0.042$).[79,90]

Extracts of the snakehead fish (*Channa striata*) have also been extensively studied as a source of protein and albumin in cases of hypoalbuminemia. Putranto et al. conducted a double-blind randomized trial in patients with end-stage renal disease, administering 500 mg of *Channa striata* extract three times daily for 14 days, and reported a significant increase in serum albumin and a significant decrease in high-sensitivity C-reactive protein in the treatment group compared to the control group, both with $p < 0.001$. Although this population differs from that of colorectal cancer, the biological mechanism is relevant for oral protein interventions targeting albumin levels and inflammation.[91]

Setya et al. also reported in burn patients that administration of 500 mg of snakehead fish extract capsules three times daily for 10 days was associated with increased albumin levels, with significant results in the treatment group ($p = 0.020$), whereas the control group showed no significant difference ($p = 0.243$). Since the study population did not consist of colorectal cancer patients, this study is more appropriately used as supporting evidence regarding the effects of snakehead fish extract on albumin levels.[92]

The association between oral albumin and mGPS should not be limited solely to an increase in serum albumin. Since mGPS is also influenced by CRP, an improvement in the score can occur through changes in one or both of these components. In cases of cancer and surgery, inflammatory status can affect albumin as a negative acute-phase protein. Son et al. explain that an increase in the C-reactive protein/albumin ratio or mGPS is usually associated with a poorer prognosis because both reflect the relationship between inflammation and nutrition.[11]

Colorectal cancer patients undergoing surgery are in a state of metabolic stress that can increase their energy and protein requirements. Weimann et al. note that early oral feeding is the primary option for surgical patients, whereas avoiding nutritional therapy may increase the risk of underfeeding following major surgery. The same source also emphasizes that malnutrition and undernutrition are risk factors for postoperative complications.[88]

The 2025 surgical nutrition guidelines from the European Society for Clinical Nutrition and Metabolism reaffirm that nutritional therapy is necessary for surgical patients at nutritional risk, particularly those undergoing major gastrointestinal surgery and cancer surgery. These recommendations include initiating oral feeding as early as possible, providing nutritional therapy when nutritional risk arises, managing catabolic stress, and promoting early mobilization to support protein synthesis and muscle function.[93]

The administration of oral nutritional supplements during the perioperative period is also consistent with the Enhanced

Recovery After Surgery (ERAS) approach. Weimann et al. explain that ERAS recommends the use of oral nutritional supplements during the perioperative period and positions nutritional therapy as an integral part of care for surgical cancer patients. This concept supports the use of oral interventions as a means to improve metabolic status before or after definitive therapy.[93]

Improvements in mGPS scores in the intervention group should still be interpreted as changes in an indicator, not as direct evidence of reduced mortality or increased survival. However, because mGPS has consistently been associated with colorectal cancer outcomes across various studies, changes in these scores still hold clinical significance as an indicator of shifts in inflammatory-nutritional status. Boukovala et al. identified mGPS as a prognostic biomarker in patients with metastatic colorectal cancer receiving first-line chemotherapy in the Phase III XELAVIRI trial.[86]

LIMITATIONS AND FUTURE WORK

The first limitation is the relatively small number of subjects—10 patients in each group. This number is sufficient for simple nonparametric analysis but not robust enough for more detailed subgroup analysis. Differences in stage, tumor location, baseline nutritional status, baseline inflammatory status, type of surgery, and additional oncological therapies may influence the mGPS. Cotan et al. also noted the need for studies with a larger number of subjects to clarify the role of the mGPS in decision-making for colorectal cancer.[84]

The second limitation is that the assessment of outcomes focused on the mGPS score. Albumin and CRP levels—as components of the score—were not discussed as separate outcomes. Consequently, the direction of change for each component could not be specifically explained; it remains unclear whether a decrease in the score was primarily driven by changes in CRP, changes in albumin, or a combination of both. Son et al. demonstrated that the mGPS and the C-reactive protein/albumin ratio can provide complementary information because they use the same laboratory components but employ different grouping methods.[11]

The third limitation is the absence of direct measurements of long-term clinical outcomes, such as overall survival, progression-free survival, recurrence, postoperative complications, surgical site infections, or length of hospital stay. Therefore, improvements in mGPS cannot be directly equated with improvements in long-term clinical outcomes. Other studies linking mGPS to overall survival and progression-free survival generally use cohort designs with longer follow-up periods and survival analyses.[84]

The fourth limitation relates to daily nutritional factors and adherence to consumption. The effects of oral protein interventions may be influenced by daily food intake, protein intake from other sources, gastrointestinal symptoms, appetite, intolerance, and adherence to taking supplements. Weimann et al. noted that the benefits of oral nutritional supplements are linked to adherence to consumption; therefore, educating patients about the benefits of supplementation is an important part of nutritional therapy.[88]

The results of this study support the use of mGPS as a simple parameter for monitoring changes in inflammatory-nutritional status in colorectal cancer patients receiving oral albumin intervention. This score is easy to apply because it requires only CRP and albumin, two tests that are commonly available in hospitals. Yamamoto et al. also noted that inflammatory biomarkers from routine blood tests have practical value because they are easily obtained and can aid in the risk stratification of colorectal cancer patients.[87]

A further implication is the need to incorporate oral albumin intervention as part of a perioperative nutritional approach, rather than as a standalone therapy. For cancer patients, Muscaritoli et al. recommend nutritional assessment starting at diagnosis and ongoing assessments based on clinical stability, including nutritional intake, muscle mass, physical performance, and the degree of systemic inflammation. Such an approach can help identify patients most likely to benefit from oral protein interventions.[85]

These results also open the door to further evaluation using a more robust study design. Future research could consider a larger sample size, serial measurements of CRP and albumin, recording of daily protein intake, monitoring of supplement adherence, and clinical outcomes such as postoperative complications, length of hospital stay, and survival. Liao et al. demonstrated that CRP- and albumin-based indicators are strongly associated with overall survival and disease-free survival or progression-free survival; therefore, combining the mGPS score with clinical outcomes will provide a more comprehensive assessment of colorectal cancer patients.[89]

CONCLUSION AND RECOMMENDATIONS

Conclusion

1. Oral albumin administration affected changes in the Modified Glasgow Prognostic Score (mGPS) in patients with colorectal cancer. Overall, 11 patients (36.7%) showed improvement in mGPS, and 19 patients (63.3%) had a stable mGPS. No patients experienced a worsening of mGPS.
2. In the Albumed/egg white extract group, 6 patients (60.0%) showed an improvement in mGPS, and 4 patients (40.0%) had a stable mGPS. The results of the Wilcoxon signed-rank test showed a statistically significant difference between mGPS before and after the intervention, with a p-value of 0.014.
3. In the snakehead fish extract group, 5 patients (50.0%) showed improvement in mGPS, and 5 patients (50.0%) had stable mGPS. The results of the Wilcoxon signed-rank test showed a statistically significant difference between mGPS before and after the intervention, with a p-value of 0.025.
4. In the control group, all patients had stable mGPS scores, totaling 10 patients (100.0%). The results of the Wilcoxon signed-rank test showed no significant difference between

mGPS scores before and after observation, with a p-value of 1.000.

5. There were significant differences in mGPS changes among the study groups based on the Kruskal–Wallis test, with a p-value of 0.014.
6. Further analysis using the Mann–Whitney U test with Bonferroni correction showed that changes in mGPS in the Albumed/egg white extract group differed significantly from those in the control group, with a p-value of 0.004. Changes in mGPS in the kutuk fish extract group also differed significantly from those in the control group, with a p-value of 0.012. There was no significant difference between the Albumed/egg white extract group and the kutuk fish extract group, with a p-value of 0.661.
7. The results of this study showed no statistically significant difference between the administration of albumin derived from egg white extract and that from *Ophiocephalus striatus* extract; however, there was a difference in the price of the albumin preparations, with the egg white extract albumin sachets being more cost-effective than those containing *Ophiocephalus striatus* extract. Additionally, the egg white extract was found to be more convenient to consume than the *Ophiocephalus striatus* extract.

Recommendations

1. Future studies should involve a larger number of subjects so that changes in mGPS between groups can be analyzed with greater statistical power.
2. Future studies could include measurements of albumin and C-reactive protein (CRP) levels before and after the intervention, so that changes in each component of mGPS can be analyzed in greater detail.
3. The recording of daily nutrient intake, adherence to oral albumin consumption, and patient tolerance to supplementation should be conducted in a more structured manner in future studies.
4. Future studies could assess clinical outcomes such as postoperative complications, length of hospital stay, surgical site infections, recurrence, or survival, so that changes in mGPS can be linked to clinical outcomes in colorectal cancer patients.
5. Albumed (egg white extract) and kutuk fish extract may be considered as adjunct oral nutritional interventions for colorectal cancer patients, particularly those at risk for nutritional status impairment and inflammation, while taking into account clinical condition, gastrointestinal tolerance, and evaluation by the patient's attending physician.
6. Future research is recommended to compare the effectiveness of Albumed (egg white extract) and kutuk fish extract using a more robust study design, a uniform intervention duration, and serial laboratory monitoring to assess changes in mGPS more objectively.
7. The results of this study showed no statistically significant difference between the administration of egg white extract and *Ophiocephalus striatus* extract; however, there was a difference in the price of the albumin preparations, with the egg white extract sachets being more cost-effective than the *Ophiocephalus striatus* extract, and the egg white extract was found to be more practical for consumption compared to the *Ophiocephalus striatus* extract, which can serve as a recommendation for future research.

DECLARATIONS

Ethics approval: [To be completed by the authors: name of the Health Research Ethics Committee, approval number and date.]

Author contributions: [To be completed by the authors.]

Funding: [To be completed by the authors.]

Conflict of interest: [To be completed by the authors.]

Data availability: [To be completed by the authors.]

REFERENCES

[1]. World Health Organization. Cancer [Internet]. Geneva: World Health Organization; 2022 [cited 2026 Oct 31]. Available from: https://www.who.int/news-room/fact-sheets/detail/cancer

[2]. International Agency for Research on Cancer, World Health Organization. Global Cancer Observatory: Indonesia fact sheet [Internet]. Lyon: International Agency for Research on Cancer; 2020 [cited 2026 Oct 31]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/populations/360-indonesia-fact-sheet.pdf

[3]. Lv L, Sun X, Liu B, Song J, Wu DJH, Gao Y, et al. Genetically predicted serum albumin and risk of colorectal cancer: a bidirectional Mendelian randomization study. Clin Epidemiol. 2022;14:771–8. doi:10.2147/CLEP.S367547. Available from: https://doi.org/10.2147/CLEP.S367547

[4]. Jiang Y, Yang Z, Wu Q, Cao J, Qiu T. The association between albumin and C-reactive protein in older adults. Medicine (Baltimore). 2023;102(34):e34726. doi:10.1097/MD.0000000000034726. Available from: https://doi.org/10.1097/MD.0000000000034726

[5]. Fernández J, Clària J, Amorós A, Aguilar F, Castro M, Casulleras M, et al. Effects of albumin treatment on systemic and portal hemodynamics and systemic inflammation in patients with decompensated cirrhosis. Gastroenterology. 2019;157(1):149–62. doi:10.1053/j.gastro.2019.03.021. Available from: https://doi.org/10.1053/j.gastro.2019.03.021

[6]. Ngwa DN, Pathak A, Agrawal A. IL-6 regulates induction of C-reactive protein gene expression by activating STAT3 isoforms. Mol Immunol. 2022;146:50–6. doi:10.1016/j.molimm.2022.04.003. Available from: https://doi.org/10.1016/j.molimm.2022.04.003

[7]. Nazha B, Moussaly E, Zaarour M, Weerasinghe C, Azab B. Hypoalbuminemia in colorectal cancer prognosis: nutritional marker or inflammatory surrogate? World J Gastrointest Surg. 2015;7(12):370–7. doi:10.4240/wjgs.v7.i12.370. Available from: https://doi.org/10.4240/wjgs.v7.i12.370

[8]. Kang B, Zhao ZQ, Liu XY, Cheng YX, Tao W, Wei ZQ, et al. Effect of hypoalbuminemia on short-term outcomes after colorectal cancer surgery: a propensity score matching analysis. Front Nutr. 2022;9:925086. doi:10.3389/fnut.2022.925086. Available from: https://doi.org/10.3389/fnut.2022.925086

[9]. Almasaudi AS, Dolan RD, Edwards CA, McMillan DC. Hypoalbuminemia reflects nutritional risk, body composition and systemic inflammation and is independently associated with survival in patients with colorectal cancer. Cancers (Basel). 2020;12(7):1986. doi:10.3390/cancers12071986. Available from: https://doi.org/10.3390/cancers12071986

[10]. Dolan RD, McMillan DC. The prevalence of cancer associated systemic inflammation: implications of prognostic studies using the Glasgow Prognostic Score. Crit Rev Oncol Hematol. 2020;150:102962. doi:10.1016/j.critrevonc.2020.102962. Available from: https://doi.org/10.1016/j.critrevonc.2020.102962

[11]. Son W, Shin SJ, Park SH, Lee SK, Park EJ, Baik SH, et al. Clinical impact of combined modified Glasgow Prognostic Score and C-reactive protein/albumin ratio in patients with colorectal cancer. Diagnostics (Basel). 2020;10(11):859. doi:10.3390/diagnostics10110859. Available from: https://doi.org/10.3390/diagnostics10110859

[12]. Gatta A, Verardo A, Bolognesi M. Hypoalbuminemia. Intern Emerg Med. 2012;7 Suppl 3:S193–9. doi:10.1007/s11739-012-0802-0. Available from: https://doi.org/10.1007/s11739-012-0802-0

[13]. Syamsiatun NH, Siswati T. Pemberian ekstra jus putih telur terhadap kadar albumin dan Hb pada penderita hipoalbuminemia [The effect of egg white juice on the albumin and hemoglobin levels in patients with hypoalbuminemia]. J Gizi Klin Indones. 2015;12(2):54–61. doi:10.22146/ijcn.22919. Available from: https://doi.org/10.22146/ijcn.22919

[14]. Saputra DH. Suplemen putih telur dalam tatalaksana hipoalbuminemia [Egg white supplementation in the management of hypoalbuminemia]. Cermin Dunia Kedokt. 2021;48(10):410–3. Available from: https://cdkjournal.com/index.php/cdk/article/view/138

[15]. Jaya W, Fatoni AZ, Iradat P, Laksono BH. The efficacy of high-albumin formula supplementation (Albumed milk) on serum albumin levels in critically ill patients with sepsis. J Anestesiol Indones. 2026;18(1):44–55. doi:10.14710/jai.v0i0.71031. Available from: https://doi.org/10.14710/jai.v0i0.71031

[16]. Pratiwi AT. Potensi ikan gabus (Ophiocephalus striatus) untuk meningkatkan kadar albumin penderita hipoalbuminemia [Potency of snakehead fish (Ophiocephalus striatus) for increasing albumin levels of hypoalbuminemia patients]. J Ilm Mhs Kedokt Indones. 2021;8(3):204–10. doi:10.53366/jimki.v8i3.254. Available from: https://doi.org/10.53366/jimki.v8i3.254

[17]. Mulyana R, Setiati S, Martini RD, Harimurti K, Dwimartutie N. The effect of Ophiocephalus striatus extract on the levels of IGF-1 and albumin in elderly patients with hypoalbuminemia. Acta Med Indones. 2017;49(4):324–9. Available from: https://pubmed.ncbi.nlm.nih.gov/29348382/

[18]. American Cancer Society. Colorectal cancer facts & figures 2020–2022. Atlanta: American Cancer Society; 2020. Available from: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2020-2022.pdf

[19]. Testa U, Pelosi E, Castelli G. Colorectal cancer: genetic abnormalities, tumor progression, tumor heterogeneity, clonal evolution and tumor-initiating cells. Med Sci (Basel). 2018;6(2):31. doi:10.3390/medsci6020031. Available from: https://doi.org/10.3390/medsci6020031

[20]. Zannah SJ, Murti IS, Sulistiawati S. Hubungan usia dengan stadium saat diagnosis penderita kanker kolorektal di RSUD Abdul Wahab Sjahranie Samarinda [Relationship between age and stage at diagnosis in colorectal cancer patients at Abdul Wahab Sjahranie Hospital, Samarinda]. J Sains Kes. 2021;3(5):701–5. doi:10.25026/jsk.v3i5.629. Available from: https://doi.org/10.25026/jsk.v3i5.629

[21]. Islami F, Goding Sauer A, Miller KD, Siegel RL, Fedewa SA, Jacobs EJ, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018;68(1):31–54. doi:10.3322/caac.21440. Available from: https://doi.org/10.3322/caac.21440

[22]. Kohler LN, Garcia DO, Harris RB, Oren E, Roe DJ, Jacobs ET. Adherence to diet and physical activity cancer prevention guidelines and cancer outcomes: a systematic review. Cancer Epidemiol Biomarkers Prev. 2016;25(7):1018–28. doi:10.1158/1055-9965.EPI-16-0121. Available from: https://doi.org/10.1158/1055-9965.EPI-16-0121

[23]. Jones WF, Ahnen DJ, Schroy PC 3rd. Improving on-time colorectal cancer screening through lead time messaging. Cancer. 2020;126(2):247–52. doi:10.1002/cncr.32535. Available from: https://doi.org/10.1002/cncr.32535

[24]. Yurgelun MB, Kulke MH, Fuchs CS, Allen BA, Uno H, Hornick JL, et al. Cancer susceptibility gene mutations in individuals with colorectal cancer. J Clin Oncol. 2017;35(10):1086–95. doi:10.1200/JCO.2016.71.0012. Available from: https://doi.org/10.1200/JCO.2016.71.0012

[25]. Møller P, Seppälä TT, Bernstein I, Holinski-Feder E, Sala P, Gareth Evans D, et al. Cancer risk and survival in path_MMR carriers by gene and gender up to 75 years of age: a report from the Prospective Lynch Syndrome Database. Gut. 2018;67(7):1306–16. doi:10.1136/gutjnl-2017-314057. Available from: https://doi.org/10.1136/gutjnl-2017-314057

[26]. Oh M, McBride A, Yun S, Bhattacharjee S, Slack M, Martin JR, et al. BRCA1 and BRCA2 gene mutations and colorectal cancer risk: systematic review and meta-analysis. J Natl Cancer Inst. 2018;110(11):1178–89. doi:10.1093/jnci/djy148. Available from: https://doi.org/10.1093/jnci/djy148

[27]. Rawla P, Sunkara T, Barsouk A. Epidemiology of colorectal cancer: incidence, mortality, survival, and risk factors. Prz Gastroenterol. 2019;14(2):89–103. doi:10.5114/pg.2018.81072. Available from: https://doi.org/10.5114/pg.2018.81072

[28]. Teepen JC, Kok JL, van Leeuwen FE, Tissing WJE, Dolsma WV, van der Pal HJ, et al. Colorectal adenomas and cancers after childhood cancer treatment: a DCOG-LATER record linkage study. J Natl Cancer Inst. 2018;110(7):758–67. doi:10.1093/jnci/djx266. Available from: https://doi.org/10.1093/jnci/djx266

[29]. Groot HJ, Lubberts S, de Wit R, Witjes JA, Kerst JM, de Jong IJ, et al. Risk of solid cancer after treatment of testicular germ cell cancer in the platinum era. J Clin Oncol. 2018;36(24):2504–13. doi:10.1200/JCO.2017.77.4174. Available from: https://doi.org/10.1200/JCO.2017.77.4174

[30]. Li S, Zhang J, Zheng H, Wang X, Liu Z, Sun T. Prognostic role of serum albumin, total lymphocyte count, and mini nutritional assessment on outcomes after geriatric hip fracture surgery: a meta-analysis and systematic review. J Arthroplasty. 2019;34(6):1287–96. doi:10.1016/j.arth.2019.02.003. Available from: https://doi.org/10.1016/j.arth.2019.02.003

[31]. Xu F, Dahlhamer JM, Zammitti EP, Wheaton AG, Croft JB. Health-risk behaviors and chronic conditions among adults with inflammatory bowel disease — United States, 2015 and 2016. MMWR Morb Mortal Wkly Rep. 2018;67(6):190–5. doi:10.15585/mmwr.mm6706a4. Available from: https://doi.org/10.15585/mmwr.mm6706a4

[32]. Murphy N, Jenab M, Gunter MJ. Adiposity and gastrointestinal cancers: epidemiology, mechanisms and future directions. Nat Rev Gastroenterol Hepatol. 2018;15(11):659–70. doi:10.1038/s41575-018-0038-1. Available from: https://doi.org/10.1038/s41575-018-0038-1

[33]. Liu PH, Wu K, Ng K, Zauber AG, Nguyen LH, Song M, et al. Association of obesity with risk of early-onset colorectal cancer among women. JAMA Oncol. 2019;5(1):37–44. doi:10.1001/jamaoncol.2018.4280. Available from: https://doi.org/10.1001/jamaoncol.2018.4280

[34]. Vieira AR, Abar L, Chan DSM, Vingeliene S, Polemiti E, Stevens C, et al. Foods and beverages and colorectal cancer risk: a systematic review and meta-analysis of cohort studies, an update of the evidence of the WCRF-AICR Continuous Update Project. Ann Oncol. 2017;28(8):1788–802. doi:10.1093/annonc/mdx171. Available from: https://doi.org/10.1093/annonc/mdx171

[35]. Schmitt M, Greten FR. The inflammatory pathogenesis of colorectal cancer. Nat Rev Immunol. 2021;21(10):653–67. doi:10.1038/s41577-021-00534-x. Available from: https://doi.org/10.1038/s41577-021-00534-x

[36]. Vacante M, Ciuni R, Basile F, Biondi A. Gut microbiota and colorectal cancer development: a closer look to the adenoma-carcinoma sequence. Biomedicines. 2020;8(11):489. doi:10.3390/biomedicines8110489. Available from: https://doi.org/10.3390/biomedicines8110489

[37]. Turri G, Barresi V, Valdegamberi A, Gecchele G, Conti C, Ammendola S, et al. Clinical significance of preoperative inflammatory markers in prediction of prognosis in node-negative colon cancer: correlation between neutrophil-to-lymphocyte ratio and poorly differentiated clusters. Biomedicines. 2021;9(1):94. doi:10.3390/biomedicines9010094. Available from: https://doi.org/10.3390/biomedicines9010094

[38]. Mármol I, Sánchez-de-Diego C, Pradilla Dieste A, Cerrada E, Rodriguez Yoldi MJ. Colorectal carcinoma: a general overview and future perspectives in colorectal cancer. Int J Mol Sci. 2017;18(1):197. doi:10.3390/ijms18010197. Available from: https://doi.org/10.3390/ijms18010197

[39]. Krasteva N, Georgieva M. Promising therapeutic strategies for colorectal cancer treatment based on nanomaterials. Pharmaceutics. 2022;14(6):1213. doi:10.3390/pharmaceutics14061213. Available from: https://doi.org/10.3390/pharmaceutics14061213

[40]. Lotfollahzadeh S, Recio-Boiles A, Cagir B. Colon cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470380/

[41]. Nayor J, Saltzman JR. Colonoscopy quality: measuring the patient experience. Endoscopy. 2018;50(1):4–5. Available from: https://pubmed.ncbi.nlm.nih.gov/29268293/

[42]. Das V, Kalita J, Pal M. Predictive and prognostic biomarkers in colorectal cancer: a systematic review of recent advances and challenges. Biomed Pharmacother. 2017;87:8–19. doi:10.1016/j.biopha.2016.12.064. Available from: https://doi.org/10.1016/j.biopha.2016.12.064

[43]. Kamel F, Eltarhoni K, Nisar P, Soloviev M. Colorectal cancer diagnosis: the obstacles we face in determining a non-invasive test and current advances in biomarker detection. Cancers (Basel). 2022;14(8):1889. doi:10.3390/cancers14081889. Available from: https://doi.org/10.3390/cancers14081889

[44]. Chang JC, Kundranda M. Novel diagnostic and predictive biomarkers in pancreatic adenocarcinoma. Int J Mol Sci. 2017;18(3):667. doi:10.3390/ijms18030667. Available from: https://doi.org/10.3390/ijms18030667

[45]. Brar B, Ranjan K, Palria A, Kumar R, Ghosh M, Sihag S, et al. Nanotechnology in colorectal cancer for precision diagnosis and therapy. Front Nanotechnol. 2021;3:699266. doi:10.3389/fnano.2021.699266. Available from: https://doi.org/10.3389/fnano.2021.699266

[46]. Xie YH, Chen YX, Fang JY. Comprehensive review of targeted therapy for colorectal cancer. Signal Transduct Target Ther. 2020;5(1):22. doi:10.1038/s41392-020-0116-z. Available from: https://doi.org/10.1038/s41392-020-0116-z

[47]. Wang H, Wu J, Xu L, Xie K, Chen C, Dong Y. Albumin nanoparticle encapsulation of potent cytotoxic therapeutics shows sustained drug release and alleviates cancer drug toxicity. Chem Commun (Camb). 2017;53(17):2618–21. doi:10.1039/c6cc08978j. Available from: https://doi.org/10.1039/c6cc08978j

[48]. Alibolandi M, Taghdisi SM, Ramezani P, Hosseini Shamili F, Farzad SA, Abnous K, et al. Smart AS1411-aptamer conjugated pegylated PAMAM dendrimer for the superior delivery of camptothecin to colon adenocarcinoma in vitro and in vivo. Int J Pharm. 2017;519(1–2):352–64. doi:10.1016/j.ijpharm.2017.01.044. Available from: https://doi.org/10.1016/j.ijpharm.2017.01.044

[49]. Yu Z, Li X, Duan J, Yang XD. Targeted treatment of colon cancer with aptamer-guided albumin nanoparticles loaded with docetaxel. Int J Nanomedicine. 2020;15:6737–48. doi:10.2147/IJN.S267177. Available from: https://doi.org/10.2147/IJN.S267177

[50]. Barontini J, Antinucci M, Tofanelli S, Cammalleri M, Dal Monte M, Gemignani F, et al. Association between polymorphisms of TAS2R16 and susceptibility to colorectal cancer. BMC Gastroenterol. 2017;17(1):104. doi:10.1186/s12876-017-0659-9. Available from: https://doi.org/10.1186/s12876-017-0659-9

[51]. He L, Li H, Cai J, Chen L, Yao J, Zhang Y, et al. Prognostic value of the Glasgow Prognostic Score or modified Glasgow Prognostic Score for patients with colorectal cancer receiving various treatments: a systematic review and meta-analysis. Cell Physiol Biochem. 2018;51(3):1237–49. doi:10.1159/000495500. Available from: https://doi.org/10.1159/000495500

[52]. Arfa N, Hamdani I, Gharbi L, Ben Abid S, Ghariani B, Mannai S, et al. Survie et facteurs pronostiques des adénocarcinomes colorectaux: étude analytique uni- et multifactorielle de 150 cas [Survival and prognostic factors of colorectal adenocarcinoma: uni- and multivariate analysis of 150 cases]. Ann Chir. 2006;131(2):104–11. doi:10.1016/j.anchir.2005.12.012. Available from: https://doi.org/10.1016/j.anchir.2005.12.012

[53]. Kanemitsu Y, Kato T, Hirai T, Yasui K, Morimoto T, Shimizu Y, et al. Survival after curative resection for mucinous adenocarcinoma of the colorectum. Dis Colon Rectum. 2003;46(2):160–7. doi:10.1007/s10350-004-6518-0. Available from: https://doi.org/10.1007/s10350-004-6518-0

[54]. Jin LJ, Chen WB, Zhang XY, Bai J, Zhao HC, Wang ZY. Analysis of factors potentially predicting prognosis of colorectal cancer. World J Gastrointest Oncol. 2019;11(12):1206–17. doi:10.4251/wjgo.v11.i12.1206. Available from: https://doi.org/10.4251/wjgo.v11.i12.1206

[55]. Dolan RD, Laird BJA, Horgan PG, McMillan DC. The prognostic value of the systemic inflammatory response in randomised clinical trials in cancer: a systematic review. Crit Rev Oncol Hematol. 2018;132:130–7. doi:10.1016/j.critrevonc.2018.09.016. Available from: https://doi.org/10.1016/j.critrevonc.2018.09.016

[56]. Sunakawa Y, Yang D, Cao S, Zhang W, Moran M, Astrow SH, et al. Immune-related genes to dominate neutrophil-lymphocyte ratio (NLR) associated with survival of cetuximab treatment in metastatic colorectal cancer. Clin Colorectal Cancer. 2018;17(4):e741–9. doi:10.1016/j.clcc.2018.08.002. Available from: https://doi.org/10.1016/j.clcc.2018.08.002

[57]. Meng Y, Long C, Huang X, Huang L, Liao L, Tang W, et al. Prognostic role and clinical significance of C-reactive protein-lymphocyte ratio in colorectal cancer. Bioengineered. 2021;12(1):5138–48. doi:10.1080/21655979.2021.1960768. Available from: https://doi.org/10.1080/21655979.2021.1960768

[58]. Xiao X, Wang S, Long G. C-reactive protein is a significant predictor of improved survival in patients with advanced non-small cell lung cancer. Medicine (Baltimore).

2019;98(26):e16238. doi:10.1097/MD.0000000000016238. Available from: https://doi.org/10.1097/MD.0000000000016238

[59]. Araki K, Ito Y, Fukada I, Kobayashi K, Miyagawa Y, Imamura M, et al. Predictive impact of absolute lymphocyte counts for progression-free survival in human epidermal growth factor receptor 2-positive advanced breast cancer treated with pertuzumab and trastuzumab plus eribulin or nab-paclitaxel. BMC Cancer. 2018;18(1):982. doi:10.1186/s12885-018-4888-2. Available from: https://doi.org/10.1186/s12885-018-4888-2

[60]. Oh SY, Heo J, Noh OK, Chun M, Cho O, Oh YT. Absolute lymphocyte count in preoperative chemoradiotherapy for rectal cancer: changes over time and prognostic significance. Technol Cancer Res Treat. 2018;17:1533033818780065. doi:10.1177/1533033818780065. Available from: https://doi.org/10.1177/1533033818780065

[61]. Suzuki R, Wei X, Allen PK, Cox JD, Komaki R, Lin SH. Prognostic significance of total lymphocyte count, neutrophil-to-lymphocyte ratio, and platelet-to-lymphocyte ratio in limited-stage small-cell lung cancer. Clin Lung Cancer. 2019;20(2):117–23. doi:10.1016/j.cllc.2018.11.013. Available from: https://doi.org/10.1016/j.cllc.2018.11.013

[62]. Wang F, Li P, Li FS. Prognostic role of C-reactive protein to albumin ratio in colorectal cancer: a meta analysis. Medicine (Baltimore). 2019;98(29):e16064. doi:10.1097/MD.0000000000016064. Available from: https://doi.org/10.1097/MD.0000000000016064

[63]. Tuomisto AE, Mäkinen MJ, Väyrynen JP. Systemic inflammation in colorectal cancer: underlying factors, effects, and prognostic significance. World J Gastroenterol. 2019;25(31):4383–404. doi:10.3748/wjg.v25.i31.4383. Available from: https://doi.org/10.3748/wjg.v25.i31.4383

[64]. Li H, Zhao Y, Zheng F. Prognostic significance of elevated preoperative neutrophil-to-lymphocyte ratio for patients with colorectal cancer undergoing curative surgery: a meta-analysis. Medicine (Baltimore). 2019;98(3):e14126. doi:10.1097/MD.0000000000014126. Available from: https://doi.org/10.1097/MD.0000000000014126

[65]. Tan D, Fu Y, Tong W, Li F. Prognostic significance of lymphocyte to monocyte ratio in colorectal cancer: a meta-analysis. Int J Surg. 2018;55:128–38. doi:10.1016/j.ijsu.2018.05.030. Available from: https://doi.org/10.1016/j.ijsu.2018.05.030

[66]. Lu X, Guo W, Xu W, Zhang X, Shi Z, Zheng L, et al. Prognostic value of the Glasgow prognostic score in colorectal cancer: a meta-analysis of 9,839 patients. Cancer Manag Res. 2019;11:229–49. doi:10.2147/CMAR.S185350. Available from: https://doi.org/10.2147/CMAR.S185350

[67]. Inamoto S, Kawada K, Okamura R, Hida K, Sakai Y. Prognostic impact of the combination of neutrophil-to-lymphocyte ratio and Glasgow prognostic score in colorectal cancer: a retrospective cohort study. Int J Colorectal Dis. 2019;34(7):1303–15. doi:10.1007/s00384-019-03316-z. Available from: https://doi.org/10.1007/s00384-019-03316-z

[68]. Mishra V, Heath RJ. Structural and biochemical features of human serum albumin essential for eukaryotic cell culture. Int J Mol Sci. 2021;22(16):8411. doi:10.3390/ijms22168411. Available from: https://doi.org/10.3390/ijms22168411

[69]. Tao C, Chuah YJ, Xu C, Wang DA. Albumin conjugates and assemblies as versatile bio-functional additives and carriers for biomedical applications. J Mater Chem B. 2019;7(3):357–67. doi:10.1039/c8tb02477d. Available from: https://doi.org/10.1039/c8tb02477d

[70]. Chen WS, Huang YS, Xu LB, Shi MM, Chen XD, Ye GQ, et al. Effects of sarcopenia, hypoalbuminemia, and laparoscopic surgery on postoperative complications in elderly patients with colorectal cancer: a prospective study. Neoplasma. 2020;67(4):922–32. doi:10.4149/neo_2020_190908N882. Available from: https://doi.org/10.4149/neo_2020_190908N882

[71]. Christina NM, Tjahyanto T, Lie JG, Santoso TA, Albertus H, Octavianus D, et al. Hypoalbuminemia and colorectal cancer patients: any correlation?: a systematic review and meta-analysis. Medicine (Baltimore). 2023;102(8):e32938. doi:10.1097/MD.0000000000032938. Available from: https://doi.org/10.1097/MD.0000000000032938

[72]. Akirov A, Masri-Iraqi H, Atamna A, Shimon I. Low albumin levels are associated with mortality risk in hospitalized patients. Am J Med. 2017;130(12):1465.e11–9. doi:10.1016/j.amjmed.2017.07.020. Available from: https://doi.org/10.1016/j.amjmed.2017.07.020

[73]. Arques S. Human serum albumin in cardiovascular diseases. Eur J Intern Med. 2018;52:8–12. doi:10.1016/j.ejim.2018.04.014. Available from: https://doi.org/10.1016/j.ejim.2018.04.014

[74]. Ling HH, Pan YP, Fan CW, Tseng WK, Huang JS, Wu TH, et al. Clinical significance of serum glutamine level in patients with colorectal cancer. Nutrients. 2019;11(4):898. doi:10.3390/nu11040898. Available from: https://doi.org/10.3390/nu11040898

[75]. McMillan DC, Maguire D, Talwar D. Relationship between nutritional status and the systemic inflammatory response: micronutrients. Proc Nutr Soc. 2019;78(1):56–67. doi:10.1017/S0029665118002501. Available from: https://doi.org/10.1017/S0029665118002501

[76]. Liao LM, Loftfield E, Etemadi A, Graubard BI, Sinha R. Substitution of dietary protein sources in relation to colorectal cancer risk in the NIH-AARP cohort study. Cancer Causes Control. 2019;30(10):1127–35. doi:10.1007/s10552-019-01210-1. Available from: https://doi.org/10.1007/s10552-019-01210-1

[77]. Watt DG, McSorley ST, Park JH, Horgan PG, McMillan DC. A postoperative systemic inflammation score predicts short- and long-term outcomes in patients undergoing surgery for colorectal cancer. Ann Surg Oncol. 2017;24(4):1100–9. doi:10.1245/s10434-016-5659-4. Available from: https://doi.org/10.1245/s10434-016-5659-4

[78]. Bektiwibowo S, Munasir Z, Nasar SS. Pemberian nutrisi enteral kasus bedah anak: pengaruh pada status nutrisi [Enteral nutrition in paediatric surgical cases: effect on nutritional status]. Sari Pediatri. 2005;7(3):136–42. doi:10.14238/sp7.3.2005.136-42. Available from: https://doi.org/10.14238/sp7.3.2005.136-42

[79]. Detarun P, Srichamnanturakit V, Isaramalai SA, Rakpanusit T. Enhancing nutritional care with egg white supplementation on serum albumin level for home-based bed-ridden elderly patients. Funct Foods Health Dis. 2022;12(6):308–24. doi:10.31989/ffhd.v12i6.932. Available from: https://doi.org/10.31989/ffhd.v12i6.932

[80]. Mustafa A, Khoirunnisa AA, Rahman N. Effect of giving snakehead fish extract (Channa striata) on albumin, neutrophil, and lymphocyte levels in hypoalbuminemia patients. J Local Ther. 2022;1(2):56–62. doi:10.31290/jlt.v1i2.3457. Available from: https://doi.org/10.31290/jlt.v1i2.3457

[81]. Dahlan MS. Besar sampel dan cara pengambilan sampel dalam penelitian kedokteran dan kesehatan [Sample size and sampling methods in medical and health research]. 3rd ed. Jakarta: Salemba Medika; 2010.

[82]. World Health Organization. Colorectal cancer [Internet]. Geneva: World Health Organization; 2023 [cited 2026 Oct 31]. Available from: https://www.who.int/news-room/fact-sheets/detail/colorectal-cancer

[83]. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin.

2024;74(3):229–63. doi:10.3322/caac.21834. Available from: https://doi.org/10.3322/caac.21834

[84]. Cotan H, Iaciu C, Nitipir C. Role of the modified Glasgow Prognostic Score (mGPS) as a prognostic factor in metastatic colorectal cancer. Cureus. 2024;16(7):e64916. doi:10.7759/cureus.64916. Available from: https://doi.org/10.7759/cureus.64916

[85]. Muscaritoli M, Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, et al. ESPEN practical guideline: clinical nutrition in cancer. Clin Nutr. 2021;40(5):2898–913. doi:10.1016/j.clnu.2021.02.005. Available from: https://doi.org/10.1016/j.clnu.2021.02.005

[86]. Boukovala M, Modest DP, Ricard I, Fischer von Weikersthal L, Decker T, Vehling-Kaiser U, et al. Evaluation of the inflammation-based modified Glasgow Prognostic Score (mGPS) as a prognostic and predictive biomarker in patients with metastatic colorectal cancer receiving first-line chemotherapy: a post hoc analysis of the randomized phase III XELAVIRI trial (AIO KRK0110). ESMO Open. 2024;9(5):103374. doi:10.1016/j.esmoop.2024.103374. Available from: https://doi.org/10.1016/j.esmoop.2024.103374

[87]. Yamamoto T, Kawada K, Obama K. Inflammation-related biomarkers for the prediction of prognosis in colorectal cancer patients. Int J Mol Sci. 2021;22(15):8002. doi:10.3390/ijms22158002. Available from: https://doi.org/10.3390/ijms22158002

[88]. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, et al. ESPEN practical guideline: clinical nutrition in surgery. Clin Nutr. 2021;40(7):4745–61. doi:10.1016/j.clnu.2021.03.031. Available from: https://doi.org/10.1016/j.clnu.2021.03.031

[89]. Liao CK, Yu YL, Lin YC, Hsu YJ, Chern YJ, Chiang JM, et al. Prognostic value of the C-reactive protein to albumin ratio in colorectal cancer: an updated systematic review and meta-analysis. World J Surg Oncol. 2021;19(1):139. doi:10.1186/s12957-021-02253-y. Available from: https://doi.org/10.1186/s12957-021-02253-y

[90]. Gong EJ, Bang CS, Lee JJ, Shin YS. Oral egg-derived protein and peptide supplementation for health outcomes in adults: systematic review and meta-analysis. Nutrients. 2026;18(7):1054. doi:10.3390/nu18071054. Available from: https://doi.org/10.3390/nu18071054

[91]. Putranto W, Hestiningrum S, Febriani NIM, Kusmardi K, Dewi RTK, Perdhana SAP, et al. The effect of Channa striata extract on serum albumin and high sensitive C-reactive protein in end-stage renal disease patients: a randomized controlled trial. Pharmacogn J. 2023;15(1):1–5. doi:10.5530/pj.2023.15.1. Available from: https://doi.org/10.5530/pj.2023.15.1

[92]. Setya AMH, Saputro ID, Zarasade LZ. The effect of giving snakehead fish extract capsules on increasing albumin levels in burn patients at RSUD Dr. Soetomo Surabaya. Bali Med J. 2024;13(2):796–9. doi:10.15562/bmj.v13i2.5179. Available from: https://doi.org/10.15562/bmj.v13i2.5179

[93]. Weimann A, Bezmarevic M, Braga M, Correia MITD, Funk-Debleds P, Gianotti L, et al. ESPEN guideline on clinical nutrition in surgery – update 2025. Clin Nutr. 2025;53:222–61. doi:10.1016/j.clnu.2025.08.029. Available from: https://doi.org/10.1016/j.clnu.2025.08.029