



Predicting morbidity and mortality in laparoscopic cholecystectomy: Preoperative serum albumin still matters



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ABSTRACT

Background: This study examined the association of preoperative serum albumin with outcomes for laparoscopic cholecystectomy.

Methods: The American College of Surgeons National Surgical Quality Improvement Program was retrospectively analyzed from 2005 to 2016 for adult patients undergoing laparoscopic cholecystectomy. Patients were stratified into four groups: <3.0 g/dL (*Severe Malnutrition*), 3.0–<3.5 (*Moderate Malnutrition*), 3.5–<4.0 (*Mild Malnutrition*), and ≥4.0 g/dL (*Normal Nutrition*). The primary outcome of 30-day mortality was evaluated with multivariable regression.

Results: Of 131,855 patients, 14.0% had *Severe*, 22.8% *Moderate*, and 29.7% *Mild Malnutrition*, with 33.5% classified as *Normal Nutrition*. Adjusted multivariable regressions demonstrated that relative to *Normal Nutrition*, mortality risk was increased for *Severe* (OR = 3.09 [95% Confidence Interval: 2.09–4.56]) and *Moderate* (OR = 1.83 [1.24–2.72]) *Malnutrition*. *Severe* (OR = 2.45 [1.67–3.61]) and *Moderate* (OR = 1.52 [1.04–2.24]) *Malnutrition* were also associated with increased risk of postoperative septic shock.

Conclusions: Even in less invasive laparoscopic cholecystectomy, reduced preoperative serum albumin is strongly associated with increased morbidity and mortality.

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Introduction

Laparoscopic cholecystectomy is a low-risk, minimally invasive operation frequently performed for the treatment of biliary disease.¹ Owing to its wide adoption, over 750,000 cholecystectomies are performed in the United States annually with direct and indirect costs exceeding \$6.2 billion.^{1,2} Despite the volume and experience with this procedure, laparoscopic cholecystectomy carries relatively substantial risks for mortality (0.3%) and 30-day hospital readmission (7.0%).³ While increasing age and emergent case status have been previously associated with adverse postoperative outcomes, efforts to further identify and mitigate factors associated with mortality and complications are needed.¹

Nearly two decades ago, the National Veterans Administration Surgical Risk Study established serum albumin level as a powerful predictor of postoperative outcomes for general, orthopedic, and

thoracic operations.^{4,5} Hypoalbuminemia, a marker for malnutrition that is defined as preoperative serum albumin <3.5 g/dL, is considered an excellent predictor of mortality and complications for open surgical procedures.^{6,7} Specifically, low albumin levels have been linked to increased risk of infectious complications, length of stay, readmission, and mortality, independent of body mass index (BMI) and other comorbidities.^{6–8} The predictive value of preoperative serum albumin levels has been revisited more recently in gastrointestinal surgery.^{9,10} Such studies have reaffirmed the independent predictive value of albumin levels in open abdominal operations.

While low serum albumin has been associated with conversion from laparoscopic to open cholecystectomy, the value of this marker as a predictor of mortality following less invasive operations has not been explored thus far. Since laparoscopic cholecystectomy is one of the most commonly performed operations worldwide, identification of clinically predictive factors might lead to better risk stratification, patient selection, and modification of perioperative methods. Therefore, we utilized a national cohort of laparoscopic cholecystectomy patients to evaluate whether low preoperative serum albumin levels are independently predictive of

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mortality, postoperative infection, and 30-day readmissions.

Material and methods

This was a retrospective study using a prospectively maintained database of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP). Over 600 hospitals contribute to the NSQIP database to assess perioperative outcomes and report 30-day morbidity and mortality. All adult patients undergoing laparoscopic cholecystectomy (Current Procedural Terminology (CPT) 47562, 47563, and 47564) between 2005 and 2016 with a recorded preoperative serum albumin within two days of operation were considered eligible for analysis **in order to best capture accurate nutritional status at the time of surgery** (Fig. 1).

Patients were stratified by nutrition status based on their preoperative serum albumin level: <3.0 g/dL (*Severe Malnutrition*), 3.0 to <3.5 g/dL (*Moderate Malnutrition*), 3.5 to <4.0 g/dL (*Mild Malnutrition*), and ≥ 4.0 g/dL (*Normal Nutrition*). The primary outcome was 30-day postoperative mortality. Secondary outcomes included postoperative septic shock, ventilator use >48 h, reoperation, reintubation, any postoperative infection, pneumonia, hospital length of stay (LOS), and rehospitalization within 30 days of discharge. NSQIP definitions were used for all variables.¹¹ The Kruskal-Wallis test for continuous variables and chi-squared analysis for categorical variables were utilized to identify differences in demographics, comorbidities, and outcomes by preoperative nutritional class.

Multivariable logistic and linear regression models were

constructed to assess the predictive value of preoperative serum albumin on mortality, and secondary outcomes listed above. Regressions accounted for baseline differences between groups and included patient demographics (age, gender, and race), comorbidities (congestive heart failure, hypertension, chronic obstructive pulmonary disease (COPD), smoking, diabetes mellitus, dialysis, bleeding disorders, ascites, and functional status), and perioperative variables (diagnosis, preoperative lab values, American Society of Anesthesiologists (ASA) score, surgical setting and urgency, and operation year). In all comparisons, $p < 0.05$ was considered statistically significant. All statistical analyses were performed using STATA 14.2 (StataCorp LP, College Station, TX). The study was deemed exempt by the Institutional Review Board at the University of California, Los Angeles.

Results

Of the 347,894 laparoscopic cholecystectomy patients identified, 131,855 (37.9%) met inclusion criteria (Fig. 1). A total of 18,407 (14.0%) patients were in the *Severe Malnutrition* cohort, with another 30,109 (22.8%) classified as *Moderate Malnutrition*, 39,182 (29.7%) as *Mild Malnutrition*, and 44,157 (33.5%) as *Normal Nutrition* (Table 1).

The *Severe Malnutrition* cohort was noted to be older (59.6 vs. 45.0 years, $p < 0.001$) and more likely to suffer from comorbidities such as diabetes (22.1 vs. 8.5%, $p < 0.001$), bleeding disorders (9.2 vs. 1.9%, $p < 0.001$), and hypertension (53.1 vs. 26.7%, $p < 0.001$) relative to the *Normal Nutrition* cohort. Patients with *Severe*

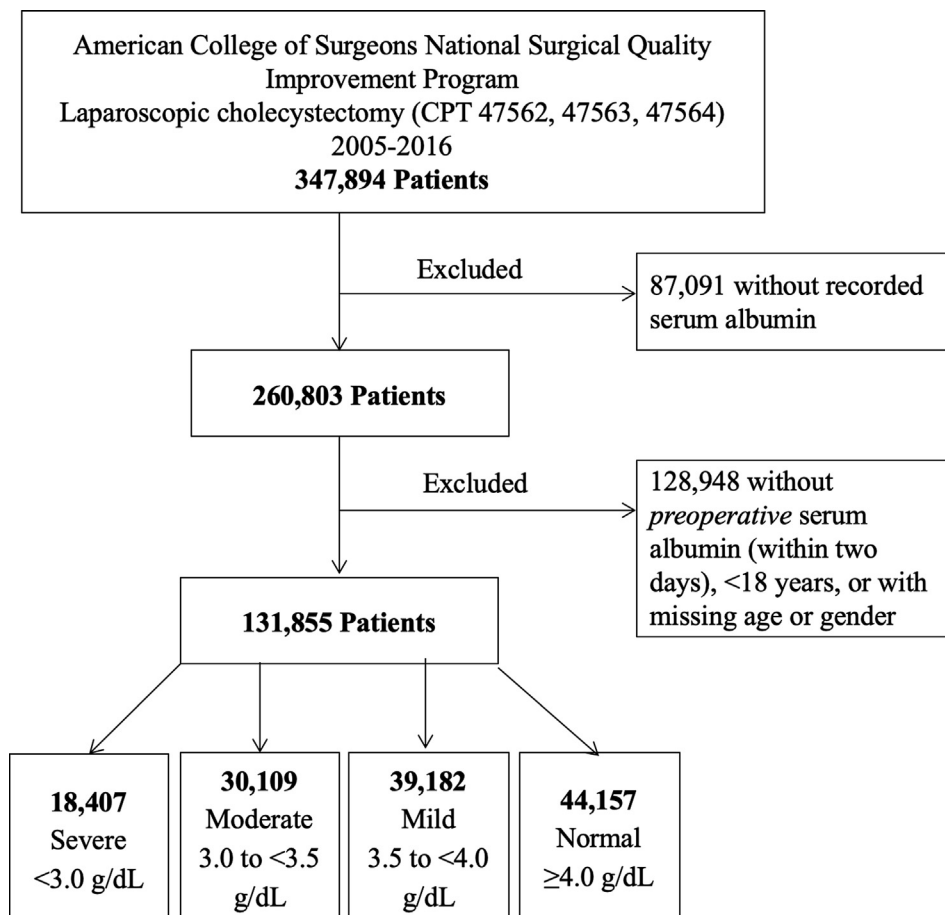


Fig. 1. Patient selection criteria. Of the 347,894 laparoscopic cholecystectomy patients identified, 131,855 (37.9%) met inclusion criteria.

Table 1
Baseline demographics and comorbidities by albumin class for laparoscopic cholecystectomy.

	Albumin <3.0 (N = 18,407)	Albumin 3.0 to <3.5 (N = 30,109)	Albumin 3.5 to <4.0 (N = 39,182)	Albumin ≥4.0 (N = 44,157)	P
Age	59.6 ± 19.4	51.0 ± 19.0	47.5 ± 17.5	45.0 ± 16.2	<0.001
Female	61.3%	69.1%	70.4%	66.9%	<0.001
Emergency	17.6%	18.5%	20.1%	22.9%	<0.001
Outpatient	5.0%	13.4%	30.4%	45.0%	<0.001
BMI (kg/m ²)	30.7 ± 8.2	31.6 ± 8.1	31.9 ± 7.9	30.8 ± 7.1	<0.001
Race					
White	74.8%	72.1%	72.1%	73.1%	<0.001
Black	12.0%	12.6%	11.3%	8.0%	<0.001
Asian/PI	3.1%	3.2%	3.0%	3.2%	<0.001
Other/Unknown	10.1%	12.2%	13.6%	14.8%	<0.001
Smoking History	16.8%	19.9%	20.8%	21.0%	<0.001
Diabetes	22.1%	14.4%	11.4%	8.5%	<0.001
COPD	6.0%	3.8%	2.4%	1.6%	<0.001
Ascites	1.7%	0.5%	0.2%	0.1%	<0.001
CHF	2.6%	1.1%	0.5%	0.2%	<0.001
Bleeding Disorders	9.2%	5.5%	3.4%	1.9%	<0.001
Hypertension	53.1%	38.1%	31.9%	26.7%	<0.001
Dialysis	2.2%	1.0%	0.6%	0.3%	<0.001
Functional Status					
Independent	90.8%	96.6%	98.3%	99.2%	<0.001
Partial	7.3%	2.7%	1.5%	0.8%	<0.001
Total	1.8%	0.5%	0.2%	0.1%	<0.001
Diagnosis					<0.001
Acute Cholecystitis	26.7%	32.4%	38.4%	41.5%	
Chronic Cholecystitis	1.7%	2.2%	3.4%	4.7%	
Biliary Colic	5.0%	6.7%	8.8%	10.1%	
Choledocholithiasis	1.0%	1.2%	0.8%	0.4%	
Pancreatitis	7.1%	5.4%	2.6%	0.9%	
Unspecified/Other	58.5%	52.2%	46.0%	42.4%	
Preoperative serum albumin (g/dL)	2.6 ± 0.3	3.2 ± 0.1	3.7 ± 0.1	4.3 ± 0.3	<0.001
Preoperative HCT (%)	34.2 ± 4.7	36.6 ± 4.5	38.6 ± 4.3	40.7 ± 4.2	<0.001
Preoperative Creatinine (mg/dL)	1.0 ± 0.9	0.9 ± 0.7	0.9 ± 0.6	0.8 ± 0.5	<0.001
Preoperative BUN (mg/dL)	13.0 ± 11.0	11.0 ± 8.0	11.8 ± 6.9	13.0 ± 6.0	<0.001
Preoperative Bilirubin (mg/dL)	1.5 ± 1.7	1.2 ± 1.3	1.0 ± 1.0	0.7 ± 0.6	<0.001

BMI = Body Mass Index; BUN = Blood Urea Nitrogen; CHF = Congestive Heart Failure; COPD = Chronic Obstructive Pulmonary Disease; HCT = Hematocrit; PI = Pacific Islander.

Malnutrition were also less likely to undergo elective procedures (8.4 vs. 26.7%, $p < 0.001$).

The univariate outcomes by serum albumin group following laparoscopic cholecystectomy are presented in [Table 2](#). Compared to those with *Normal Nutrition*, the *Severe Malnutrition* cohort experienced higher rates of mortality (1.9 vs. 0.1%, $p < 0.001$), perioperative bleeding (2.5 vs. 0.3%, $p < 0.001$), wound infection (2.2 vs. 1.0%, $p < 0.001$), ventilator use >48 h (1.2 vs. 0.1%, $p < 0.001$), and septic shock (1.2 vs. 0.1%, $p < 0.001$). The *Severe Malnutrition* group was also at an increased risk of reintubation (1.5 vs. 0.2%, $p < 0.001$), reoperation (2.3 vs. 1.0%, $p < 0.001$), and 30-day

readmission (8.3 vs. 3.7%, $p < 0.001$) relative to the *Normal Nutrition* group. As shown in [Table 2](#), those with *Moderate Malnutrition* were also at increased risk of mortality (0.5 vs. 0.1%, $p < 0.001$), bleeding (0.9 vs. 0.3%, $p < 0.001$), and additional adverse events relative to the *Normal Nutrition* group.

Results of multivariable logistic regressions evaluating the association of preoperative serum albumin with mortality and septic shock are presented in [Table 3](#). After adjusting for differences in demographics and comorbidities, *Severe* (OR = 3.09 [95% Confidence Interval (CI): 2.09–4.56], $p < 0.001$) and *Moderate* (OR = 1.83 [95% CI: 1.24–2.72], $p = 0.003$) *Malnutrition* were associated with

Table 2
Outcomes by albumin class for laparoscopic cholecystectomy.

Outcome	Albumin <3.0 (N = 18,407)	Albumin 3.0 to <3.5 (N = 30,109)	Albumin 3.5 to <4.0 (N = 39,182)	Albumin ≥4.0 (N = 44,157)	P
Mortality	1.9%	0.5%	0.2%	0.1%	<0.001
Bleeding	2.5%	0.9%	0.5%	0.3%	<0.001
Wound Infection	2.2%	0.8%	0.5%	0.3%	<0.001
Superficial Infection	0.7%	0.6%	0.7%	0.5%	0.081
Organ Infection	1.4%	0.8%	0.5%	0.4%	<0.001
Pneumonia	0.1%	0.1%	0.1%	0.0%	0.002
Septic Shock	1.2%	0.4%	0.2%	0.1%	<0.001
Ventilator >48 Hours	1.2%	0.3%	0.2%	0.1%	<0.001
DVT	0.7%	0.2%	0.2%	0.1%	<0.001
Renal Failure	0.5%	0.1%	0.1%	0.0%	<0.001
Reintubation	1.5%	0.5%	0.3%	0.2%	<0.001
Return to OR	2.3%	1.4%	1.1%	1.0%	<0.001
30-Day Readmission	8.3%	5.6%	4.5%	3.7%	<0.001

DVT = Deep Vein Thrombosis; OR = Operating Room.

Table 3
Logistic regression on death and septic shock for laparoscopic cholecystectomy.

	Mortality				Septic Shock			
	OR	P	[95% CI]		OR	P	[95% CI]	
Serum Albumin (g/dL)	0.46	<0.001	0.39	0.54	0.53	<0.001	0.45	0.63
Albumin Class (g/dL)								
<3.0	3.09	0.000	2.09	4.56	2.45	0.000	1.67	3.61
3.0 to < 3.5	1.83	0.003	1.24	2.72	1.52	0.032	1.04	2.24
3.5 to < 4.0	1.34	0.168	0.89	2.02	1.47	0.051	1.00	2.15
≥4.0	Ref				Ref			
Age	1.04	<0.001	1.03	1.05	1.02	<0.001	1.01	1.03
Female	1.11	0.248	0.93	1.33	0.88	0.204	0.72	1.07
Inpatient	2.29	<0.001	1.46	3.58	1.91	0.005	1.22	2.99
Urgency								
Urgent	Ref				Ref			
Elective	1.24	0.172	0.91	1.68	0.69	0.086	0.45	1.05
Emergency	1.39	0.001	1.14	1.70	1.83	<0.001	1.48	2.25
Diagnosis								
Acute Cholecystitis	Ref				Ref			
Chronic Cholecystitis	1.63	0.070	0.96	2.76	0.83	0.629	0.38	1.80
Biliary Colic	0.94	0.758	0.61	1.43	0.94	0.802	0.59	1.51
Choledocholithiasis	0.49	0.323	0.12	2.01	0.65	0.555	0.16	2.68
Pancreatitis	0.77	0.259	0.48	1.22	0.56	0.070	0.30	1.05
Unspecified/other	1.10	0.373	0.90	1.34	1.23	0.069	0.98	1.55
Race								
White	Ref				Ref			
Black	1.06	0.701	0.79	1.42	1.17	0.323	0.86	1.59
Asian/PI	1.00	0.984	0.63	1.58	1.23	0.393	0.76	1.98
Other/unknown	0.82	0.236	0.59	1.14	0.95	0.745	0.68	1.32
Smoking	1.15	0.328	0.87	1.50	1.52	0.001	1.18	1.97
Functional Status								
Independent	Ref				Ref			
Partial	2.30	<0.001	1.84	2.88	2.22	<0.001	1.69	2.91
Total	4.30	<0.001	3.11	5.97	2.91	<0.001	1.87	4.52
ASA	2.59	<0.001	2.23	3.02	2.30	<0.001	1.94	2.72
CHF	1.59	0.002	1.19	2.13	1.38	0.091	0.95	1.99
Bleeding Disorder	1.38	0.003	1.11	1.72	1.23	0.122	0.95	1.60
Hypertension	0.93	0.526	0.76	1.15	1.14	0.305	0.89	1.45
COPD	1.40	0.009	1.09	1.79	1.44	0.016	1.07	1.93
Diabetes	0.88	0.186	0.72	1.07	1.27	0.031	1.02	1.57
Ascites	3.89	<0.001	2.58	5.86	2.40	0.001	1.43	4.02
Dialysis	1.59	0.073	0.96	2.65	0.93	0.808	0.52	1.66
Preoperative Hematocrit (%)	0.96	0.000	0.94	0.98	0.99	0.391	0.97	1.01
Preoperative Creatinine (mg/dL)	0.92	0.128	0.82	1.02	1.09	0.104	0.98	1.21
Preoperative BUN (mg/dL)	1.03	<0.001	1.02	1.03	1.02	<0.001	1.01	1.02
Preoperative Bilirubin (mg/dL)	1.09	<0.001	1.04	1.14	1.20	<0.001	1.14	1.25
Operating Year	1.02	0.158	0.99	1.05	1.00	0.814	0.97	1.04

ASA = American Society of Anesthesiologists classification; BUN = Blood Urea Nitrogen; CI = Confidence Interval; COPD = Chronic Obstructive Pulmonary Disease; OR = Odds Ratio; PI = Pacific Islander.

increased odds of mortality following laparoscopic cholecystectomy relative to *Normal Nutrition*. *Severe* (OR = 2.45 [95% CI: 1.67–3.61], $p < 0.001$) and *Moderate* (OR = 1.52 [95% CI: 1.04–2.24], $p = 0.032$) *Malnutrition* were also associated with increased risk of postoperative septic shock. *Mild Malnutrition* was not associated with increased risk of mortality (OR = 1.34 [95% CI: 0.89–2.02], $p = 0.168$), or septic shock (OR = 1.47 [95% CI: 1.00–2.15], $p = 0.051$), relative to *Normal Nutrition*. Such stepwise increases for mortality and septic shock are illustrated in Fig. 2. After adjustment, a 1-g/dL increase in serum albumin reduced the odds of mortality by 54% (OR = 0.46 [95% CI: 0.39–0.54], $p < 0.001$) and septic shock by 47% (OR = 0.53 [95% CI: 0.45–0.63], $p < 0.001$).

Furthermore, there was a significant stepwise increase in the risk of prolonged intubation with *Severe* (OR = 3.04 [95% CI: 1.97–4.71], $p < 0.001$), *Moderate* (OR = 1.76 [95% CI: 1.14–2.72], $p = 0.011$), and *Mild* (OR = 1.59 [95% CI: 1.02–2.47], $p = 0.042$) *Malnutrition* relative to *Normal Nutrition* (Fig. 3). A similar trend was noted for postoperative pneumonia and hospital length of stay (Table 4). *Severe Malnutrition* was a further significant predictor of readmission (OR = 1.19 [95% CI: 1.07–1.34], $p = 0.002$), reoperation (OR = 1.27 [95% CI: 1.07–1.51], $p = 0.005$), reintubation (OR = 1.65

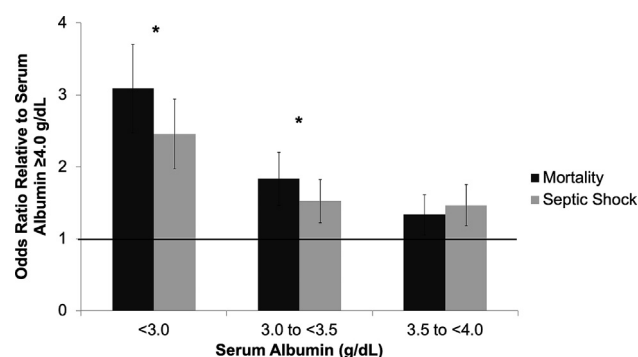


Fig. 2. Adjusted Odds Ratios by Preoperative Serum Albumin Class on Septic Shock and Mortality. The adjusted odds ratios relative to the serum albumin ≥ 4.0 cohort are presented in Fig. 2. Multivariable logistic regressions accounted for baseline differences between groups. Error bars represent standard errors. * indicates significance at $p < 0.05$.

[95% CI: 1.21–2.26], $p = 0.002$), infection (OR = 1.30 [95% CI: 1.10–1.54], $p = 0.002$), and LOS ($\beta = 2.30$ days [95% CI: 2.18–2.43

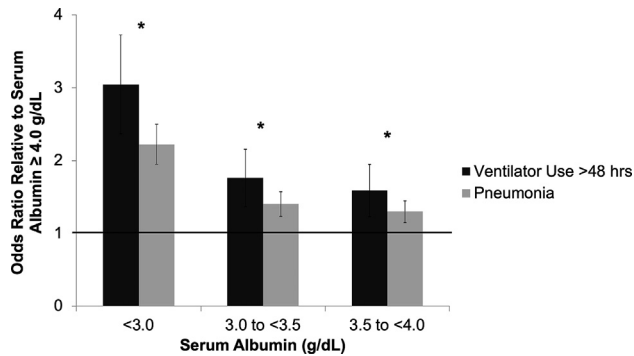


Fig. 3. Adjusted Odds Ratios for Ventilator Use > 48 Hours and Postoperative Pneumonia by Serum Albumin Class. The adjusted odds ratios relative to the serum albumin ≥ 4.0 cohort are presented in Fig. 3. Multivariable logistic regressions accounted for baseline differences between groups. Error bars represent standard errors. * indicates significance at $p < 0.05$.

days], $p < 0.001$) relative to *Normal Nutrition* (Table 4).

Discussion

Given the nearly universal adoption of laparoscopic cholecystectomy for the management of biliary disease, there is an increased focus on identifying predictors of postoperative outcomes to improve patient safety and optimize healthcare expenditures.^{1,2} While serum albumin is a well-established predictor of outcomes in open surgery, its utility with minimally invasive surgery has not been investigated in large cohorts.^{4,5} The present study, to our knowledge, is the first to use a large national database to demonstrate the impact of hypoalbuminemia on mortality and complications following laparoscopic surgery. We found an inverse but significant relationship between preoperative serum albumin levels and the risk of mortality, septic shock, prolonged intubation, and pneumonia following laparoscopic cholecystectomy. Several of our findings deserve further discussion.

Albumin is an established marker of malnutrition and frailty, and therefore resilience to disease and surgical stress.¹² Sepsis induces oxidation of albumin, leading to proteolysis and further depletion of albumin reserves in patients who are already high-risk at baseline.¹² This may explain our finding that patients with severe malnutrition were at an increased risk of postoperative infection, as well as mortality.¹³ While the inverse relationship between serum albumin and morbidity and mortality had been previously established in open procedures,^{8,9,14} our study confirms that serum albumin persists as a critical marker of surgical stress even in the less invasive laparoscopic cholecystectomy. The hypothesis of an albumin reserve is supported by the significant, stepwise increase in

morbidity and mortality observed by serum albumin class.

Moreover, our study has shown that the severity of malnutrition is an important factor that must also be considered when risk stratifying patients. Although serum albumin levels below 3.5 g/dL characterize the present definition of hypoalbuminemia, a notable finding of our study is the further sharp increase in mortality associated with serum albumin levels below 3.0 g/dL.^{6,15–17} This marked increase in risk for patients with serum albumin < 3.0 g/dL persists across additional measures of adverse outcomes, including postoperative pneumonia, prolonged ventilator use, and increased length of stay. The exponential, rather than linear, relationship of serum albumin with morbidity and mortality has been previously acknowledged in the National Veterans Administration Surgical Risk Study⁵ and remains critical to help prognosticate postoperative outcomes.

Surgery triggers a multitude of metabolic stress pathways that may correlate with the degree of invasiveness, underlying disease, nutritional status, and operative variables such as blood loss and extent of resection.¹⁸ While the rise of laparoscopic surgery has mitigated the impact of these factors, resulting in shorter hospital stay with no increase in the risk of bile duct injuries,¹⁹ continuing efforts to identify patient factors associated with postoperative morbidity is essential. Our findings confirm the predictive value of serum albumin in laparoscopic procedures. This laboratory value can be used in a simple risk stratification scheme and allow for mitigation of risk via preoperative optimization or choice of alternate methods.

Exogenous perioperative albumin supplementation in patients with hypoalbuminemia has shown mixed results.^{20–22} Huang et al. (2013) found that preoperative correction of malnutrition in patients undergoing gastrectomy reduced the incidence of surgical site infections,²³ with promising results also noted in the colorectal patient population.^{24,25} However, Hergouth and Kompan (2007) did not identify mortality reductions with preoperative correction and instead concluded that hypoalbuminemia remains a marker of inflammatory response to surgery that replacement cannot alter,²⁶ a conclusion supported by additional literature.^{27,28} Importantly, we stratified patients by their serum albumin in the 48 h prior to surgery in order to best capture a patient's nutritional status at the time of surgery and avoid confounding by those who may have undergone preoperative correction. This methodology allows for a simple risk stratification scheme to highlight the disparities in morbidity and mortality by serum albumin at the time of surgery. Additional investigation is warranted to assess the case of preoperative albumin correction and nutrition optimization in laparoscopic cholecystectomy.

There are several limitations to this study inherent to its retrospective nature. First, the majority of patients did not have a measured preoperative serum albumin level within the time

Table 4
Additional adjusted regressions for predictive effect of serum albumin in laparoscopic cholecystectomy.

	Albumin Class*					
	Albumin <3.0 g/dL		Albumin 3.0 to <3.5 g/dL		Albumin 3.5 to <4.0 g/dL	
	OR [95% CI]	P	OR [95% CI]	P	OR [95% CI]	P
Bleeding	1.03 [0.82–1.31]	0.776	0.88 [0.69–1.11]	0.271	0.88 [0.69–1.12]	0.300
Readmission	1.19 [1.07–1.34]	0.002	1.06 [0.96–1.16]	0.253	1.02 [0.93–1.11]	0.678
Reoperation	1.27 [1.07–1.51]	0.005	1.06 [0.91–1.23]	0.456	1.01 [0.88–1.16]	0.921
Reintubation	1.65 [1.21–2.26]	0.002	1.25 [0.92–1.70]	0.154	1.19 [0.87–1.61]	0.273
Prolonged Ventilator Use	3.04 [1.97–4.71]	<0.001	1.76 [1.14–2.72]	0.011	1.59 [1.02–2.47]	0.042
Any Infection	1.30 [1.10–1.54]	0.002	1.03 [0.88–1.20]	0.721	1.09 [0.95–1.25]	0.210
Pneumonia	2.22 [1.74–2.83]	<0.001	1.40 [1.11–1.77]	0.005	1.30 [1.03–1.64]	0.027
Hospital LOS	2.30 [2.18–2.43]	<0.001	0.89 [0.79–0.99]	<0.001	0.34 [0.25–0.43]	<0.001

LOS = Length of Stay; * = Relative to serum albumin ≥ 4.0 g/dL.

window of the study and were excluded. This limited our sample size and may have biased our results, as higher-risk patients may have been more likely to undergo preoperative laboratory testing. Nonetheless, we used the largest available clinical surgical database to examine this relationship. The NSQIP only follows patients for 30 days following surgery, limiting our analysis to short-term outcomes. In addition, NSQIP does not record cause of death, further limiting this work. We have utilized statistical best practices to mitigate the effect of such limitations.

Conclusions

In conclusion, preoperative hypoalbuminemia is associated with increased morbidity and mortality following laparoscopic cholecystectomy. Lower preoperative serum albumin levels are independently associated with increased mortality, postoperative septic shock, length of stay, and risk of 30-day readmission. While serum albumin <3.5 g/dL is the currently utilized threshold for hypoalbuminemia, patients with serum albumin <3.0 g/dL experience a disproportionately higher risk of septic shock and mortality. Our findings may be used to create a parsimonious risk stratification scheme for laparoscopic operations to allow for more robust risk-adjusted benchmarking of institutions and surgeons.

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Declaration of competing interest

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References

- Fry DE, Pine M, Nedza S, Locke D, Reband A, Pine G. Hospital outcomes in inpatient laparoscopic cholecystectomy in medicare patients. *Ann Surg*. 2017;265(1):178–184. <https://doi.org/10.1097/SLA.0000000000001653>.
- Manuel-Vázquez A, Latorre-Fragua R, Ramiro-Pérez C, et al. Ninety-day readmissions after inpatient cholecystectomy: a 5-year analysis. *World J Gastroenterol*. 2017;23(16):2972. <https://doi.org/10.3748/wjg.v23.i16.2972>.
- Kim Y, Wima K, Jung AD, Martin GE, Dhar VK, Shah SA. Laparoscopic subtotal cholecystectomy compared to total cholecystectomy: a matched national analysis. *J Surg Res*. 2017;218:316–321. <https://doi.org/10.1016/j.jss.2017.06.047>.
- Gibbs J, Cull W, Henderson W, Daley J, Hur K, Khuri SF. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. *Arch Surg Chic Ill*. 1960;134(1):36–42, 1999.
J Am Coll Surg. 1995;180(5):519–531.
- Bohl DD, Shen MR, Kayupov E, Della Valle CJ. Hypoalbuminemia independently predicts surgical site infection, pneumonia, length of stay, and readmission after total joint arthroplasty. *J Arthroplast*. 2016;31(1):15–21. <https://doi.org/10.1016/j.arth.2015.08.028>.
- Walls JD, Abraham D, Nelson CL, Kamath AF, Elkassabany NM, Liu J. Hypoalbuminemia more than morbid obesity is an independent predictor of complications after total hip arthroplasty. *J Arthroplast*. 2015;30(12):2290–2295. <https://doi.org/10.1016/j.arth.2015.06.003>.
- Yuwen P, Chen W, Lv H, et al. Albumin and surgical site infection risk in orthopaedics: a meta-analysis. *BMC Surg*. 2017;17(1). <https://doi.org/10.1186/s12893-016-0186-6>.
- Nisar PJ, Appau KA, Remzi FH, Kiran RP. Preoperative hypoalbuminemia is associated with adverse outcomes after ileoanal pouch surgery. *Inflamm Bowel Dis*. 2012;18(6):1034–1041. <https://doi.org/10.1002/ibd.21842>.
- Chai FY, Jiffre D. Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery. *Ann Surg*. 2011;254(4):665. <https://doi.org/10.1097/SLA.0b013e31823062f3>.
- User guide for the 2016 ACS NSQIP participant use data file (PUF). October https://www.facs.org/-/media/files/quality%20programs/nsqip/nsqip_puf_userguide_2016.ashx; 2017.
- Minasyan H. Sepsis and septic shock: pathogenesis and treatment perspectives. *J Crit Care*. 2017;40:229–242. <https://doi.org/10.1016/j.jccr.2017.04.015>.
- Kim S, McClave SA, Martindale RG, Miller KR, Hurt RT. Hypoalbuminemia and clinical outcomes: what is the mechanism behind the relationship? *Am Surg*. 2017;83(11):1220–1227.
- Ge X, Dai X, Ding C, et al. Early postoperative decrease of serum albumin predicts surgical outcome in patients undergoing colorectal resection. *Dis Colon Rectum*. 2017;60(3):326–334. <https://doi.org/10.1097/DCR.0000000000000750>.
- Adogwa O, Martin JR, Huang K, et al. Preoperative serum albumin level as a predictor of postoperative complication after spine fusion. *Spine*. 2014;39(18):1513–1519. <https://doi.org/10.1097/BRS.0000000000000450>.
- Goh SL, De Silva RP, Dhital K, Gett RM. Is low serum albumin associated with postoperative complications in patients undergoing oesophagectomy for oesophageal malignancies? *Interact Cardiovasc Thorac Surg*. 2015;20(1):107–113. <https://doi.org/10.1093/icvts/ivu324>.
- Hennessey DB, Burke JP, Ni-Dhonochu T, Shields C, Winter DC, Mealy K. Preoperative hypoalbuminemia is an independent risk factor for the development of surgical site infection following gastrointestinal surgery: a multi-institutional study. *Ann Surg*. 2010;252(2):325–329. <https://doi.org/10.1097/SLA.0b013e3181e9819a>.
- Hübner M, Mantziari S, Demartines N, Pralong F, Coti-Bertrand P, Schäfer M. Postoperative albumin drop is a marker for surgical stress and a predictor for clinical outcome: a pilot study. *Gastroenterol Res Pract*. 2016;2016, 8743187. <https://doi.org/10.1155/2016/8743187>.
- Keus F, de Jong J, Gooszen HG, Laarhoven CJ. Laparoscopic versus open cholecystectomy for patients with symptomatic cholecystolithiasis. Cochrane Hepato-Biliary Group. In: *Cochrane Database Syst Rev*. 2006. <https://doi.org/10.1002/14651858.CD006231>. October.
- Golub R, Sorrento JJ, Cantu R, Nierman DM, Moideen A, Stein HD. Efficacy of albumin supplementation in the surgical intensive care unit: a prospective, randomized study. *Crit Care Med*. 1994;22(4):613–619. <https://doi.org/10.1097/00003246-199404000-00017>.
- Mahkovic-Hergouth K, Kompan L. Is replacement of albumin in major abdominal surgery useful? *J Clin Anesth*. 2011;23(1):42–46. <https://doi.org/10.1016/j.jclinane.2010.06.007>.
- Charles A. Albumin use guidelines and outcome in a surgical intensive care unit. *Arch Surg*. 2008;143(10):935. <https://doi.org/10.1001/archsurg.143.10.935>.
- Huang R, Greenky M, Kerr GJ, Austin MS, Parvizi J. The effect of malnutrition on patients undergoing elective joint arthroplasty. *J Arthroplast*. 2013;28(8):21–24. <https://doi.org/10.1016/j.arth.2013.05.038>.
- Truong A, Hanna MH, Moghadamyeghaneh Z, Stamos MJ. Implications of preoperative hypoalbuminemia in colorectal surgery. *World J Gastrointest Surg*. 2016;8(5):353. <https://doi.org/10.4240/wjgs.v8.i5.353>.
- Al-Mulhim AS. Laparoscopic sleeve gastrectomy and nutrient deficiencies: a prospective study. *Surg Laparosc Endosc Percutaneous Tech*. 2016;26(3):208–211. <https://doi.org/10.1097/SLE.0000000000000270>.
- Hergouth KM, Kompan L. Replacement of albumin after abdominal surgery. *Crit Care*. 2007;11(Suppl 2):P405. <https://doi.org/10.1186/cc5565>.
- Boldt J. Use of albumin: an update. *Br J Anaesth*. 2010;104(3):276–284. <https://doi.org/10.1093/bja/aep393>.
- Vincent J-L, Russell JA, Jacob M, et al. Albumin administration in the acutely ill: what is new and where next? *Crit Care*. 2014;18(4):231. <https://doi.org/10.1186/cc13991>.