


The Effects of Omega-3 Supplementation on Inflammatory Markers in Colorectal Cancer Patients: Evidence-Based Case Report

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ABSTRACT

Introduction: Omega-3 polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have immunomodulatory and anti-inflammatory effects that may help reduce inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) in colorectal cancer (CRC) patients. **Methods:** A literature search was conducted in PubMed, Cochrane Library, and Google Scholar from May to June 2025. Included studies were meta-analyses or randomized controlled trials (RCTs) evaluating omega-3 supplementation in adult CRC patients, with inflammatory markers as primary outcomes. Critical assessment tools and levels of evidence of the final articles are based on the Oxford Centre for Evidence-Based Medicine. **Results:** Three meta-analyses were reviewed. Omega-3 supplementation was given orally (660 mg–4.8 g/day) or parenterally (0.1–0.2 g/kg/day) for 5 to 84 days. IL-6 and tumor necrosis factor-α (TNF-α) levels were significantly reduced in most studies. CRP showed modest and inconsistent improvement, while albumin slightly increased. High heterogeneity in dose, timing, and administration routes limited the strength of interpretation. **Conclusion**: Omega-3 supplementation appears to reduce systemic inflammation in CRC patients, particularly through IL-6 suppression. Although the effect on CRP is inconsistent and albumin improvement is mild, these findings suggest a potential benefit in inflammatory and nutritional status. Further standardized and high-quality RCTs are needed to confirm clinical utility and optimal dosing strategies.

Keywords: Colorectal cancer, CRP, immunonutrition, inflammation, omega-3.

ABSTRAK

Pendahuluan: Asam lemak tak jenuh ganda omega-3 (*polyunsaturated fatty acids*/PUFAs), khususnya EPA dan DHA, memiliki efek imunomodulator dan antiinflamasi yang berpotensi menurunkan penanda inflamasi seperti interleukin-6 (IL-6) dan *C-reactive protein* (CRP) pasien kanker kolorektal (CRC). **Metode:** Pencarian literatur dilakukan di PubMed, Cochrane Library, dan Google Scholar, dari Mei hingga Juni 2025. Studi yang disertakan merupakan meta-analisis atau uji terkontrol acak (RCT) yang mengevaluasi suplementasi omega-3 pada pasien CRC dewasa, dengan fokus pada penanda inflamasi sebagai luaran utama. Penilaian kritis dan tingkat bukti berdasarkan Oxford Centre for Evidence-Based Medicine. **Hasil:** Tiga meta-analisis ditelaah. Suplementasi omega-3 diberikan secara oral (660 mg–4,8 g/hari) atau parenteral (0,1–0,2 g/kg/hari) selama 5 hingga 84 hari. Kadar IL-6 dan TNF-α menurun signifikan dalam sebagian besar studi. CRP menunjukkan perbaikan moderat dan tidak konsisten, dengan albumin sedikit meningkat. Heterogenitas tinggi dalam dosis, waktu, dan rute pemberian membatasi kekuatan interpretasi. **Simpulan:** Suplementasi omega-3 tampak menurunkan inflamasi sistemik pada pasien CRC, terutama melalui penekanan IL-6. Meskipun efek terhadap CRP tidak konsisten dan peningkatan albumin tergolong ringan, temuan ini menunjukkan potensi manfaat terhadap status inflamasi dan nutrisi. Diperlukan RCT berkualitas tinggi dengan protokol yang distandarisasi untuk mengonfirmasi manfaat klinis dan strategi dosis optimal. **Vanessa Aryani Octavia M, Diyah Eka Andayani. Efek Suplementasi Omega-3 terhadap Petanda Inflamasi pada Pasien Kanker Kolorektal: Laporan Kasus Berbasis Bukti.**

Kata Kunci: Kanker kolorektal, CRP, imunonutrisi, inflamasi, omega-3.

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INTRODUCTION

Colorectal cancer (CRC) is the third most common cancer and the second leading cause of cancer-related death worldwide, with nearly 2 million new cases and 930,000 deaths in 2020. Most cases occur in high-

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human development index (HDI) countries, but rising trends are also seen among younger adults and in developing nations. In Indonesia, CRC ranked fourth in incidence with 35,676 new cases and was the third leading cause of cancer death in 2022. Globally, the CRC burden is projected to rise to 3.2 million cases and 1.6 million deaths by 2040.[1,2]

Colorectal cancer is commonly associated with systemic inflammation and malnutrition, both of which negatively affect clinical outcomes. Elevated C-reactive protein (CRP) is a key marker of inflammation and has been correlated with increased weight loss and cancer progression. In contrast, low serum albumin reflects poor nutritional and inflammatory status and is linked to reduced dietary intake and a higher likelihood of cancer dissemination.[3,4]

Omega-3 polyunsaturated fatty acids (PUFAs), particularly EPA and DHA, have been shown to modulate the inflammatory response in colorectal cancer by targeting several molecular pathways. They inhibit the activation of pro-inflammatory transcription factors such as NF-κB and reduce the synthesis of cytokines and mediators like COX-2 and prostaglandin E2. Moreover, omega-3 PUFAs promote the resolution of inflammation by enhancing the production of specialized pro-resolving mediators, including resolvins and protectins. Through these mechanisms, omega-3 intake may help reduce circulating levels of C-reactive protein (CRP), thereby contributing to improved inflammatory and nutritional status.[5,6]

This study aims to assess whether omega-3 supplementation as an adjunctive therapy in colorectal cancer patients can improve inflammatory status, specifically by reducing C-reactive protein (CRP) levels, which serve as key indicators of systemic inflammation and are associated with poor nutritional status and clinical outcomes in cancer patients.

CASE SCENARIO

Mr. S, a 49-year-old male, is currently hospitalized in the surgical ward following a right hemicolectomy for stage IIIC colorectal cancer. The patient is severely malnourished with low albumin (1.8 g/dL) and an elevated C-reactive protein level (61.3 mg/L). Seven days post-operation, he is clinically stable but still has a low appetite. The patient has not been able to eat according to his nutritional needs since surgery. He is scheduled to begin adjuvant chemotherapy and/or radiation therapy in the coming weeks. The attending clinical nutrition specialist considers initiating omega-3 fatty acid supplementation as part of immunonutrition therapy to reduce inflammation and enhance clinical recovery prior to starting cancer treatment.

METHOD

A literature search was independently conducted by two researchers across three electronic databases: PubMed, Cochrane Library, and Google Scholar, between May 28 and June 4, 2025. The search strategy was based on PICO components as outlined in **Table 1**.

Table 1. PICO framework.

Population	Patients aged >18 years with colorectal cancer
Intervention	Omega-3 supplementation
Comparison	No omega-3 supplementation
Outcome	Reduced inflammatory markers

Articles published between 2020 and 2025 were selected. Duplicates were removed using Covidence, and selection was performed by comparing titles and abstracts with the clinical question's PICO framework. Selected articles were then reviewed in full-text format to determine eligibility. The inclusion criteria are patients with colorectal cancer aged > 18 years who received omega-3 supplementation, with the outcome measured by reduced inflammatory markers. The study design is a systematic review/meta-analysis of randomized controlled trials (RCTs) and RCTs. Meanwhile, the exclusion criteria are studies not conducted on humans, full-text articles unavailable, and articles written in languages other than English or Indonesian. Critical appraisal tools and determination of the level of evidence were created based on the Oxford Centre for Evidence-Based Medicine.[7]

RESULT

Results of Literature Search

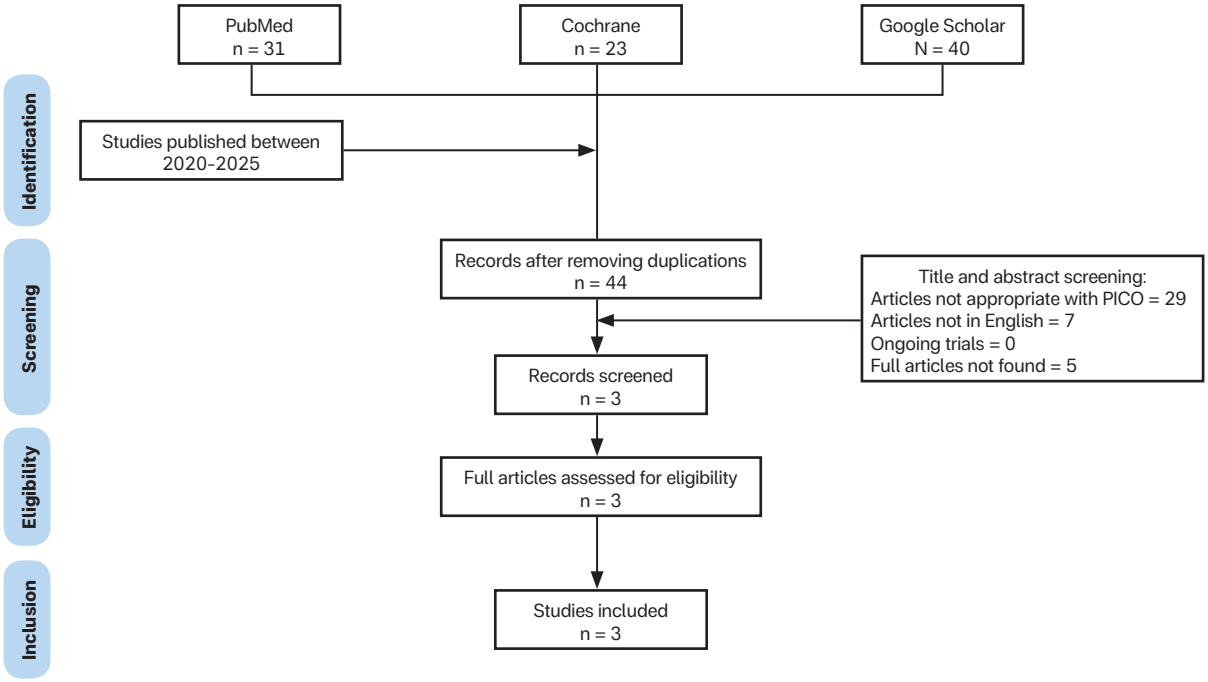
The search strategy and the number of articles retrieved from each database are summarized in **Table 2.** The process of identifying, screening, and selecting eligible articles is illustrated in the **Scheme**. From the initial 94 articles identified, duplicates were removed, followed by abstract and full-text screening. Following a comprehensive review, one study was excluded, leaving three systematic review/meta-analysis (SR/MA) for critical analysis.

The characteristics of the included studies are detailed in **Table 3**, which provides information on the study design, population, intervention, and outcomes of interest. To assess the relevance of each study to the clinical question, similarity in population, determining factors, and outcome measures was compared and is summarized in **Table 5.** Critical appraisal tools and determination of the level of evidence were created based on the Oxford Centre for Evidence-Based Medicine is presented in **Table 4.**

Table 2. Article search strategy.

Database	Search Strategy	Hits	Selected Articles
PubMed	(((((((acid, omega 3 fatty[MeSH Terms]) OR (fatty acid, omega 3[MeSH Terms])) OR (fatty acids, omega 3[MeSH Terms])) OR (omega 3 eicosapentaenoic acid[MeSH Terms])) OR (omega 3 fatty acid[MeSH Terms])) AND (((((inflammatory markers[MeSH Terms]) OR (inflammation[MeSH Terms])) AND ((((cancer, colorectal[MeSH Terms]) OR (cancers, colorectal[MeSH Terms])) OR (carcinoma, colorectal[MeSH Terms])) OR (carcinomas, colorectal[MeSH Terms]))	31	2

Database	Search Strategy	Hits	Selected Articles
Cochrane	MeSH descriptor: [Fatty Acids, Omega-3] explode all trees OR ("omega-3"):ti,ab,kw AND MeSH descriptor: [Colorectal Neoplasms] explode all trees OR (colorectal cancer):ti,ab,kw AND (inflammatory markers):ti,ab,kw	23	0
Google Scholar	All in title : omega 3 supplementation, inflammatory markers, colorectal cancer	40	1



Scheme. Prisma's flow chart.

Table 3. Study characteristics.

Researcher	Year	Study Design	Number of Patient (n)	Population	Intervention	Control	Outcome
Liu, *et al.*[7]	2022	MA	1,556	CRC patients postoperatively	Omega-3 fatty acids oral route, 2–3 g/day, for 5–7 days postoperatively	Standard nutrition/ placebo	IL-6 (MD = −4.70, 95% CI: −6.59 to −2.80, $p < 0.00001$); CRP (MD = −2.41, 95% CI: −5.45 to 0.63, $p = 0.12$); albumin levels (MD = −0.21, 95% CI: −1.02 to 0.60, $p = 0.61$)
Li, *et al.*[8]	2023	MA	702	CRC patients undergoing surgery or chemotherapy	Omega-3 2–3 g/day, administered perioperatively or during chemotherapy	No supplementation	Lower CRP level (WMD -6.12), lower IL-6 level (SMD -0.54), lower TNF-a (SMD -0.56)
Wibowo, *et al.*[9]	2024	SR/MA	2,847	CRC patients in perioperative and chemotherapy settings	Omega-3 fatty acid 1.5–3 g/day administered 5–7 days pre/post operatively or peri chemotherapy	Standard care/ placebo	Lower CRP level (WMD -6.12), lower TNF-a level (SMD -0.56)

Abbreviations: MA: Meta-analysis; SR: Systematic review; CRC: Colorectal patient; CI: Confidence interval; MD: Mean difference; CRP: C-reactive protein; WMD: Weighted mean difference; SMD: Standardized mean difference; TNF: Tumor necrosis factor.

Table 4. Validity criteria.

	Study design	Number of patients	Randomization	Similarity treatment and control	Blinding comparable treatment	Domain	Determinant	Measurement of outcomes	Quality of evidence	Level of evidence
Liu, *et al.*, 2022.[8]	+	+	?	+	-	+	+	+	Moderate	1A
Li, *et al.*, 2023.[9]	+	+	?	+	?	+	+	+	Moderate	1A
Wibowo, *et al.*, 2024.[10]	+	+	?	+	?	+	+	+	Moderate	1A

Notes:

Quality of evidence according to GRADE guidelines, https://www.ncbi.nlm.nih.gov/pubmed/21208779

Level of evidence according to Oxford Center of Evidence-based Medicine (CEBM), http://www.cebm.net.

+ clearly mentioned in the article; - not done; ? Not stated clearly

- Systematic review and meta-analysis with troublesome heterogeneity

Table 5. Relevance criteria.

Researcher	Year	Population Similarity	Determinant/Intervention/Indicators Similarity	Outcome Similarity
Liu, *et al.*[8]	2022	+	+	+
Li, *et al.*[9]	2023	+	+	+
Wibowo, *et al.*[10]	2024	+	+	+

DISCUSSION

Colorectal cancer (CRC) induces profound metabolic disturbances largely mediated by chronic systemic inflammation, which plays a central role in the development of malnutrition. Tumor-driven secretion of pro-inflammatory cytokines such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), and insulin-like growth factor 1 (IGF-1) disrupts appetite regulation, promotes proteolysis, impairs protein synthesis, and accelerates energy expenditure, leading to muscle wasting and cancer cachexia.[3] These inflammatory processes not only decrease albumin production and elevate CRP levels but also compromise gut barrier function and microbiota balance, further reducing nutrient absorption.[4] In the preoperative phase, this inflammation-driven catabolic state heightens surgical risk, prolongs recovery, and increases susceptibility to complications.[11] Conversely, in the postoperative period, persistent inflammation is exacerbated by surgical stress, leading to worsened malnutrition, delayed wound healing, and impaired treatment tolerance. Nutritional interventions in both phases—particularly immunonutrition—are thus essential to modulate inflammatory response and support metabolic balance.[12]

Omega-3s are widely recognized as immunonutrients, alongside glutamine, arginine, and nucleotides, due to their immunomodulatory effects and their role in improving clinical outcomes, particularly in oncology and surgical settings.[6,11] As part of this immunonutritional approach, omega-3 polyunsaturated fatty acids (PUFAs)—particularly EPA and DHA—play a central role in modulating inflammation in colorectal cancer. They reduce inflammatory responses by inhibiting COX-2 activity and decreasing prostaglandin E2 (PGE2) synthesis.[13] Additionally, omega-3s alter membrane lipid rafts and suppress signaling pathways such as epidermal growth factor receptor (EGFR), PI3K/AKT, and mitogen-activated protein kinase (MAPK). They also stimulate the production of specialized pro-resolving mediators like resolvins and protectins. Supplementation with omega-3 has been shown to lower IL-6 and improve CRP levels, both of which are markers of systemic inflammation in colorectal cancer patients.[6,13,14]

Liu, *et al.*,[8] conducted a meta-analysis in 2023 to assess the efficacy and safety of omega-3 polyunsaturated fatty acids (O3FAs) as adjuvant therapy in colorectal cancer (CRC) patients. Nineteen randomized controlled trials involving 1,556 participants were included, with interventions delivered perioperatively or during chemotherapy. O3FAs were administered via several formulations, including oral capsules, enteral nutrition, and parenteral routes such as lipid emulsions in total parenteral nutrition (TPN). The oral and enteral dosages ranged from 1.2 to 3.6 g/day, typically using EPA/DHA mixtures, while parenteral doses ranged from 0.1 to 0.2 g/kg/day via intravenous lipid emulsions. Intervention durations varied from 2 to 84 days across studies. Meta-analysis showed significant reductions in TNF-α (MD = −0.79, p = 0.03) and IL-6 (MD = −4.70, p < 0.00001), and a shorter hospital stay (MD = −9.36, p = 0.01). However, effects on CRP, albumin, weight, body mass index (BMI), infection rates, CRC mortality, and quality of life were not statistically significant. The strengths of this study include its large sample size, inclusion of both surgical and chemotherapy settings, and subgroup analysis by administration route. Limitations include heterogeneity in dosing regimens,

variation in timing of supplementation, and methodological variability across included trials.

Li, *et al.*,[9] conducted a meta-analysis in 2023 to evaluate the effects of polyunsaturated fatty acids (PUFAs) on postoperative complications, inflammatory markers, immune response, and nutritional status in colorectal cancer patients. The analysis included 12 randomized controlled trials involving 702 participants. Omega-3 was administered either orally (660 mg to 4.8 g/day) or parenterally (0.2 g/kg/day), using fish oil or enriched immunonutrition formulas, for durations ranging from 5 to 84 days. Subgroup analysis based on timing revealed that preoperative and postoperative supplementation significantly shortened hospital stay (WMD = −2.27 and −2.66, respectively; $p < 0.05$). Among the included studies, Braga, *et al.*,[15] administered omega-3 at approximately 2 g/day for 5–7 days preoperatively, while Mocellin, *et al.*,[16] used 2.2 g/day for 4 weeks during chemotherapy. PUFA supplementation also led to significant reductions in CRP (WMD = −6.12, $p = 0.02$), IL-6, and TNF-α levels, while albumin showed modest improvement in patients receiving chemotherapy. The strengths of this meta-analysis include subgroup analysis by timing and route of administration, and comprehensive evaluation of both nutritional and inflammatory markers. However, heterogeneity in protocols and co-interventions limits generalizability and underscores the need for standardized future trials.

Wibowo, *et al.*,[10] conducted a systematic review and meta-analysis in 2024 to evaluate the efficacy of omega-3 fatty acids (O3FAs) as a complementary treatment in colorectal cancer (CRC) patients, focusing on inflammatory markers, nutritional status, infectious complications, and recovery. The analysis included 12 randomized controlled trials. Omega-3 was administered via oral capsules (e.g., 660 mg to 4.8 g/day) and parenteral infusions (e.g., 0.2 g/kg/day), with durations ranging from 5 days to 9 weeks, depending on the intervention phase (pre-, peri-, or post-operative). The supplementation led to significant reductions in IL-6 (MD = −4.86, $p = 0.009$) and CRP (MD = −1.87, $p = 0.003$ after sensitivity analysis), with a trend toward reduced TNF-α levels ($p = 0.06$). Serum albumin levels showed slight improvement (MD = 0.13, $p = 0.18$), though not statistically significant. The incidence of post-operative infectious complications and length of hospital stay also decreased with O3FA use. Strengths of this study include its specific focus on CRC and multi-outcome evaluation. However, limitations include high heterogeneity across studies (CRP $I^2 = 75\%$, albumin $I^2 = 97\%$) and inconsistent intervention protocols, highlighting the need for standardized dosing and timing in future trials.

CONCLUSION

Omega-3 supplementation as adjunctive therapy in colorectal cancer patients demonstrates potential benefits in reducing systemic inflammation, particularly through the suppression of interleukin-6 (IL-6). These effects are likely mediated by omega-3's immunomodulatory mechanisms, including inhibition of pro-inflammatory cytokines and enhancement of inflammation-resolving mediators. While reductions in C-reactive protein (CRP) were inconsistent across studies, and albumin levels showed only modest improvements, these findings still indicate possible enhancements in both inflammatory and nutritional status. The variability in study protocols—ranging from oral to parenteral administration, with doses between 660 mg and 4.8 g/day and durations from 5 to 84 days—limits the generalizability of the evidence. Furthermore, inconsistencies in the timing of supplementation and the presence of co-interventions contribute to heterogeneity in outcomes. High-quality randomized controlled trials with standardized omega-3 regimens are needed to confirm its clinical utility, establish optimal dosing strategies, and assess its long-term impact on inflammation and nutritional recovery in colorectal cancer patients.

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