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Abstract

Serum albumin has traditionally been used as a quantitative measure of a patient’s nutritional status because of its availability and low cost. While malnutrition has a clear definition within both the American and European Societies for Parenteral and Enteral Nutrition clinical guidelines, individual surgeons often determine nutritional status anecdotally. Preoperative albumin level has been shown to be the best predictor of mortality after colorectal cancer surgery. Specifically in colorectal surgical patients, hypoalbuminemia significantly increases the length of hospital stay, rates of surgical site infections, enterocutaneous fistula risk, and deep vein thrombosis formation. The delay of surgical procedures to allow for preoperative correction of albumin levels in hypoalbuminemic patients has been shown to improve the morbidity and mortality in patients with severe nutritional risk. The importance of preoperative albumin levels and the patient’s chronic inflammatory state on the postoperative morbidity and mortality has led to the development of a variety of surgical scoring systems to predict outcomes efficiently. This review attempts to provide a systematic overview of albumin and its role and implications in colorectal surgery.

Key words: Colorectal surgery; Malnutrition; Albumin; Hypoalbuminemia; Prealbumin; Serum albumin; Nutrition

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Core tip: Although albumin remains a flawed marker of nutrition, it offers clear prognostic value in predicting patient outcomes after colorectal surgery. Hypoalbuminemia significantly influences the length of hospital stay, rates of surgical site infections, enterocutaneous fistula risk, and deep vein thrombosis formation. Despite the fact that hypoalbuminemia is classically defined $< 3.0$ g/dL, clinical judgment must account for albumin levels $\leq 3.4$ g/dL as even modest hypoalbuminemia can affect outcomes. The subjective global assessmen, modified Glasgow Prognostic Score, and Colorectal preoperative Surgical Score scoring systems provide convenient and valuable prognostic information that may help in the
counseling and risk adjustment of patients undergoing colorectal surgery.


INTRODUCTION

Albumin is a single polypeptide responsible for five main functions: (1) maintenance of colloid osmotic pressure; (2) binding and transport of solutes; (3) free radical scavenging; (4) platelet function inhibition and antithrombotic effect; and (5) beneficial effects on vascular permeability in the setting of shock and sepsis[1]. Albumin is a major source of sulfhydryl groups, which sequester both leukotoxin and nitric oxide, limiting vascular permeability and dilation respectively. Serum albumin has traditionally been used as a quantitative measure of a patient’s nutritional status because of its ready availability and low cost. The reliability of albumin as an assessment of malnutrition is controversial because hypoalbuminemia is an acute phase reactant and is affected by systemic inflammation[2]. The increased demand for specific amino acids for acute phase protein synthesis degrades available body protein, including albumin[3-5]. Therefore, nutritional status is often determined anecdotally by individual care providers based on their own clinical experience and judgment in clinical practice. In this review, we cover in-depth the clinical indications and implications of serum albumin levels in the setting of colorectal surgery. We investigate the correlation between albumin and postoperative complications, inflammatory bowel disease (IBD) treatment, nutritional response, and new prognostic models.

LITERATURE RESEARCH

We performed a systematic literature review through an electronic search of MEDLINE from PubMed and the Cochrane Library until May 2015. We used the following search terms and associations: Albumin, hypoalbuminemia, serum protein, nutrition, malnutrition, colorectal surgery, gastrointestinal (GI) surgery, complications, and mortality. Articles were assessed in a tiered fashion. We first screened the titles, assessed abstracts for relevance, then filtered the entire text of the papers. Only papers in the English language were included. After removing duplicates, 379 total records were found, 339 of which were in English. Thirty-five articles remained after screening and their full texts were analyzed. We completed this search by visiting the bibliographies of relevant articles.

HYPOALBUMINEMIA IN SURGICAL PATIENTS

In the early 1950’s, hypoalbuminemia was noted to negatively influence postoperative recovery[6,7]. This finding was followed by work from Harvey who reported that a low serum albumin was the best indicator of concurrent sepsis[8]. A high incidence of malnutrition in the hospital setting was first described in 1974 by Banh[9] and Butterworth[10]. Contemporary data currently shows that malnutrition has a prevalence of 30% to 50% in hospitalized patients, and is one of the most important patient outcome determinants, affecting length of hospitalization, cost, morbidity, and ultimately mortality[11,12]. Most notably, hypoalbuminemia is associated with poor tissue healing, decreased collagen synthesis, and granuloma formation in surgical wounds, ultimately delaying wound healing[13-17]. Serum albumin levels have traditionally been used as a biochemical marker of individual nutritional status prior to surgery. It is regarded as an accurate preoperative prognostic indicator in a variety of surgical procedures including cardiac[18], trauma[19], and general surgery[20-22]. This was perhaps best illustrated in a large-scale non-randomized retrospective study using the National Veteran’s Affairs Surgical Database of 54215 patients from 44 tertiary care centers by Gibbs et al[23] on major non-cardiac surgeries. Thirty-day morbidity and mortality were measured by C-index (C) where a value of 0.0-0.5 indicates any association between variables are likely due to chance, and C of 0.5-1.0 indicates a strong predictive value or correlation[24]. Univariate analysis revealed that albumin < 3.5 g/dL was the strongest preoperative predictor of both 30-d morbidity (C = 0.68) and mortality (C = 0.78), just ahead of American Society of Anesthesiology class. Furthermore, multivariate analysis showed that albumin levels were the strongest predictor of both morbidity (odds ratio (OR) = 0.68; 95%CI: 0.56-0.60) and mortality (OR = 0.44; 95%CI: 0.41-0.48). Albumin levels also independently predicted complication rates of systemic sepsis, acute renal failure, coma, failure to wean from ventilation, and bleeding/transfusions amongst 16 other complications (C = 0.78, 0.76, 0.76, 0.75, 0.72 respectively; all P < 0.001). Additionally, analysis of preoperative albumin and major post operative complications in 2003 by Kudsk et al[25] identified clinical hypoalbuminemia as an independent determinant of hospital stay, serious postoperative complications (albumin < 4.25 g/dL), and mortality (albumin < 3.25 g/dL).

On the other hand, an ongoing debate continues to exist regarding the value of albumin as a clinical marker of malnutrition. There is no clear consensus amongst healthcare professionals about the definition of malnutrition. Suggested markers include albumin and prealbumin, which are widely used today, and transferrin and retinol binding protein, which are newer evolving
Although the classic definition for hypoalbuminemia is < 3.0 g/dL, studies’ definitions vary widely from < 2.7 in some studies to < 3.5 g/dL in others[12,40,41]. Using the American College of Surgeons National Quality Improvement Program (NSQIP) database to measure 30-d postoperative surgical outcomes, Moghadamyeganeh et al[12] emphasized the effect of modest hypoalbuminemia as defined by serum albumin levels between 3.0 and 3.4 g/dL. The mortality rate in patients with modest hypoalbuminemia and without hypoalbuminemia was 6% and 1.7% respectively, and the morbidity risk was greater as well [adjusted odds ratio (AOR) = 1.876; 95%CI: 1.51-2.05; P < 0.01]. Not surprisingly, the highest morbidity (60.4%) and mortality (26.2%) rates occurred at serum albumin levels lower than 2 g/dL. Additionally, this study showed a linear correlation between albumin level and postoperative mortality, meaning any decrease in serum albumin level from the normal value (> 4 g/dL) had serious effects on the outcomes following colorectal resections. The rate of increase in mortality and morbidity was estimated to be approximately 49% and 24% respectively for each 1 g/dL decrease in albumin level (P < 0.05). Colon cancer patients had a higher rate of modest hypoalbuminemia compared to rectal cancer patients (AOR = 1.55; P < 0.01).

Complications

The relationship to colorectal surgery.

Hypocomplenemia and colorectal surgery

Despite the growing fund of research surrounding albumin status in general surgery patients, colorectal surgery maintains a unique relationship with nutritional status and albumin level. Colorectal surgery patients are often malnourished due to advanced malignancy or inflammatory bowel disease that results in poor oral intake, intestinal blockages, intestinal fistulas, poor absorptive capacity, and large volume losses from the GI tract[32]. Kudsk et al[33] emphasized the potential for bias if the surgical site is not considered. Malnutrition is observed in up to 80% of patients with advanced colorectal cancer putting them at increased risk for postoperative complications[25-30]. Burden et al[34] showed that 1 in 5 pre-operative colorectal cancer patients undergoing surgery were malnourished when measuring body weight (weight loss > 10%) and had a significantly lower handgrip strength (P = 0.013), a measure of nutritional status[37]. Hypoalbuminemia has also been associated with delayed recovery of postoperative bowel function, further worsening postoperative nutritional recovery[38]. Preoperative albumin levels have been shown to be the best predictor of mortality after colorectal cancer surgery[12,39]. It is important to concede that the current research surrounding albumin levels is limited and heterogeneous; each study uses different qualifications and methods. Below is a review of the current literature surrounding hypoalbuminemia and its relationship to colorectal surgery.

ILEUS

Postoperative bowel function is a major determinant of the length of hospital stay and nutritional recovery of a patient. A key retrospective study of 80 patients undergoing right hemicolectomy by Lohsiriwat et al[36] showed that an albumin level < 3.5 g/dL compared to...
an albumin > 3.5 g/dL was associated with increased postoperative complications (0 and 14 respectively; \( P < 0.001 \)), time to first bowel movement (55.3 and 69.5 h respectively; \( P = 0.018 \)), and time to resume a normal diet (4.0 to 4.9 d respectively; \( P < 0.001 \)). In multivariate analysis, only delayed time to first bowel movement was associated with preoperative hypoalbuminemia. Similarly, Millan et al.\(^{42} \) showed that albumin levels < 35 mg/dL were significantly associated with postoperative ileus (\( P = 0.042 \)) in a retrospective study of 773 patients. Kronberg et al.\(^{43} \) also showed in a study of 413 patients that preoperative serum albumin concentration was lower in patients who developed postoperative ileus (3.83 mg/dL vs 4.09 mg/dL; \( P = 0.039 \); OR = 0.90). Prolonged postoperative ileus symptoms include nausea and vomiting, inability to tolerate an oral diet, abdominal distention, and delayed passage of flatus and stool\(^{44,45} \). Decreasing preoperative albumin was a predictor for prolonged postoperative ileus (OR = 1.11 per gram per litre unit change; 95%CI: 1.02-1.22; \( P = 0.047 \))\(^{46} \).

**SURGICAL SITE INFECTION**

A study of 524 patients undergoing GI surgery [of which 339 (64%) underwent colorectal surgery] in 4 institutions in Ireland showed that patients who developed a surgical site infection had a lower median preoperative serum albumin than those who did not develop an infection, 3.0 g/dL and 3.6 g/dL respectively (\( P < 0.001 \))\(^{47} \). One hundred and thirty-eight patients (26.3%) had a low preoperative albumin level (< 3.0 g/dL) and were found to be at increased risk for severe surgical site infections. Of the patients developing a superficial wound infection, 46.4% had a low albumin level (\( P = 0.001 \)). In those with deep wound infections, 80% had low albumin levels (\( P = 0.004 \)), and in those with organ space infection, 83.3% had low albumin levels (\( P = 0.397 \)).

**FISTULAS**

Enteric or enterocutaneous fistulas are abnormal communications between the gastrointestinal tract to another cavity or through the skin respectively. Although uncommon, they are a significant concern within colorectal surgery due to their relatively high incidence and considerable morbidity and mortality, first described in a classic case study of 157 patients in 1960\(^{47,49} \). An estimated 75%-85% of enterocutaneous fistulas are postoperative complications following bowel injury via inadvertent enterotomy and/or anastomotic leakage\(^{50} \) and 30%-80% eventually require surgical treatment despite advances in medical treatment\(^{51-53} \).

Not surprisingly, serum albumin level has been shown to be a vital prognostic factor of healing enteric fistulas\(^{49,54} \). In a retrospective chart review of 53 GI cancer patients with postoperative enteric fistula complications, Lu et al.\(^{49} \) showed a significant correlation between enteric fistula healing/recovery and an increased serum albumin level (\( P = 0.029 \)) and lower fistula drainage amount (< 500 mL/d) (\( P = 0.013 \)) after multivariate analysis. Additionally, amongst patients with both increasing albumin levels and < 500 mL/d of fistula drainage, over 90% of fistulas fully resolved with conservative therapy after total parenteral nutrition (TPN)\(^{49,55} \). However, although TPN nutritional support has been shown to aid recovery, careful monitoring for underlying or uncontrolled sepsis is required as patients are prone to rapidly deteriorate\(^{52} \).

Once it is obvious that operative repair is unavoidable, the decision between early surgical fistula treatment vs initial nutritional support with delayed surgery is a difficult one. In a report of 135 consecutive patients with enterocutaneous fistulas by Visschers et al.\(^{53,56} \) hypoalbuminemic patients failed to recover well after restorative surgery. Patients with an albumin level below 2.5 g/dL continued to show signs of inflammation postoperatively despite being treated for infection, which lead to eventual deterioration and death in the majority (17/25; 68%) of patients while those who had albumin > 2.5 g/dL had lower mortality (8/25; 32%). Operative fistula repair in hypoalbuminemic patients is therefore recommended only after a nutritive recovery period of at least 6 wk.

**DEEP VEIN THROMBOSIS/PULMONARY EMBOLISM**

There is limited data regarding the predictive factors of postoperative venous thromboembolism in patients undergoing colorectal resection. Using data from the large national NSQIP database from 2005 to 2011, Moghadamyeghanesh et al.\(^{41} \) showed that a serum albumin < 3.5 mg/dL significantly increased the risk of developing a postoperative deep vein thrombosis (DVT) (AOR = 1.69; 95%CI: 1.49-1.93; \( P < 0.01 \)). Additionally, hypoalbuminemia was also associated with an increased risk of pulmonary embolism (PE) (AOR = 1.21; 95%CI: 1.02-1.42; \( P < 0.02 \)) although the strongest risk factor for PE was not surprisingly a DVT.

**INFLAMMATORY BOWEL DISEASE AND HYPOALBUMINEMIA**

Inflammatory bowel disease is broadly classified into two variants, ulcerative colitis (UC) and Crohn’s disease (CD). The mainstay of UC and CD therapy is medical management, however up to 1/3 of Crohn’s patients will undergo abdominal surgery within the first 5 years of diagnosis\(^{47} \). In CD, hypoalbuminemia has been shown to be a predictor of intraabdominal septic complications after intestinal anastomosis by Yamamoto et al.\(^{50} \) in a retrospective chart review of 343 patients undergoing 1008 intestinal anastomoses between 1980 and 1997. In this study, albumin levels < 3.0 g/dL were considered hypoalbuminemic and significantly affected
the incidence of intra-abdominal sepsis in univariate
and multivariate analysis with P values of 0.01 and 0.04
respectively. Intra-abdominal sepsis occurred in 21% of
patients with hypoalbuminemia in contrast to 12% in
those without. If all significant risk factors in this study
(hypoalbuminemia, steroid use at least one month
immediately before surgery, and abscess or fistula at
the time of laparotomy) were present, the incidence
of sepsis reached 50%. Because reoperations for early
postoperative complications were not included in this
study, the impact of serious postoperative or refractory
hypoalbuminemia could not be assessed.

Intra-abdominal sepsis and delayed wound healing
are significant consequences of hypoalbuminemia in
IBD patients[69]. For these reasons, ileal pouch anal
anastomosis (IPAA), the treatment of choice for UC,
has traditionally been avoided due to the large number
of suture or staple lines and wide pelvic dissection in
malnourished patients[60,61]. An 8-year single-institution
prospective study identifying 405 patients showed
that an albumin level < 3.5 g/dL was significantly
associated with IPAA pouch failure within 30 d to 10
years, development of anastomotic leak, postopera-
tive transfusion, and prolonged inpatient stay using
univariate analysis[62]. Multivariate analysis revealed
preoperative hypoalbuminemia as a strong predictor
for anastomatic leak and prolonged median length of
stay after pouch surgery, which was 60% longer than in
patients with normal albumin levels.

Because of the high complication rate of pouch
creation in IBD patients, a staged operation is favored.
Nisar et al[62] showed that hypoalbuminemic patients
with IBD who underwent a single-stage total procto-
colectomy (TPC) with concurrent pouch creation had
a significantly longer inpatient stay and increased
postoperative transfusion requirements compared to
two-stage subtotal colectomy (STC) with subsequent
completion proctocolectomy and IPAA. A higher risk
of anastomotic leak in hypoalbuminemic patients was
found in single-stage TPC and IPAA (22%) compared to
initial STC with follow-up completion proctectomy and
IPAA (11%). However, the sample only comprised 24
TPC patients and 10 with STC. Interestingly, this study
was one of very few which analyzed serum albumin
levels as a continuous variable and thus found that the
improvement in albumin between the time of STC and
IPAA correlated significantly with the baseline albumin (R²
= 0.814), (P < 0.0001).

In a retrospective case series of 78 patients with CD
but without hypoalbuminemia, Zerbib et al[63] showed
that weaning steroids and applying enteral nutrition at
> 30 kcal/kg ideal body weight/day in intestinal non-
occluded patients or TPN in patients with intestinal occlusion together with abscess drainage and antibio-
tic therapy for 2-3 wk preoperatively minimized the
usage of a temporary diverting stoma [7.7% (6/78) of
patients] while achieving uneventful operative outcomes
in 58% of the total patients. This rate of diverting stoma
utilization was significantly lower than a previously
reported series for penetrating CD by Goyer et al[64]
who reported a rate of 39%. This suggests a strong
correlation between preoperative nutrition and Crohn’s
disease surgical outcomes.

**PREOPERATIVE TREATMENT OF HYPOALBUMINEMIA**

While the deleterious effects of hypoalbuminemia on
the rate of postoperative complications have been well
established, pre-surgical correction of hypoalbuminemia
remains a subject of debate. While some believe a low
albumin level indicates malnutrition, others postulate
that the hypoalbuminemia stems from the chronic
disease state and resultant inflammation and is not
due to malnutrition, thus hindering any beneficial effects
of nutritional therapy[3]. Although enteral and parenteral
nutrition have been shown to improve outcomes in
malnourished patients undergoing major elective sur-
gery[65], preoperative nutrition not been well studied
in populations undergoing colorectal surgery. The con-
sensus is to stabilize baseline nutritional status and to
administer enteral or parenteral nutrition to severely
hypoalbuminemic patients preoperatively, even if a delay
in surgery is necessary.

In 1982, a study by Rombeau et al[66] of 33 con-
secutive IBD patients demonstrated that preoperative TPN
given for at least 5 d resulted in significantly fewer post-
operative complications (P < 0.05). All patients had an
albumin < 3.5 g/dL or a transferrin level < 150 mg/dL.
In a case series by Jacobson, 15 consecutive CD patients
given preoperative TPN were compared to 105 control
patients matched for known postoperative complication
factors[67]. TPN was given between 18 and 90 (avg = 46)
d preoperatively before undergoing intestinal resection
with primary hand-sewn anastomoses. In this study
the average albumin level was significantly increased
from 3.4 to 3.9 g/dL (P < 0.01) through TPN. There
was a significantly higher rate of complications in the
non-TPN group (29/105) compared to the TPN group
(0/15) (P < 0.05). Although the TPN group was without
postoperative complications, the risk of preoperative
complications should be recognized. In the TPN group,
repeated central venous catheter thromboses requiring
up to 5 replacements occurred in 4 patients and a
pneumothorax which resolved after 5 d of evacuation
occurred in one other patient.

Lashner et al[68] further quantified the significance of
preoperative TPN. In a retrospective single-center/single-
surgical team study of 103 CD patients, preoperative
TPN was only beneficial to CD patients by reducing the
length of bowel resection during small bowel resection
by more than 20 cm (P < 0.05). There was no difference
in complication rates. During ileectomy, TPN patients
had a shorter resection by approximately 11 cm when
compared to non-TPN patients (P < 0.02). However,
it appears that the cost of shorter bowel resections
in TPN patients was longer hospital stays (12 d; P <
0.001). Although this study included patients undergoing
large bowel resection, none of them received preoperative TPN. In this study, TPN was given between 5-7 d and administration > 10 d was not recommended. In contrast, the European Society for Clinical Nutrition and Metabolism guidelines state that if a severe nutritional risk is present, preoperative nutrition therapy, if possible, by enteral route for 10-14 d before surgery is recommended even if the surgery has to be delayed. Additionally, Visschers et al[53] recommended delaying enterocutaneous fistula repair at least 6 wk to stabilize baseline nutritional status in severely malnourished patients.

NEW COLORECTAL SURGERY SCORING SYSTEMS

Broad efforts have been made to use albumin levels together with other clinical markers to create a scoring system predicting postoperative morbidity or mortality. The Subjective Global Assessment (SGA) scale combines both subjective aspects of the patient’s history such as gastrointestinal symptoms and dietary change and objective aspects such as ankle edema, albumin levels, and tumor grade.[70]. The SGA stratifies patients into A, B and C categories yielding significant differences in median survival in their cohort of 235 patients (log rank 13.36; P = 0.0013). The SGA provides useful prognostic information in patients with advanced colorectal cancer and may identify malnourished patients quickly but suffers due to the inclusion of subjective measures exposing it to observer bias.

The modified Glasgow Prognostic Score (mGPS) ranges from 0-2 and is composed of C-reactive protein (CRP) and albumin levels. mGPS was shown by Park et al[71] in a retrospective single-center study to tightly correlate with overall survival (OS) in patients undergoing elective resection of colon cancer (P < 0.001). When mGPS and tumor-node-metastasis (TNM) staging were combined, they effectively stratified outcomes of patients undergoing potentially curative resection of colorectal cancer. A TNM stage I/mGPS = 0 yielded a 5-year cancer specific survival (CSS) and overall survival of 97% and 87% respectively; whereas a TNM stage III/ mGPS = 2 exhibited a 5-year CSS and OS of 32% and 26% respectively (P < 0.001). Additionally, the mGPS stratified the survival of patients who received adjuvant chemotherapy after resection of stage III colon cancer. Patients with mGPS = 0 had a 50% relative increase in survival at 5 years with adjuvant therapy, whereas those with mGPS = 1-2 received no benefit (P = 0.003). The mGPS provides important prognostic information in patients undergoing colorectal resections and can help guide adjuvant therapy, especially when combined together with TNM staging.

The Colorectal preoperative Surgical Score (CrOSS) was proposed by Kong et al[39] in 2015 as a response to other scoring systems, which require postoperative variables or may be too complex or difficult to assess at the patient’s bedside. Their multivariate logistic regression analysis of 46 variables yielded 4 independent predictors for mortality following colorectal surgery: Age ≥ 70, urgent surgery, albumin level ≤ 3.0 g/dL, and congestive heart failure, together composing the CrOSS score. CrOSS accurately predicted mortality with a receiver operating characteristic (ROC) of 0.870 and calibration P-value of 0.937. The score was internally and externally validated to the Portsmouth and Colorectal Physiological and Operative Severity Score for enUmeration of Mortality and Morbidity and the 2012 Barwon Health model (ROC = 0.788, P = 0.24). CrOSS offers a simple yet robust preoperative risk stratification model, specifically tested in colorectal surgery.

NEW MARKERS FOR MALNUTRITION AND INFLAMMATION

Although albumin remains the widest studied marker for malnutrition, several other markers have been proposed to aid perioperative assessment of a colorectal surgery patient. Prealbumin, transferrin and retinol binding protein are considered traditional markers of nutrition; however, recent data demonstrates their poor relationship to nutrition status. Because the markers for a patient’s nutrition status are often negative acute-phase reactants, efforts have been made to quantify a patient’s inflammatory status as an indirect measure of nutrition and postoperative morbidity and mortality.

In 2012, Oberhofer et al[72] showed an increase in CRP in the early postoperative period after colorectal surgery was correlated with a significant increase in complication rates (P < 0.001), which agreed with Welsch et al[73] who demonstrated that CRP values greater than 140 mg/L on postoperative day 3 or 4 predicted infectious complications and anastomotic leaks after colorectal surgery. Conversely, preoperative CRP levels were not correlated with postoperative complication incidence. Oberhofer et al[72] also concluded that postoperative procalcitonin increased significantly more in patients with postoperative complications than those patients without complications, with the highest predictive value on postoperative day 5 (P < 0.001). Procalcitonin is also a reliable laboratory marker for early diagnosis of surgical site infection and sepsis after colorectal cancer surgery (P < 0.001).[74-75]

Prealbumin (PAB), also known as transthyretin, is a visceral protein and a negative acute phase reactant similar to albumin. PAB’s advantage over albumin is its shorter half-life (2-3 d), thus it may be more useful for detecting acute changes in nutritional status. However, similar to albumin, PAB has been shown to be a poor marker of nutritional status as evidenced by studies of extreme cases of starvation, which fail to show consistent or reversible decreases in PAB levels.[76-77] In addition, PAB has been shown to be inferior to albumin as a predictor of colon cancer recurrence. A study of 158 patients with operable colorectal carcinoma in Japan,
56 patients (35.4%) with decreased preoperative PAB and 15 patients (9.5%) with decreased preoperative albumin levels, showed that both a low preoperative serum PAB and albumin were associated with early disease recurrence (P = 0.0005 and P = 0.0002 respectively) [79]. However, only albumin maintained its significance in multivariate analysis (P = 0.048) while PAB lost significance, indicating that only albumin is an independent predictor of early colorectal carcinoma recurrence.

Additionally, interleukin-6 has recently been shown to correlate with more advanced colorectal cancer [79] and was found to cause reactive thrombocytosis, upregulation of CRP, and downregulation of albumin production by the liver, all processes of acute inflammation [80]. Preoperative thrombocytosis with a platelet count greater than 300 × 10^9/L was related to overall survival in multivariate analysis (P = 0.039; OR = 1.642; 95%CI: 1.025-2.629) [81].

Recent studies demonstrate positive survival outcomes after colorectal surgery by targeting the systemic inflammatory response with anti-inflammatory agents such as broad-spectrum nonsteroidal anti-inflammatory drugs or aspirin [82,83]. Adequate dietary habits are also associated with both decreased colorectal cancer risk and postoperative outcomes. Increased marine n-3 polyunsaturated fatty acids consumption was protective against postoperative complications after colorectal cancer surgery [84-86].

**CONCLUSION**

Although albumin remains a flawed marker of nutrition, it offers clear prognostic value in predicting patient outcomes after colorectal surgery. Hypoalbunemia significantly influences the length of hospital stay and complication rates, specifically surgical site infection, enterocutaneous fistula, and DVT formation. However, these studies are mostly small-cohort non-randomized retrospective studies or large scale studies using national data bases and this topic would benefit from further study. Although clinical hypoalbunemia is classically defined as serum concentrations < 3.0 g/dL, clinical judgment must account for albumin levels ≤ 3.4 g/dL as even modest hypoalbunemia can affect outcomes. Surgical delay for preoperative nutrition has been shown to improve the morbidity and mortality in patients with severe nutritional risk. Hypoalbuminemic patients may benefit from a staged colorectal resection vs a single operation, especially in the setting of IBD. Efforts to quantify a patient's nutritional status indirectly with inflammatory markers show promise, but the data is superficial and overall inferior to albumin. However, addressing systemic inflammation with anti-inflammatory agents has demonstrated positive survival outcomes in pilot studies. How these developing new markers will be used in combination with albumin is an interesting frontier, meanwhile the SGA, mGPS, and CrOSS scoring systems provide convenient and valuable prognostic information that may help in the counseling and risk adjustment of patients undergoing colorectal surgery.

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