

Hypoalbuminemia is associated with surgical site infection, septic shock, and mortality after major lower extremity amputation

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INTRODUCTION: Wound healing complications are common after major lower extremity amputation. Hypoalbuminemia can prolong the inflammatory phase of wound healing and lead to tissue edema, increasing the risk of delayed wound healing and surgical site infection. The purpose of this study was to determine the association between preoperative serum albumin level and various complications after below- and above- knee amputation.

METHODS: Patients undergoing below- or above-knee amputation between January 1, 2015 and December 31, 2020 were identified on the American College of Surgeons National Surgical Quality Improvement (ACS NSQIP) database using Current Procedural Terminology (CPT codes) 27880, 27881, 27590, and 27591. Patients were categorized into two groups: those with and without clinically significant hypoalbuminemia (<2.5 g/dL). Baseline demographics and medical comorbidities were reported for each patient. Propensity score matching was used to match the two cohorts based on sex, age, body mass index (BMI), American Society of Anesthesiologists (ASA) class, and degree of wound contamination. The incidence of 30-day outcome measures, including mortality, readmission, reoperation, and various surgical and medical complications, were compared between groups. Binary logistic regression was used to identify variables independently associated with the outcomes of interest. Statistical significance was defined as p<0.05.

RESULTS:

A total of 16,587 patients were included in the final cohort – 5,293 with clinically significant hypoalbuminemia (<2.5 g/dL). The cohort had a high burden of medical comorbidity; most patients were ASA class 3 (51.0%) or 4 (46.2%). After matching, the hypoalbuminemia group had a higher incidence of mortality (6.8% vs. 4.6%, p=0.009), superficial surgical site infection (3.5% vs. 1.8%, p=0.006), septic shock (2.6% vs. 1.0%, p=0.001), postoperative blood transfusion (28.6% vs. 17.3%, p<0.001), pneumonia (4.2% vs. 2.8%, p=0.035), reintubation (3.5% vs. 1.7%, p<0.001), and prolonged ventilation (2.4% vs. 1.0%, p=0.002). On multivariate logistic regression, hypoalbuminemia was independently associated with superficial surgical site infection, septic shock, postoperative blood transfusion, pneumonia, reintubation, and prolonged ventilation (p<0.05).

DISCUSSION AND CONCLUSION:

Clinically significant hypoalbuminemia (<2.5 g/dL) was independently associated with various 30-day complications after major lower extremity amputation, including mortality, superficial surgical site infection, septic shock, postoperative blood transfusion, pneumonia, reintubation, and prolonged ventilation.

Table 1. Demographics, comorbidities, and surgical variables of the cohort prior to matching

	Albumin <2.5 g/dL (n=5,293)	Albumin ≥2.5 g/dL (n=11,294)	P
Sex			
Male	3,499 66.1%	7,460 66.1%	0.946
Female	1,794 33.9%	3,834 33.9%	
Age			
18-39 years	152 2.9%	402 3.6%	0.022
40-49 years	430 8.1%	430 3.8%	0.603
50-59 years	1,174 22.2%	2,321 20.6%	0.016
60-69 years	1,638 30.9%	3,258 28.8%	0.006
70-79 years	1,160 21.9%	2,278 20.3%	0.011
80+ years	739 14.0%	1,744 15.4%	0.013
BMI (kg/m²)			
Underweight	486 9.2%	890 7.9%	0.005
Normal	1,681 31.8%	3,470 30.7%	0.179
Overweight	1,844 34.8%	3,072 27.2%	0.184
Obesity Class I	858 16.2%	1,967 17.4%	0.054
Obesity Class II	460 8.7%	1,036 9.2%	0.312
Obesity Class III	424 8.0%	859 7.6%	0.363
Comorbidities			
Diabetes			
No	1,619 30.6%	4,132 36.6%	<0.001
Non-insulin dependent	663 12.5%	1,637 14.5%	
Insulin dependent	3,011 56.9%	5,525 48.9%	
Smoking	1,454 27.5%	3,339 29.6%	0.006
COPD	535 10.1%	1,456 12.9%	<0.001
Ascites	77 1.5%	50 0.4%	<0.001
Congestive Heart Failure	561 10.6%	898 8.0%	<0.001
Hypertension	4,186 79.1%	8,964 80.1%	0.074
Renal Failure	405 7.7%	470 4.2%	<0.001
Dialysis	1,435 27.1%	2,171 19.2%	<0.001
Cancer	62 1.2%	123 1.1%	0.638
Chronic Steroid Use	286 5.4%	786 7.0%	<0.001
Bleeding Disorder	1,259 23.8%	2,843 25.2%	0.054
Pre-Op Blood Transfusion	1,021 19.3%	883 7.8%	<0.001
Pre-Op Sepsis	1,006 19.0%	1,250 11.1%	<0.001
Sepsis	292 5.5%	175 1.5%	
Septic Shock	943 17.8%	1,602 14.2%	
SIRS			
Wound Classification			
Clean	2,741 51.8%	6,540 57.9%	<0.001
Clean/Contaminated	395 7.5%	901 8.0%	0.249
Contaminated	538 10.2%	1,184 10.5%	0.530
Dirty/Infected	1,619 30.6%	2,669 23.6%	<0.001
ASA Class			
Class 1 (No disturbance)	1 <0.1%	12 0.1%	0.061
Class 2 (Mild disturbance)	60 1.1%	269 2.4%	<0.001
Class 3 (Severe disturbance)	2,316 43.8%	6,141 54.4%	<0.001
Class 4 (Life threatening)	2,450 46.3%	4,808 42.6%	<0.001

Table 2. 30-day outcome measures and complications after matching

	Albumin <2.5 g/dL (n=1,466)	Albumin ≥2.5 g/dL (n=1,466)	P
Readmission	205 14.0%	201 13.7%	0.831
Reoperation	100 6.8%	97 6.6%	0.825
Mortality	100 6.8%	67 4.6%	0.009
Surgical Complications			
Superficial surgical site infection	51 3.5%	27 1.8%	0.006
Wound infection	20 1.4%	20 1.4%	>0.999
Deep surgical site infection	17 1.2%	27 1.8%	0.129
Dehiscence	17 1.2%	18 1.2%	0.865
Blood loss requiring transfusion	420 28.6%	254 17.3%	<0.001
Medical Complications			
Pneumonia	62 4.2%	41 2.8%	0.035
Unplanned intubation	51 3.5%	23 1.6%	<0.001
Pulmonary embolism	8 0.5%	5 0.3%	0.404
Ventilator >48 hours	35 2.4%	14 1.0%	0.002
Renal insufficiency	19 1.3%	9 0.6%	0.058
Renal failure	18 1.2%	13 0.9%	0.367
Urinary tract infection	35 2.4%	35 2.4%	>0.999
Cerebrovascular accident	10 0.7%	12 0.8%	0.669
Cardiac arrest	30 2.0%	25 1.7%	0.496
Myocardial infarction	31 2.1%	25 1.7%	0.418
Deep venous thromboembolism	10 0.7%	7 0.5%	0.466
Sepsis	70 4.8%	54 3.7%	0.142
Septic Shock	38 2.6%	15 1.0%	0.001

Table 3. Risk factors associated with 30-day outcome measures/complications

	Relative Risk [95% C.I.]
Readmission	
>80 years-old	1.311 [1.015 – 1.746]
Reoperation	
Pre-operative sepsis	2.137 [1.117 – 4.088]
Mortality	
50-59 years-old	0.356 [0.191 – 0.665]
>80 years-old	1.935 [1.126 – 3.327]
Underweight	1.935 [1.126 – 3.327]
Contaminated wound	2.184 [1.146 – 4.161]
ASA Class 4	2.038 [1.402 – 2.963]
Surgical Complications	
Superficial SSI	
Albumin <2.5	1.919 [1.197 – 3.077]
Post-Op Transfusion	
Smoking	1.646 [1.288 – 2.104]
Albumin <2.5	1.938 [1.623 – 2.315]
ASA Class 4	1.484 [1.243 – 1.772]
Medical Complications	
Pneumonia	
70-79 years-old	2.125 [1.310 – 3.448]
80+ years-old	2.565 [1.551 – 4.242]
Albumin <2.5	1.553 [1.034 – 2.331]
ASA Class 4	1.562 [1.026 – 2.379]
Unplanned Intubation	
Albumin <2.5	2.310 [1.390 – 3.802]
ASA Class 4	3.327 [1.953 – 5.669]
Ventilator >48 hours	
Albumin <2.5	2.617 [1.387 – 4.950]
ASA Class 4	2.856 [1.507 – 5.413]
Septic Shock	
80+ years-old	1.962 [1.047 – 3.687]
Albumin <2.5	2.740 [1.466 – 5.263]
ASA Class 4	2.476 [1.357 – 4.516]