

Additional Value of Preoperative Albumin for Surgical Risk Stratification among Colorectal Cancer Patients

David W. Larson^a Mohamed A. Abd El Aziz^a William Perry^a
Anne-Lise D'Angelo^a Kevin T. Behm^a Kellie L. Mathis^a Fabian Grass^b

^aDivision of Colon and Rectal Surgery, Department of Surgery, Mayo Clinic, Rochester, MN, USA; ^bDepartment of Visceral Surgery, Lausanne University Hospital CHUV, University of Lausanne, Lausanne, Switzerland

Keywords

European Society for Clinical Nutrition and Metabolism · Malnutrition · Colorectal cancer · Surgery · Hypoalbuminemia

Abstract

Background: BMI ≤ 18.5 kg/m² and preoperative weight loss may lead to inaccurate assessment of nutritional status, given the increasing prevalence of obesity. The aim of this study was to assess whether clinical evaluation of malnutrition based on these parameters is sufficient to predict complications after colorectal cancer surgery. **Materials and Methods:** The American College of Surgeons-National Quality Improvement Program database was queried from 2005 to 2018. Patients undergoing elective colorectal cancer surgery were divided into 4 groups: (1) albumin < 3.1 g/dL within 21 days of surgery, (2) European Society for Clinical Nutrition and Metabolism (ESPEN) 2 clinical parameters for malnutrition ($\geq 10\%$ loss of weight/6 months plus [BMI < 20 kg/m² if age < 70 years OR BMI < 22 kg/m² if age ≥ 70 years]), (3) both aforementioned criteria, and (4) none of aforementioned criteria. **Results:** Of 82,280 patients, 5,932 (7.2%) had hypoalbuminemia < 3.1 g/dL, 764 (0.9%) fulfilled clinical ESPEN 2 parameters, and 338 (0.4%) met both criteria. After adjusting for baseline confounders, patients in the hypoalbuminemia

group had a higher risk of overall complications (odds ratio [OR] 1.92, $p < 0.05$ vs. OR 1.18 in the ESPEN 2 group, $p < 0.05$), major complications (OR 1.98, $p < 0.05$ vs. OR 1.20, $p < 0.05$), surgical complications (OR 1.77, 95% $p < 0.05$ vs. OR 1.1, $p > 0.05$), medical complications (OR 1.73, $p < 0.05$ vs. OR 1.16, $p > 0.05$), surgical site infection (OR 1.32, $p < 0.05$ vs. OR 0.86, $p > 0.05$), and prolonged hospitalization (OR 1.79, $p < 0.05$ vs. OR 1.22, $p < 0.05$). Patients who met both criteria were at highest risk. **Conclusions:** Preoperative measurement of serum albumin appears to be essential to identify patients at risk for complications after colorectal cancer surgery. Clinical evaluation through BMI and weight loss alone may underestimate surgery-associated risks in the USA.

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Introduction

Malnutrition is common in patients with colorectal cancer and associated with increased surgical morbidity, mortality, and compromised long-term outcomes [1–5]. Preoperative nutritional screening is mandatory to identify patients who may benefit from nutritional therapy [6].

David W. Larson and Mohamed A. Abd El Aziz shared first authorship.

However, defining universal diagnostic criteria for malnutrition independent of etiology and clinical setting represents a challenge [7]. A wide array of both clinical and laboratory parameters are available as nutritional screening tools [8–10]. However, there is no formal consensus regarding accuracy and value of different assessment methods in patients with colorectal cancer [11, 12], with differing guidelines between European and American nutritional societies [6, 10, 13]. Official screening tools as suggested by the European Society for Clinical Nutrition and Metabolism (ESPEN) integrate, besides measurements of body composition (muscle mass), low BMI and significant preoperative weight loss as mandatory clinical parameters [10, 14]. Due to limited resources in a busy practice, measurement of body composition may not be routinely performed by many centers, leading to overly simplistic nutritional assessment through easily available clinical tools such as BMI and weight loss [15]. However, in countries with an increasing prevalence of obesity such as the USA, clinical evaluation based on BMI and weight loss alone may lead to an under-detection of patients at surgical risk [6, 16, 17]. In the absence of body composition as essential nutritional screening tool, serum albumin, often routinely assessed during preoperative screening, may help to refine surgical risk stratification [18].

Preoperative hypoalbuminemia of <3.1 g/dL has been recently identified as a critical threshold for postoperative adverse events [19]. However, systematic measurement of laboratory parameters such as serum albumin represents an additional cost burden to the chronically stressed health care system and a potential benefit remains questionable [6, 10, 20]. Since serum albumin does not represent a nutritional parameter but rather reflects disease severity, it was suggested as a helpful adjunct for risk stratification in ESPEN guidelines 2006 and the updated 2017 version [20, 21]. The aim of this study was to evaluate a potential benefit of serum albumin as an adjunct to the clinical nutritional parameters BMI and weight loss in a representative US population undergoing colorectal cancer surgery.

Methods

Data Source

The American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) Public User File from January 2005 to December 2018 provided the study cohort. ACS-NSQIP is an established, externally validated, and outcome-based clinical database that was created for quality improvement purposes. Trained data abstractors use standardized data extraction sheets to

report demographic, anthropometric, and perioperative data from the participant sites, which represent a 20% random sample of the US surgical population.

Cohort Selection

All adult (≥ 18 years) patients undergoing elective colorectal surgery for colon or rectal cancer using the Current Procedure Terminology codes and the International Classification of Diseases codes as specified in Figure 1 were included. Patients with missing anthropometric measures, missing albumin levels, albumin measurements deriving from outside the suggested preoperative 21-day window (half-life of albumin) [22], and American Society of Anesthesiologists (ASA) class V were excluded. Due to a potential impact on albumin levels, patients with preoperative ascites, preoperative sepsis, preoperative acute renal failure or hemodialysis, and ventilator dependence were excluded from the study.

Patients were divided into 4 non-overlapping, mutually exclusive groups: (1) severe hypoalbuminemia <3.1 g/dL [19], (2) clinical nutritional parameters for malnutrition ($\geq 10\%$ weight loss over 6 months PLUS [BMI <20 kg/m² in patients <70 years OR BMI <22 kg/m² in patients ≥ 70 years] [10]), defined as ESPEN 2 parameters [7] (3) both aforementioned criteria, and (4) none of aforementioned criteria. For comparative purposes of the different groups, 2 additional definitions were used: ESPEN 1 (BMI <18.5 kg/m²) and moderate hypoalbuminemia (albumin <3.5 g/dL). Of note, body composition (i.e., measurement of muscle mass) as a mandatory parameter for assessment of nutritional status according to ESPEN guidelines was not considered in this assessment. Therefore, the used clinical nutritional parameters should not be considered as officially recommended ESPEN screening tools.

ACS-NSQIP reported baseline demographics, laboratory parameters (albumin, hematocrit, platelet count, liver function tests i.e., serum glutamic oxaloacetic transaminase [SGOT]), and surgical details (approach, operating time, and extent of resection) were compared between the 4 groups [23]. Primary study outcomes of interest were postoperative 30-day complications according to standardized ACS-NSQIP definitions, which were regrouped as surgical (including surgical site infection [SSI], wound disruption, systemic sepsis, and need for blood transfusion), medical including urinary tract infection, respiratory complications (pneumonia, unplanned intubation, and/or on mechanical ventilator ≥ 48 h), renal complications (progressive renal failure, and/or acute kidney injury), major adverse cardiovascular events (MACE: stroke, cardiac arrest requiring cardiopulmonary resuscitation, and/or myocardial infarction) and vascular thromboembolism (VTE: pulmonary embolism and/or deep venous thrombosis), minor complications (including urinary tract infection and superficial SSI), and major complications (including myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, deep venous thrombosis, pulmonary embolism, pneumonia, unplanned intubation, need for mechanical ventilator for ≥ 48 h after surgery, acute kidney injury, progressive renal insufficiency, stroke, blood transfusion, deep SSI, organ space infection, wound disruption, and systemic sepsis). Further assessed were unplanned reoperation if the indication was related to the index operation, unplanned readmission related to the index operation, index length of stay (LOS), whereas prolonged LOS was defined as ≥ 7 days according to the upper quartile of the entire cohort), and 30-day mortality. Postoperative complications were risk-adjusted and compared between the 3 groups (albumin <3.1 g/dL, ESPEN 2, both criteria).

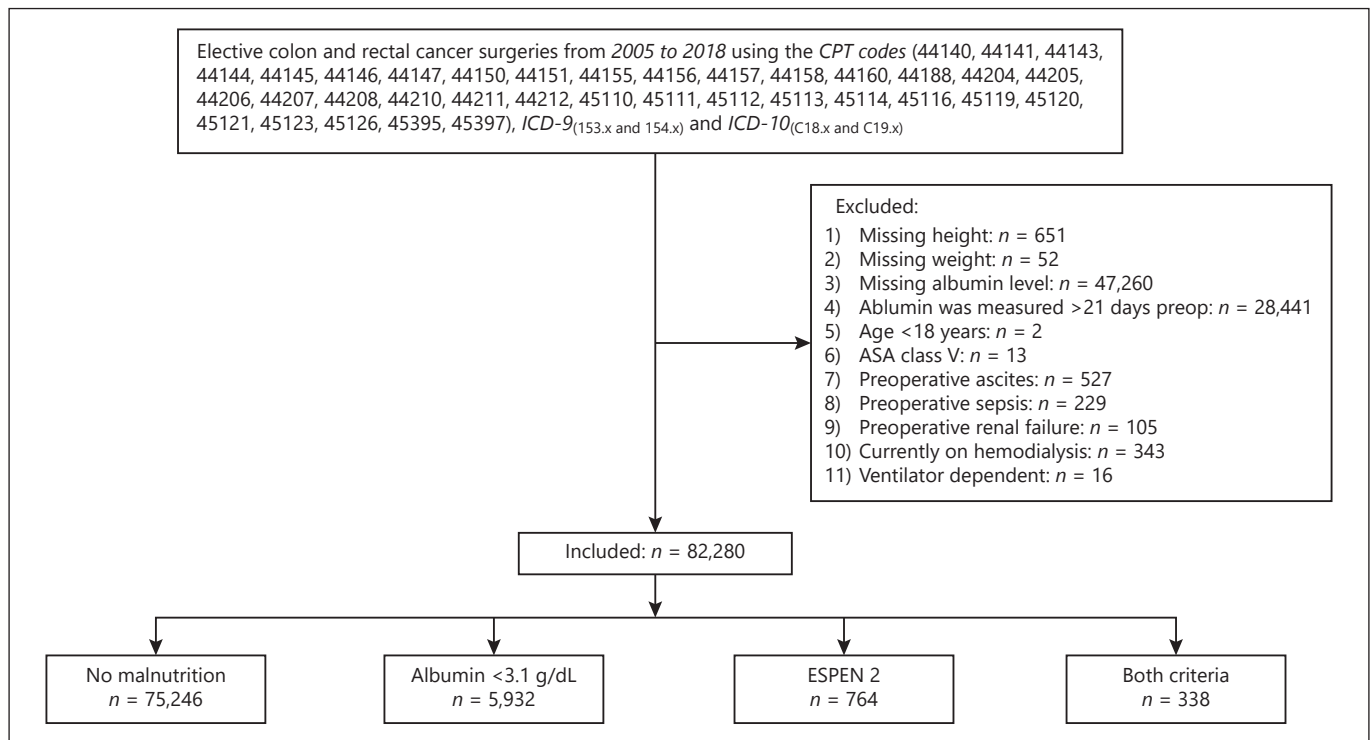


Fig. 1. Study's flow diagram. ESPEN, European Society for Clinical Nutrition and Metabolism.

Statistical Analysis

Descriptive statistics were reported as percentages and frequencies for categorical variables and as median (interquartile range) for continuous variables. The differences between exposure groups and outcomes were examined using the χ^2 test for categorical variables and the Kruskal-Wallis test for continuous variables. Outcomes with an alpha level of less than 0.1 after univariable analysis were further evaluated by multivariable binary logistic regression to compute adjusted odds ratios (ORs). For all the analyses, an alpha level of less than 0.05 was considered statistically significant. Data analysis was performed using Statistical Package for the Social Sciences SPSS Advanced Statistics 25 (IBM Software Group, Inc., Armonk, NY, USA).

Results

A total of 82,280 patients constituted the study cohort. Of these, 5,932 (7.2%) patients had preoperative hypoalbuminemia <3.1 g/dL, 764 (0.9%) met the definition of ESPEN 2 clinical nutritional parameters, and 338 (0.4%) met both criteria (hypoalbuminemia <3.1 g/dL and ESPEN 2), as detailed in Figure 1. Figure 2 illustrates the distribution of 3 different risk stratification methods ($\geq 10\%$ weight loss in the last 6 preoperative months, albumin <3.5 g/dL, and BMI <18.5 kg/m²) among the 4 co-

horts according to suggested definitions (ESPEN 1, ESPEN 2 clinical nutritional parameters, severe hypoalbuminemia, and moderate hypoalbuminemia). Patients with severe hypoalbuminemia <3.1 g/dL were older, predominantly male, and had a higher rate of preoperative comorbidities, including diabetes mellitus, cardiac disorders, chronic steroid use, bleeding disorders, preoperative anemia, and high ASA class compared to patients who met clinical ESPEN 2 parameters (Table 1).

Patients with hypoalbuminemia <3.1 g/dL presented more overall complications (58.9 vs. 44.3%), major complications (34.2 vs. 21.5%), surgical complications (31.6 vs. 20.3%), medical complications (17.4 vs. 10.2%), unplanned readmission (11.1 vs. 7.9%), unplanned reoperation (5.4 vs. 4.6%), prolonged LOS (40.3 vs. 29.6%), and 30-day mortality (5.2 vs. 2.2%) than patients in the ESPEN 2 group (all $p < 0.05$). Patients who met both criteria (albumin <3.1 g/dL and ESPEN 2) presented consistently the highest complication rates, as detailed in Table 2.

After adjusting for baseline confounders (using the baselined cohort not meeting any of the 3 suggested criteria as a reference), patients in the hypoalbuminemia group had a higher adjusted odds of overall complications (OR 1.92, 95% CI [1.80–2.04] vs. OR 1.184, 95% CI

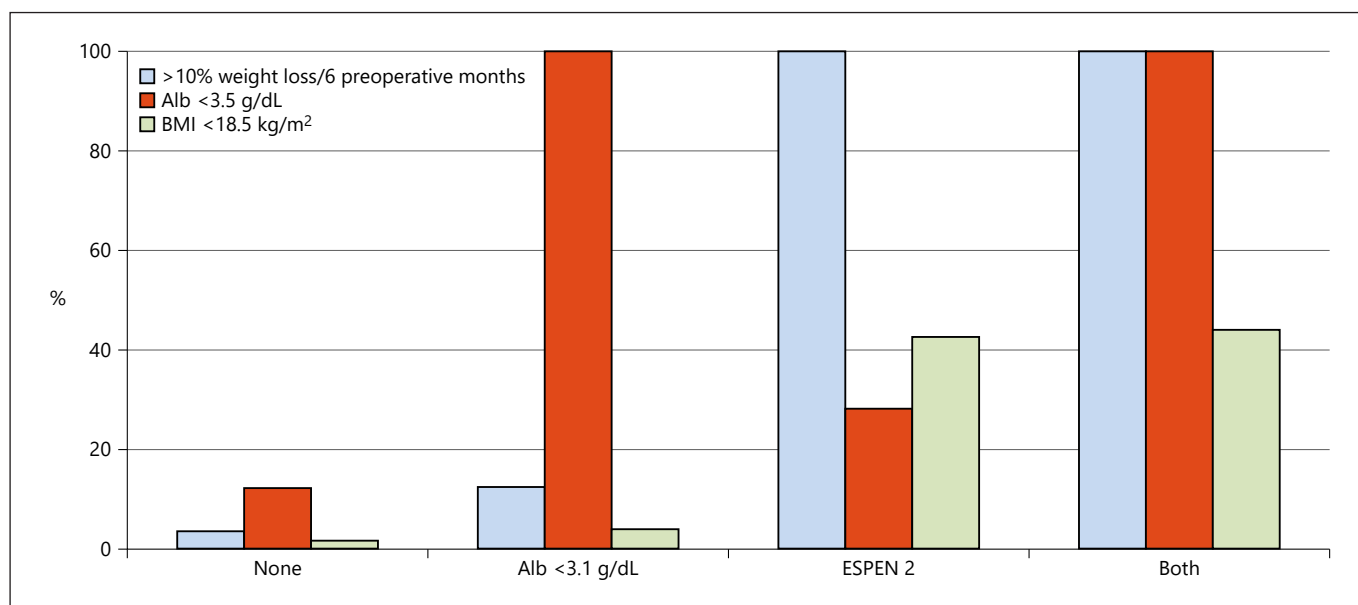


Fig. 2. Prevalence of different criteria of assessment among the study cohorts. ESPEN 2 defined as $\geq 10\%$ weight/6 months plus [BMI < 20 kg/m² in patients < 70 years OR BMI < 22 kg/m² in patients ≥ 70 years]). ESPEN, European Society for Clinical Nutrition and Metabolism.

[1.01–1.39] in the ESPEN 2 group), major complications (OR 1.98, 95% CI [1.86–2.11] vs. OR 1.20, 95% CI [1.00–1.45]), surgical complications (OR 1.77, 95% CI [1.66–1.88] vs. OR 1.1, 95% CI [0.90–1.33]), medical complications (OR 1.73, 95% CI [1.59–1.87] vs. OR 1.16, 95% CI [0.90–1.48]), SSI (OR 1.32, 95% CI [1.21–1.44] vs. OR 0.86, 95% CI [0.66–1.12]), prolonged hospitalization (OR 1.79, 95% CI [1.68–1.91] vs. OR 1.22, 95% CI [1.03–1.46]) compared to patients in the ESPEN 2 group (Fig. 3 and see online suppl. Table 1; for all online suppl. material, see www.karger.com/doi/10.1159/000514058). Patients who met both criteria (severe hypoalbuminemia and clinical ESPEN 2 parameters) were at highest risk of overall complications (OR 2.6, 95% CI [2.03–3.33]), major complications (OR 2.51, 95% CI [1.98–3.18]), and surgical complications (OR 2.26, 95% CI [1.79–2.87]) (Fig. 3; online suppl. Table 1).

Discussion

This large-scale analysis derived from a national, validated data registry of elective surgical colorectal cancer patients revealed important differences in risk stratification depending on the screening modality. While less than 1% of this representative US cohort presented with

malnutrition according to the suggested clinical nutritional parameters (BMI, weight loss), 7.2% of patients were at surgical risk according to the previously identified critical albumin threshold of 3.1 g/dL. Given the significant association of hypoalbuminemia and postoperative morbi-mortality, preoperative albumin levels may represent a critical adjunct to clinical screening tools to prevent under-detection of surgical risk patients. This is important, given the challenges to adopt the full panel of nutritional screening tools as recommended by ESPEN in an everyday practice setting [15].

Clinical tools integrating BMI may underestimate the presence of malnutrition, especially in the context of an increasing prevalence of obesity in the USA [17]. This was also acknowledged by the respective European consensus statements [10, 24]. BMI has been criticized as an inaccurate measure of body fat content as it does not take into account muscle mass, bone density, overall body composition including fluid homeostasis, and racial and sex differences [25]. Furthermore, patients with obesity presenting with significant preoperative cachexia may remain undetected despite the important impact on biochemical, metabolic, and anthropometric body composition, while BMI scores remain within normal limits [16]. In this present study, only 4% of patients with severe preoperative hypoalbuminemia < 3.1 g/dL had a BMI < 18.5 kg/m² (ES-

Table 1. Baseline demographic, anthropometric, and preoperative characteristics

	Severe malnutrition					<i>p</i> value ^a
	No (<i>N</i> = 75,246)	Albumin <3.1 g/dL (<i>N</i> = 5,932)	ESPEN 2 (<i>N</i> = 764)	Both criteria (<i>N</i> = 338)	Total (<i>N</i> = 82,280)	
Age ≥ 80 years, <i>n</i> (%)	10,099 (13.4)	1,750 (29.5)	192 (25.1)	112 (33.1)	12,153 (14.8)	<0.0001
Gender: male, <i>n</i> (%)	40,278 (53.6)	2,756 (46.5)	333 (43.6)	152 (45.0)	43,519 (52.9)	<0.0001
Race, <i>n</i> (%)						
White	55,043 (73.2)	4,414 (74.4)	552 (72.3)	240 (71.0)	60,249 (73.2)	<0.0001
African American	6,925 (9.2)	701 (11.8)	84 (11.0)	49 (14.5)	7,759 (9.4)	
Asian	3,592 (4.8)	174 (2.9)	55 (7.2)	23 (6.8)	3,844 (4.7)	
Others	619 (0.8)	60 (1.0)	3 (0.4)	6 (1.8)	688 (0.8)	
Unknown/not reported	9,067 (12.0)	583 (9.8)	70 (9.2)	20 (5.9)	9,740 (11.8)	
ASA class ≥ ASA 3, <i>n</i> (%)	43,162 (57.4)	4,648 (78.6)	517 (67.7)	268 (79.3)	48,595 (59.1)	<0.0001
Diabetes mellitus, <i>n</i> (%)	13,820 (18.4)	1,281 (21.6)	69 (9.0)	29 (8.6)	15,199 (18.5)	<0.0001
Current smoker, <i>n</i> (%)	10,674 (14.2)	922 (15.5)	248 (32.5)	101 (29.9)	11,945 (14.5)	<0.0001
Dyspnea, <i>n</i> (%)	6,458 (8.6)	976 (16.5)	109 (14.3)	60 (17.8)	7,603 (9.2)	<0.0001
History of severe COPD, <i>n</i> (%)	3,602 (4.8)	544 (9.2)	84 (11.0)	31 (9.2)	4,261 (5.2)	<0.0001
Functional health status, <i>n</i> (%)						
Independent	73,399 (97.8)	5,086 (86.0)	726 (95.0)	275 (81.4)	79,486 (96.8)	<0.0001
Dependent	1,677 (2.2)	828 (14.0)	38 (5.0)	63 (18.6)	2,606 (3.2)	
CHF within 30 days of surgery, <i>n</i> (%)	565 (0.8)	200 (3.4)	3 (0.4)	8 (2.4)	776 (0.9)	<0.0001
Hypertension requiring medication, <i>n</i> (%)	39,679 (52.7)	3,487 (58.8)	307 (40.2)	143 (42.3)	43,616 (53.0)	<0.0001
Disseminated cancer, <i>n</i> (%)	7,097 (9.4)	943 (15.9)	141 (18.5)	73 (21.6)	8,254 (10.0)	<0.0001
>10% loss of body weight/last 6 months, <i>n</i> (%)	2,744 (3.6)	753 (12.7)	764 (100.0)	338 (100.0)	4,599 (5.6)	<0.0001
Chronic steroid use, <i>n</i> (%)	2,038 (2.7)	265 (4.5)	27 (3.5)	20 (5.9)	2,350 (2.9)	<0.0001
Bleeding disorder, <i>n</i> (%)	2,156 (2.9)	387 (6.5)	22 (2.9)	26 (7.7)	2,591 (3.1)	<0.0001
PRBC transfusion 72 h before surgery, <i>n</i> (%)	599 (0.8)	317 (5.3)	11 (1.4)	11 (3.3)	938 (1.1)	<0.0001
Underlying disease, <i>n</i> (%)						
Colon cancer	48,939 (65.0)	4,579 (77.2)	458 (59.9)	231 (68.3)	54,207 (65.9)	<0.0001
Rectal cancer	26,307 (35.0)	1,353 (22.8)	306 (40.1)	107 (31.7)	28,073 (34.1)	
Minimally invasive surgery, <i>n</i> (%)	41,917 (55.7)	2,150 (36.2)	316 (41.4)	96 (28.4)	44,479 (54.1)	<0.0001
Extent of resection, <i>n</i> (%)						
Subtotal colectomy	50,835 (67.6)	4,910 (82.8)	541 (70.8)	276 (81.7)	56,562 (68.7)	<0.0001
Total colectomy	1,344 (1.8)	144 (2.4)	11 (1.4)	9 (2.7)	1,508 (1.8)	
Proctectomy	23,067 (30.7)	878 (14.8)	212 (27.7)	53 (15.7)	24,210 (29.4)	
Operation time, median (IQR), min	173 (121–246)	146 (101–216)	154 (104–224)	133 (93–200)	170 (119–244)	<0.0001
Days between albumin measurement and operation, median (IQR)	7 (4–12)	4 (1–9)	6.5 (3–11)	3 (1–7)	7 (3–12)	<0.0001
Preoperative hematocrit, median (IQR)	38.1 (34–41.6)	31.5 (28.8–34.7)	35.2 (32–39)	31 (28–34)	37.8 (34–41.3)	<0.0001
Preoperative platelet count, median (IQR)	251 (204–310)	295 (224–390)	293 (229–363)	353 (265–461)	254 (206–316)	<0.0001
Preoperative SGOT, median (IQR)	20 (16–26)	19 (15–27)	20 (15–25)	19 (14–26)	20 (16–26)	<0.0001

ESPEN 2: ≥10% weight/6 months plus (BMI <20 kg/m² in patients <70 years OR BMI <22 kg/m² in patients ≥70 years) (body composite was not considered for our analysis). ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; PRBC, packed red blood cells; IQR, interquartile range; ESPEN, European Society for Clinical Nutrition and Metabolism; SGOT, serum glutamic oxaloacetic transaminase. ^a Derived from the χ^2 test for categorical variables and Independent sample Kruskal-Wallis test for continuous variables.

PEN 1 definition), while 13% lost ≥10% of their body weight (Fig. 2). This raises the question of insufficient performance of simplified clinical nutritional assessment in the US population. This is supported by the more significant correlation of hypoalbuminemia and risk-adjusted postoperative complications (Fig. 3).

While the expert panel reached a consensus regarding clinical criteria for malnutrition, systematic biochemical

assessment was considered but ultimately excluded from the recommendation [10]. Additional costs with a questionable additional benefit in the decision-making process may have been prevailing arguments [26], despite the proven association of hypoalbuminemia and worse short-term outcomes [19, 27–29]. The critical cutoff value of 3.1 g/dL has recently been identified by Haskins et al. [19], yielding 80% specificity for adverse events in patients

Table 2. Postoperative complications

	Severe malnutrition				Total (N = 82,280)	p value ^a
	No (N = 75,246)	Albumin <3.1 g/dL (N = 5,932)	ESPEN 2 (N = 764)	Both criteria (N = 338)		
Overall complications,* n (%)	26,780 (35.6)	3,481 (58.9)	338 (44.3)	227 (67.6)	30,826 (37.5)	<0.0001
Minor complications, n (%)	5,516 (7.3)	634 (10.7)	53 (6.9)	38 (11.2)	6,241 (7.6)	<0.0001
Major complications, n (%)	12,316 (16.4)	2,027 (34.2)	164 (21.5)	136 (40.2)	14,643 (17.8)	<0.0001
Surgical complications, n (%)	12,922 (17.2)	1,877 (31.6)	155 (20.3)	128 (37.9)	15,082 (18.3)	<0.0001
Any SSI	7,097 (9.4)	780 (13.1)	67 (8.8)	45 (13.3)	7,989 (9.7)	<0.0001
Superficial incisional	3,749 (5.0)	397 (6.7)	28 (3.7)	25 (7.4)	4,199 (5.1)	<0.0001
Deep incisional	767 (1.0)	100 (1.7)	4 (0.5)	4 (1.2)	875 (1.1)	<0.0001
Organ/space	2,895 (3.8)	319 (5.4)	38 (5.0)	18 (5.3)	3,270 (4.0)	<0.0001
Wound disruption	704 (0.9)	91 (1.5)	13 (1.7)	6 (1.8)	814 (1.0)	<0.0001
Systemic sepsis	2,813 (3.7)	503 (8.5)	36 (4.7)	33 (9.8)	3,385 (4.1)	<0.0001
Sepsis	1,995 (2.7)	315 (5.3)	28 (3.7)	18 (5.3)	2,356 (2.9)	<0.0001
Septic shock	858 (1.1)	200 (3.4)	8 (1.0)	15 (4.4)	1,081 (1.3)	<0.0001
Need for blood transfusion	5,514 (7.3)	1,061 (17.9)	86 (11.3)	80 (23.7)	6,741 (8.2)	<0.0001
Medical complications, n (%)	5,782 (7.7)	1,035 (17.4)	78 (10.2)	64 (18.9)	6,959 (8.5)	<0.0001
UTI	1,983 (2.6)	278 (4.7)	27 (3.5)	18 (5.3)	2,306 (2.8)	<0.0001
Respiratory complication	2,183 (2.9)	524 (8.8)	39 (5.1)	36 (10.7)	2,782 (3.4)	<0.0001
Renal complication	930 (1.2)	145 (2.4)	3 (0.4)	6 (1.8)	1,084 (1.3)	<0.0001
MACE	866 (1.2)	181 (3.1)	15 (2.0)	13 (3.8)	1,075 (1.3)	<0.0001
VTE	1,044 (1.4)	200 (3.4)	8 (1.0)	11 (3.3)	1,263 (1.5)	<0.0001
LOS, median (IQR), days	5 (3–7)	7 (5–10)	6 (4–8)	7 (5–11)	5 (4–7)	<0.0001
LOS >7 days (Q3), n (%)	16,385 (21.8)	2,382 (40.3)	226 (29.6)	150 (44.6)	19,143 (23.3)	<0.0001
Unplanned readmission related to the primary procedure, [#] n (%)	4,723 (8.8)	357 (11.1)	38 (7.9)	22 (13.4)	5,140 (8.9)	<0.0001
Unplanned reoperation related to the primary procedure, [#] n (%)	2,140 (4.0)	173 (5.4)	22 (4.6)	6 (3.7)	2,341 (4.0)	<0.0001
Mortality (within 30 days), n (%)	662 (0.9)	310 (5.2)	17 (2.2)	32 (9.5)	1,021 (1.2)	<0.0001

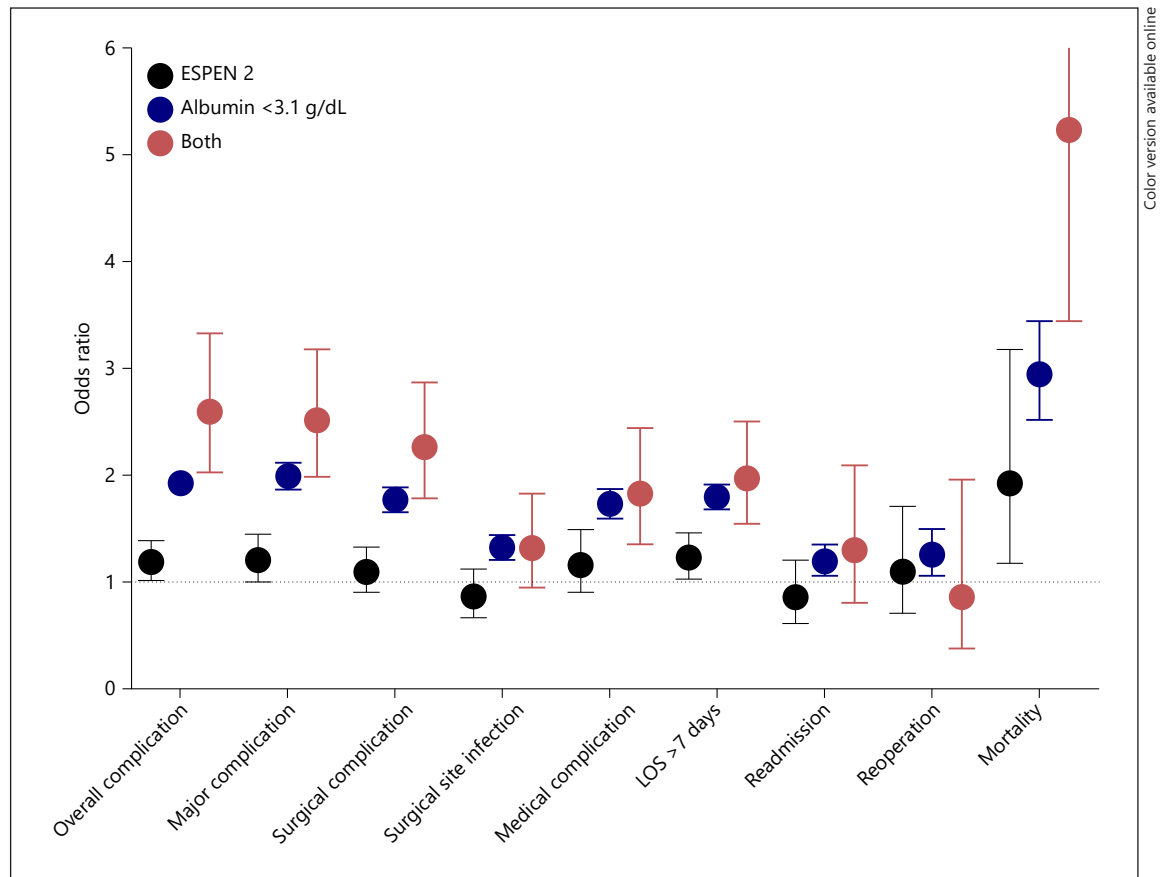
ESPEN 2: $\geq 10\%$ weight/6 months plus (BMI < 20 kg/m² in patients < 70 years OR BMI < 22 kg/m² in patients ≥ 70 years) (body composite was not considered for our analysis). ESPEN, European Society for Clinical Nutrition and Metabolism; SSI, surgical site infection; UTI, urinary tract infection; MACE, major adverse cardiovascular events; VTE, vascular thromboembolism; LOS, length of stay. * Overall complications include any surgical complication, any medical complication, LOS > 7 days, unplanned readmission related to the primary operation, unplanned reoperation related to the primary operation, and 30-day mortality. [#] Analyzed from 2012 to 2018 only (not captured before 2012). ^a Derived from χ^2 test for categorical variables and independent-sample Kruskal-Wallis test for continuous variables.

with colon cancer. Our analysis revealed that only 0.9% of the entire cohort met the suggested cutoffs for clinical nutritional parameters (BMI and weight loss) without concomitant severe hypoalbuminemia (albumin < 3.1 g/dL, Fig. 1). Among all patients meeting our suggested clinical “ESPEN 2” parameters, only 31% presented with albumin < 3.1 g/dL. On the other hand, 95% (7.2% of the entire cohort) of patients with albumin < 3.1 g/dL did not meet the suggested clinical nutritional parameters. Taken together, a significant proportion of patients at risk may remain undetected without additional assessment of albumin levels. However, it is important to mention that

nutritional assessment in the present study did not include measurement of body composition, as recommended by ESPEN guidelines.

The additional use of serum albumin as an adjunct to clinical assessment has been recommended by ESPEN guidelines [10, 20, 21, 30]. In addition, it was also recommended by the American Society of Enhanced Recovery and Perioperative Quality [6]. Nevertheless, albumin does not represent a nutritional marker per se but rather an additional tool for preoperative risk stratification.

Taken together, our findings suggest that clinical nutritional parameters (BMI and weight loss) may be insuf-



Color version available online

Fig. 3. Risk-adjusted comparison of postoperative outcomes. Comparison of postoperative outcomes between the 3 groups albumin <3.1 g/dL, ESPEN 2, and both. Displayed are OR and 95% confidence interval. ESPEN 2: $\geq 10\%$ weight/6 months plus (BMI <20 kg/m² in patients <70 years OR BMI <22 kg/m² in patients ≥ 70 years) (body composite was not considered for our analysis). None of the 3 criteria met was used as a reference. Adjusted for age >80 years, gender, race, ASA class ≥ 3 , diabetes mellitus, current smoker within 1 year of surgery, dyspnea, history of severe COPD, functional status, hypertension requiring medication, disseminated

cancer, steroid use for chronic condition, bleeding disorders, blood transfusion ≥ 1 units within 72 h of surgery, underlying disease (colon or rectal cancer), operative approach, extent of surgical resection, total operation time, preoperative SGOT. CHF (low event rate), platelets, and hematocrit (inconsistent assessment) not retained for regression model. ASA, American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; ESPEN, European Society for Clinical Nutrition and Metabolism; LOS, length of stay; SSI, surgical site infection; OR, odds ratio.

efficient for preoperative risk stratification in the US population with colorectal cancer. Validated nutritional screening tools (i.e., Nutritional Risk Score *NRS-2002* [14], Malnutrition Universal Screening Tool *MUST* [31]), measurement of body composition (i.e., muscle mass) and close collaboration with nutritional specialists remain mandatory to tailor individual nutritional support strategies [17, 32]. Albumin measurement may thus be critical to refine indications for preoperative nutritional conditioning [33–35]. This strategy is in line with the preoperative nutrition screening (PONS score) algorithm, which has been proposed by The American Society for Enhanced Recovery and Perioperative Quality

(ASER): Referral to a dietician if BMI <18.5 kg/m² (<20 kg/m² if age >65) or unintentional weight loss of >10% in last 6 months or eating less than 50% of a normal diet in the last week, and/or albumin <3 g/dL [6]. Furthermore, new Global Leadership Initiative in Malnutrition (GLIM) criteria, which were elaborated in dedicated consensus conferences in collaboration with different nutritional societies, have endorsed albumin <3 g/dL as a criterion of severe surgical risk, in line with the (updated) ESPEN guidelines for surgical patients [20, 24]. The present study stresses the importance of albumin measurement as an important additional tool when nutritional screening is performed through clinical evaluation alone, espe-

cially when screening is not performed by nutritional experts.

Arguably, preoperative albumin measurement comes with additional cost and systematic measurement within 21 days from surgery may represent a logistical challenge. However, severe hypoalbuminemia was associated with cost drivers prolonged LOS, unplanned readmission, and unplanned reoperation, in the present study and previous studies [1, 19, 36]. It has been shown that every dollar spent on nutritional therapy in hospitalized patients saves USD 52 of in-hospital costs [6, 37]. Nevertheless, cost-effectiveness of systematic albumin measurement needs to be further assessed. Adding albumin to conventional clinical screening may be most useful given the significant impact on postoperative outcomes if all analyzed criteria (BMI, weight loss, and hypoalbuminemia) were met (Fig. 3). Importantly, the benefits of preoperative nutritional therapy and prehabilitation have to be carefully balanced given a potential compromise of overall survival with delayed surgical management [38, 39].

The present results must be interpreted within the context of several limitations. First, patients with missing values were removed from our analysis, which may lead to selection bias. Furthermore, albumin levels may have been drawn based on clinical suspicion of malnutrition, potentially explaining the overrepresentation of the group with severe hypoalbuminemia. Second, the comparative baseline group with no severe malnutrition based on chosen criteria may have met other criteria for malnutrition that were not accounted for (Fig. 2). More specifically, ESPEN guidelines also endorse a wide range of measurements of body composition (i.e., lean body mass or muscle mass), which however were not available in the setting of this dataset. Moreover, details about screening modalities and institutional practice of participating centers were not available either. This needs to be considered when interpreting the results, especially regarding the baseline group, which may include patients fulfilling malnutrition criteria based on other definitions. Third, ACS-NSQIP does not report cancer-specific outcomes, impeding investigation of long-term outcomes. Finally, albumin represents an unspecific marker for different disease states, which were excluded for this present analysis. However, albumin should not be considered a specific nutritional marker nor replace dedicated nutritional screening. In other words, this demonstrated that simplified nutritional screening through clinical parameters alone (particularly in a population with high average BMI) may lead to an underestimation of surgical risk. Hence, hypoalbuminemia as a surrogate of disease sever-

ity could be a relevant additional tool in an “everyday” practice where systematic, comprehensive nutritional screening according to guidelines might be challenging.

In conclusion, this study revealed a strong association of severe hypoalbuminemia and postoperative morbidity-mortality in an unselected US cohort undergoing colorectal cancer surgery. Simplified clinical nutritional screening may lead to under-detection of patients at surgical risk. Further studies are needed to evaluate the cost-effectiveness of systematic serum albumin measurement.

Statement of Ethics

No ethical approval was needed as this study utilized a national database with no attempt to identify the patients.

Conflict of Interest Statement

There are no conflicts of interest to declare.

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Author Contributions

Conception and design: F.G., M.A.A., W.P., K.T.B., A.D., K.L.M., and D.W.L. Acquisition of data: M.A.A. and F.G. Analysis and interpretation of data: M.A.A., F.G., W.P., K.T.B., A.D., K.L.M., and D.W.L. Drafting of the manuscript: F.G., M.A.A., W.P., K.T.B., A.D., K.L.M., and D.W.L. Critical revision of the manuscript: all authors. Final approval of the version to be published: all authors

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