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ORIGINAL ARTICLE

Hypoalbuminemia Is a Better Predictor than Obesity of Complications After Total Knee Arthroplasty: a Propensity Score-Adjusted Observational Analysis

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Abstract *Background:* Obesity is an established risk factor for complications after total knee arthroplasty (TKA) and is often associated with malnutrition. *Questions/Purposes:* 1. What is the prevalence of hypoalbuminemia in obese patients undergoing TKA? 2. What is the independent morbidity risk of malnutrition relative to obesity? *Methods:* TKA cases were identified from the National Surgical Quality Improvement Program from 2005 to 2013. Propensity scores for having preoperative albumin measurements were calculated using demographics, BMI, and modified Charlson Comorbidity Index (CCI). Malnutrition was defined as hypoalbuminemia (<3.5 g/dL). Patients were classified by BMI as follows: non-obese (18.5–29.9), obese I (30–34.9), obese II (35–39.9), or obese III (≥40). Postoperative complications were compared across obesity and nutritional statuses. Multivariable propensity-adjusted logistic regressions were performed to determine associations between malnutrition, obesity, and 30-day outcomes. *Results:* There were 71,599 cases identified, with 34,800 (48.6%) having albumin measurements. Propensity score adjustment adequately accounted for selection bias, with adjusted $p > 0.05$ for observable characteristics. Malnutrition prevalence increased with BMI (6.1% in obese III vs. 3.7% in non-obese). With propensity-adjusted multivariable analysis, obese III was the only obesity class associated with any complication, wound complication, and reoperation. Hypoalbuminemia was a stronger and more consistent independent risk factor, for any complication, wound, cardiac, or respiratory complications, and death. *Conclusions:* Hypoalbuminemia is a more consistent independent predictor of complications after TKA than obesity. Strategies for medical optimization of these conditions should be investigated.

Keywords hypoalbuminemia · malnutrition · total knee arthroplasty

Introduction

Obesity is increasingly prevalent in both developed and emerging nations [23]. In the USA, more than one third of adults are obese [24], defined as a body mass index (BMI) ≥30 kg/m^2. While obesity is a known risk factor for medical comorbidities, it is also an established risk factor for developing knee osteoarthritis [14, 28]. Each unit increase in age-adjusted BMI is associated with an approximately 4% increase in the incidence of general osteoarthritis (OA) [26]. Further, increasing BMI is the most substantial driver of the differential growth rates between total knee arthroplasty (TKA) and total hip arthroplasty (THA) in the USA [12]. The increasing obesity prevalence among TKA patients is worrisome, since obesity has been associated with elevated risk for perioperative morbidity and mortality [21].

Recently, orthopedic surgeons are becoming increasingly aware of the importance of nutritional status prior to elective surgery [9, 18, 22, 27]. To define malnutrition, most surgeons use serum laboratory values such as albumin concentration and total lymphocyte count. Obese patients are known to have micronutrient deficiencies such as iron and 25-hydroxy vitamin D [11, 15, 30], but the prevalence and significance of protein malnutrition in obese and non-obese patients undergoing TKA are not well characterized. Furthermore, it is unclear whether obesity and malnutrition are

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independently associated with adverse perioperative events. Given its potentially modifiable nature, preoperative malnutrition could significantly impact complication rates following TKA.

Using a large multi-center prospective clinical outcomes database, the research questions in this study were (1) What is the prevalence of malnutrition across various obesity classes in patients undergoing primary elective TKA? And the purpose of this study was to determine the prevalence of malnutrition across various obesity classes in patients undergoing primary elective TKA and to compare (2) What are the independent associations between malnutrition, obesity, and postoperative complications following TKA?.

Patients and Methods

The institutional review board at our institution granted an exemption prior to starting the study. A retrospective cohort study was performed using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. In NSQIP, more than 150 patient variables are recorded prospectively from more than 370 participating hospitals across the USA by trained clinical reviewers using a combination of chart reviews and provider interviews [1]. Among the collected variables are preoperative laboratory values including albumin concentration. NSQIP performs frequent data auditing to assess the quality of the data collected, with an overall inter-rater disagreement rate of 2% [1]. Further, patient data is collected up to the 30th postoperative day regardless of date of hospital discharge.

TKA cases were extracted from the NSQIP database from 2005 to 2013 using Current Procedural Terminology (CPT) code 27447, with International Classification of Diseases, Ninth Revision (ICD-9) codes 715.16, 715.36, and 715.96 for knee OA. Emergent cases, those with previous infections, and patients with missing age, gender, height, and weight were excluded. Patient demographics and medical comorbidities were collected. BMI was calculated from height and weight, and a modified Charlson Comorbidity Index (CCI) [7] was calculated for each patient as a measure of overall comorbidity burden, from data available in the NSQIP. A modified CCI has been shown to have similar efficacy to the original CCI and has been used in the orthopedic literature [2, 4, 29].

A total of 71,599 TKA cases were identified, of which 34,800 (48.6%) had preoperative serum albumin measurements. Compared to patients without measurements, those with albumin data had higher obesity classifications and modified CCI ($p < 0.05$) (Table 1), suggesting that there exists a bias towards obtaining a preoperative albumin level in patients with elevated comorbidity burden. To control for this potential selection bias between patients with and without preoperative albumin measurements, propensity scores were determined based on patient demographics, BMI, and modified CCI. The propensity score adjusted for the conditional probability of having a preoperative albumin measurement in this nonrandomized sample. The propensity-adjusted p values indicated a successful reduction in selection bias, with adjusted p values >0.05 for all patient variables. Thus, the remainder of the analysis was performed with the 34,800 patients with albumin measurements, while carrying forward the propensity scores.

Patients were categorized by BMI into the following World Health Organization obesity categories: non-obese (18.5–29.9 kg/m^2), obese I (30–34.9 kg/m^2), obese II (35–39.9 kg/m^2), or obese III (≥40 kg/m^2). This is an established classification for outcomes research using the NSQIP [6]. While malnutrition can occur in individuals with a BMI <18.5, these were excluded as the purpose of this study was to investigate the associations between malnutrition and obesity, in relation to normal weight patients.

Patient demographics, obesity classifications, and modified CCI were compared between patients with and without preoperative albumin measurements. Of a total of 71,599 TKA cases identified, 34,800 (48.6%) had preoperative serum albumin measurements. Compared to patients without measurements, those with albumin data had higher obesity classifications and modified CCI ($p < 0.05$) (Table 1), suggesting that there exists a bias towards obtaining a preoperative albumin level in patients with elevated comorbidity burden. To control for selection bias in the cases with albumin data, propensity scores were determined, defined as the conditional probability of having an albumin measurement based on the observed demographics, obesity classification, and comorbidity burden. Propensity scores have been used previously for this purpose [2, 10]. The propensity score adjusted for the conditional probability of having a preoperative albumin measurement in this nonrandomized sample. The propensity-adjusted p values indicated a successful reduction in selection bias, with adjusted p values >0.05 for all patient variables. Thus, the remainder of the analysis was performed with the 34,800 patients with albumin measurements, while carrying forward the propensity scores. Patients were categorized by serum albumin as normal (≥3.5 g/dL) or hypoalbuminemic (<3.5 g/dL). For the purposes of this study, malnutrition was defined as hypoalbuminemia.

Demographics and comorbidities were compared across obesity and albumin classes in bivariate fashion. Pearson's chi-square for categorical variables was used. The study endpoints included wound complications (superficial infection, deep surgical site infection, organ space surgical site infection, or wound dehiscence), septic complications (sepsis or septic shock), cardiac complications (cardiac arrest or myocardial infarction), respiratory complications (pneumonia, intubation, or ventilator requirement), blood transfusions (intra- or postoperative), urinary tract infection, return to the operating room within 30 days, deep vein thrombosis (DVT) or pulmonary embolism (PE), extended length of stay (LOS, defined as 4 days or longer), and death. Major complications were defined as any septic, cardiac, or respiratory complications, as well as DVT, PE, return to OR, and death.

Bivariate regressions were performed to compare the study endpoints across obesity and nutritional classes. The Bonferroni correction was applied to multiple comparisons

Table 1 Overall patient demographic characteristics and comorbidities with and without albumin measurements, with propensity score adjustment

	All patients $N = 71{,}599$	With preoperative albumin $N = 34{,}800$	Without preoperative albumin $N = 36{,}799$	Unadjusted p value	Adjusted p value[a]
Overall	100.0%	48.6%	51.4%		
Male gender	37.0%	36.8%	37.3%	0.134	0.999
Age group (years)				0.258	0.829
18–64	39.3%	39.2%	39.4%		
65–79	49.3%	49.6%	49.1%		
80+	11.3%	11.2%	11.5%		
Obesity classification				0.001	0.890
Non-obese (18.5–29.9 kg/m^2)	38.2%	37.7%	38.7%		
Obese I (30–34.9 kg/m^2)	28.3%	28.3%	28.4%		
Obese II (35–39.9 kg/m^2)	18.5%	18.5%	18.4%		
Obese III (≥40 kg/m^2)	15.0%	15.5%	14.5%		
Modified Charlson Comorbidity Index				<0.001	0.081
0 to 2	21.4%	20.9%	21.9%		
3	32.5%	32.3%	32.7%		
≥4	46.1%	46.8%	45.5%		

[a] To control for selection bias between the groups with and without preoperative serum albumin measurements, propensity scores were used, with the propensity score defined as the conditional probability of having a preoperative albumin measurement based on the observed patient characteristics. Propensity-adjusted p values for demographics, obesity classification, and modified CCI are reported. The model successfully reduced selection bias by eliminating significant differences in preoperative variables (adjusted p all >0.05)

to determine the level of significance for each analysis. Complications that were statistically significant either between obesity or albumin classes were carried into a propensity-adjusted multivariable logistic regression model. For each study outcome, the multivariable logistic regression adjusted for baseline patient demographic characteristics, comorbidities, type of anesthesia used, and propensity scores as a covariate. Regressions were repeated for each of the obesity classes as well as for hypoalbuminemia. The odds ratios were relative to non-obese patients for the obese classes and to patients with normal albumin for the hypoalbuminemia model. Obesity models were adjusted for hypoalbuminemia, and the albumin models were adjusted for BMI as a continuous variable. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated. The level of significance was set at $p < 0.05$. Analysis was performed using SPSS 22 (IBM Corp., Armonk, NY).

Results

Among this cohort of 34,800 TKA cases, the prevalence of malnutrition ranged from 3.5 to 6.1% depending on obesity classification (Table 2). There was a significant increase in the prevalence of hypoalbuminemia in the obese III patients (6.1%) compared to the non-obese (3.7%, $p < 0.001$). In addition, as obesity increased, patients were more likely to be female, African-American, younger in age, higher in ASA class, receive general anesthesia, and to be hypoalbuminemic (all $p < 0.001$). Relative to patients with normal albumin, the hypoalbuminemic patients were more likely to be female, African-American, older in age, higher in ASA class, and to receive general anesthesia (all $p < 0.001$). With increasing obesity, patients were more likely to have hypertension, dyspnea, chronic obstructive pulmonary disease (COPD), and diabetes ($p < 0.05$) (Table 3). Patients with preoperative hypoalbuminemia had higher rates of many comorbidities including hypertension, any of the pulmonary comorbidities, renal disease requiring dialysis, cerebrovascular history, diabetes, and chronic corticosteroid use ($p < 0.05$).

In the analysis of the associations between malnutrition, obesity, and postoperative complications following TKA, hypoalbuminemia was a more robust and consistent predictor of complications than obesity. With unadjusted analysis, as the obesity class increased, patients had higher rates of any complication(s), wound complications, and return to OR (Table 4). The rate of blood transfusions decreased with increasing obesity. Between the normal albumin and the hypoalbuminemic groups, patients with low albumin had higher rates of having any complication(s), any major complication(s), wound complications, cardiac complications, respiratory complications, blood transfusions, extended LOS, and death. With propensity-adjusted multivariable logistic regressions, obese III was the only obesity class to reach statistical significance as a predictor of postoperative complications, for any complication(s) (OR 1.31, $p = 0.005$), wound complications (OR 1.99, $p = 0.001$), and return to the operating room (OR 1.59, $p = 0.011$) (Table 5). Obese I and obese II were not statistically different from non-obese patients for any of the study outcomes. No obesity class was a significant predictor of major complications, cardiac complications, or death. Preoperative hypoalbuminemia was a stronger and more consistent independent risk factor for multiple complications while adjusting for BMI, as a predictor of any complication(s) (OR 1.37, $p = 0.003$), any major complication (OR 1.32, $p = 0.024$), wound

Table 2 Preoperative demographics and characteristics by obesity classification and serum albumin

Demographic and clinical characteristic (%)	Non-obese N = 13,099	Obese I N = 9811	Obese II N = 6427	Obese III N = 5386	p value	Normal albumin N = 33,400	Hypoalbuminemic N = 1400	p value
Gender					<0.001			<0.001
Women	59.8	59.4	66.7	74.3		63.0	69.4	
Men	40.2	40.6	33.3	25.7		37.0	30.6	
Race					<0.001			<0.001
White	82.9	83.1	82.2	81.1		82.7	79.7	
African-American	4.7	6.1	8.1	10.7		6.5	11.3	
Hispanic	5.4	5.9	5.3	4.5		5.4	5.2	
Other	3.3	2.4	1.8	1.6		2.6	2.2	
Unknown	7.6	7.2	6.6	5.1		7.0	4.9	
Age group (years)					<0.001			<0.001
18–64	28.6	37.0	47.4	59.6		39.4	35.6	
65–79	52.3	53.2	47.9	38.5		49.7	46.6	
80+	19.1	9.8	4.7	2.0		10.9	17.7	
ASA classification					<0.001			<0.001
1–2	62.0	55.7	42.3	25.0		51.7	32.0	
3–4	38.0	44.3	57.7	75.0		48.3	68.0	
Anesthesia type					<0.001			<0.001
General	54.5	55.3	56.8	59.2		55.6	62.3	
Regional/spinal/epidural	40.8	40.2	38.7	36.6		39.9	33.6	
Other	4.7	4.5	4.5	4.2				
Preoperative albumin					<0.001			
Normal (≥3.5 g/dL)	96.3	96.5	96.2	93.9				
Hypoalbuminemic (<3.5 g/dL)	3.7	3.5	3.8	6.1				

complications (OR 1.78, $p = 0.005$), cardiac complications (OR 2.23, $p = 0.010$), respiratory complications (OR 3.75, $p < 0.001$), and death (OR 3.17, $p = 0.004$) (Fig. 1). Unadjusted postoperative complications by obesity and serum class were also compared in bivariate fashion (Table 4). The Bonferroni correction was used to set statistical significance at $p < 0.004$. As the obesity class increased, patients had higher rates of any complication(s), wound complications, and return to OR. The rate of blood transfusions decreased with increasing obesity. Between the normal albumin and the hypoalbuminemic groups, patients with low albumin had higher rates of having any complication(s), any major complication(s), wound complications, cardiac complications, respiratory complications, blood transfusions, extended LOS, and death.

Table 3 Preoperative comorbidities by obesity classification and serum albumin

Comorbidity (%)	Non-obese N = 13,099	Obese I N = 9811	Obese II N = 6427	Obese III N = 5386	p value	Normal albumin N = 33,400	Hypoalbuminemic N = 1400	p value
Cardiovascular								
Congestive heart failure	0.2	0.3	0.2	0.3	0.348	0.2	0.6	0.010
Previous PCI	1.9	2.0	1.8	1.4	0.036	1.8	2.3	0.173
Previous cardiac surgery	1.4	1.1	1.0	0.6	<0.001	1.1	1.0	0.698
Angina	0.1	0.1	0.1	0.1	0.405	0.1	0.1	0.610
Hypertension requiring medication	60.7	70.0	74.3	77.9	<0.001	68.2	74.5	<0.001
Peripheral vascular disease	0.1	0.2	0.1	0.0	0.008	0.1	0.2	0.410
Pulmonary								
Current smoker	8.2	8.2	9.0	9.3	0.041	8.4	11.9	<0.001
Dyspnea	5.2	7.4	9.8	13.5	<0.001	7.7	14.3	<0.001
COPD	3.2	3.8	4.5	5.4	<0.001	3.8	7.9	<0.001
Renal								
Currently on dialysis	0.2	0.2	0.1	0.2	0.810	0.1	1.2	<0.001
Cerebrovascular								
Stroke with or without deficits	0.7	0.7	0.8	0.5	0.141	0.7	1.9	<0.001
Transient ischemic attacks	0.6	0.7	0.6	0.6	0.648	0.6	1.1	<0.001
Other								
Weight loss	0.3	0.1	0.1	0.1	0.007	0.1	0.6	<0.001
Diabetes	11.3	18.9	25.1	30.0	<0.001	18.7	23.6	<0.001
Alcohol use	0.7	0.4	0.4	0.3	0.003	0.5	0.8	<0.001
Chronic corticosteroid use	3.9	3.0	3.2	3.8	0.001	3.3	8.5	<0.001
Bleeding disorder	2.7	3.0	2.8	2.3	0.077	2.6	6.1	<0.001
Disseminated cancer	0.1	0.2	0.2	0.0	0.180	0.1	0.2	0.260

PCI percutaneous coronary intervention, *COPD* chronic obstructive pulmonary disease

Table 4 Postoperative events by obesity classification and serum albumin

Comorbidity (%)	Non-obese $N = 13{,}099$	Obese I $N = 9811$	Obese II $N = 6427$	Obese III $N = 5386$	p value[a]	Normal albumin $N = 33{,}400$	Hypoalbuminemic $N = 1400$	p value[a]
Any complication(s)	4.9	5.0	4.9	6.3	0.001	5.0	7.7	<0.001
Any major complication(s)	3.6	3.7	3.5	4.4	0.040	3.7	5.4	0.001
Wound complications	0.8	0.9	1.0	1.7	<0.001	1.0	2.0	<0.001
Septic complications	0.3	0.3	0.3	0.5	0.114	0.3	0.7	0.016
Cardiac complications	0.4	0.3	0.3	0.3	0.603	0.3	0.9	<0.001
Respiratory complications	0.6	0.4	0.4	0.4	0.183	0.4	2.0	<0.001
Blood transfusions (intra-/postoperative)	17.3	13.7	12.9	11.2	<0.001	14.3	19.4	<0.001
Urinary complications	1.1	1.0	1.1	1.4	0.225	1.1	1.4	0.354
Return to OR within 30 days	1.2	1.1	1.2	1.9	<0.001	1.2	1.6	0.269
DVT/PE	1.5	1.8	1.6	1.6	0.264	1.6	1.7	0.805
Death	0.1	0.2	0.1	0.2	0.371	0.1	0.6	<0.001
Extended length of stay (LOS)	9.0	8.2	8.7	9.7	0.020	8.6	14.2	<0.001

[a] Using the Bonferroni correction, significant values were set at $p < 0.004$

Propensity-adjusted multivariable logistic regressions were performed to determine the independent morbidity risk of each obesity class as well as hypoalbuminemia for each of the study outcomes (Table 5, Fig. 1), with adjusted OR and 95% CI. Obese III was the only obesity class to reach statistical significance as a predictor of postoperative complications, for any complication(s) (OR 1.31, $p = 0.005$), wound complications (OR 1.99, $p = 0.001$), and return to the operating room (OR 1.59, $p = 0.011$). Obese I and obese II were not statistically different from non-obese patients for any of the study outcomes. No obesity class was a significant predictor of major complications, cardiac complications, or death. With propensity-adjusted multivariable analysis, preoperative hypoalbuminemia was a stronger and more consistent independent risk factor for multiple complications while adjusting for BMI, as a predictor of any complication(s) (OR 1.37, $p = 0.003$), any major complication (OR 1.32, $p = 0.024$), wound complications (OR 1.78, $p = 0.005$), cardiac complications (OR 2.23, $p = 0.010$), respiratory complications (OR 3.75, $p < 0.001$), and death (OR 3.17, $p = 0.004$) (Fig. 1).

Discussion

Malnutrition is a common yet under-studied risk factor for complications in patients undergoing TKA, and its association with obesity is poorly understood. The aims of this study were to determine (1) the prevalence of hypoalbuminemia in non-obese and obese patients undergoing TKA and (2) the independent effects of hypoalbuminemia and obesity on 30-day postoperative complications following primary elective TKA. After statistical and propensity score adjustment for patient demographics, comorbidities, and whether preoperative serum albumin measurement was performed, the results show that being obese I or obese II with a BMI between 30 and 40 kg/m^2 did not confer increased risk for postoperative complications, while obese III was associated with increased postoperative morbidity, including any complications, wound complications, and return to OR within 30 days. In addition, while adjusting for patient BMI, preoperative serum hypoalbuminemia was identified as a robust independent risk factor for postoperative adverse events, most notably wound complications, cardiac complications, respiratory complications, and death. Hypoalbuminemia was overall a more consistent and robust predictor of postoperative complications than any obesity class.

This current study is subject to several limitations, the most important of which was that out of a total of 71,599 TKA cases, 34,800 (48.6%) had preoperative albumin measurements. As a large multi-center, multi-year clinical outcomes database, this may be due to heterogeneity across preoperative risk stratification protocols, preoperative medical workup differences, data collection practices, and patient demographics. Additionally, as shown in the results, patients with preoperative serum albumin measurements had higher obesity classes and modified CCI. To account for this selection bias, a propensity score adjustment model was used, which successfully eliminated statistically significant differences between groups with and without a preoperative albumin. Furthermore, the subsequent multivariable analysis used only the cases that had preoperative albumin measurements, while adjusting for the same propensity scores, accounting for any initial selection bias of the cohort. An additional limitation was that albumin was the only nutritional marker available in the NSQIP, and other markers such as transferrin and lymphocyte count would have potentially captured more patients with poor nutritional status. Furthermore, patients were followed for just 30 days postoperatively, and complications or deaths occurring after the 30th day were not captured. Lastly, there were no functional outcomes in the NSQIP.

A number of prospective and retrospective studies have demonstrated the adverse effect of obesity on outcomes following TKA [8, 13, 16, 17]. In these studies, obese patients have higher rates of infection and revision for infectious and non-infectious reasons, as well as decreased improvement in functional outcome scores compared to the non-obese. While the NSQIP does not have functional outcome scores or data regarding adverse events after the 30th postoperative day, our results are largely consistent with prior literature that demonstrated increased postoperative morbidity following TKA in obese patients. This was

Table 5 Adjusted odds ratios for postoperative events by obesity classification and preoperative hypoalbuminemia

Complication	Odds ratio	95% CI Lower	95% CI Upper	Propensity-adjusted p value[a]
Any complication(s)				
Obese I (30–34.9 kg/m^2)	1.01	0.89	1.15	0.853
Obese II (35–39.9 kg/m^2)	1.05	0.90	1.24	0.525
Obese III (≥40 kg/m^2)	1.31	1.08	1.58	0.005
Hypoalbuminemia (<3.5 g/dL)	1.37	1.11	1.68	0.003
Any major complication(s)				
Obese I (30–34.9 kg/m^2)	1.02	0.88	1.18	0.817
Obese II (35–39.9 kg/m^2)	1.00	0.83	1.21	0.963
Obese III (≥40 kg/m^2)	1.18	0.95	1.47	0.130
Hypoalbuminemia (<3.5 g/dL)	1.32	1.04	1.68	0.024
Wound complications				
Obese I (30–34.9 kg/m^2)	1.09	0.81	1.47	0.579
Obese II (35–39.9 kg/m^2)	1.37	0.95	1.98	0.092
Obese III (≥40 kg/m^2)	1.99	1.33	2.98	0.001
Hypoalbuminemia (<3.5 g/dL)	1.78	1.20	2.64	0.005
Cardiac complications				
Obese I (30–34.9 kg/m^2)	1.00	0.61	1.64	0.989
Obese II (35–39.9 kg/m^2)	0.84	0.45	1.57	0.579
Obese III (≥40 kg/m^2)	0.96	0.45	2.06	0.910
Hypoalbuminemia (<3.5 g/dL)	2.23	1.21	4.12	0.010
Respiratory complications				
Obese I (30–34.9 kg/m^2)	0.70	0.47	1.04	0.078
Obese II (35–39.9 kg/m^2)	0.75	0.45	1.23	0.255
Obese III (≥40 kg/m^2)	0.52	0.29	0.95	0.033
Hypoalbuminemia (<3.5 g/dL)	3.75	2.46	5.71	<0.001
Return to OR within 30 days				
Obese I (30–34.9 kg/m^2)	0.90	0.69	1.17	0.441
Obese II (35–39.9 kg/m^2)	1.04	0.76	1.44	0.798
Obese III (≥40 kg/m^2)	1.59	1.11	2.27	0.011
Hypoalbuminemia (<3.5 g/dL)	1.10	0.71	1.71	0.658
Death				
Obese I (30–34.9 kg/m^2)	1.75	0.84	3.63	0.133
Obese II (35–39.9 kg/m^2)	1.47	0.51	4.22	0.472
Obese III (≥40 kg/m^2)	1.40	0.47	4.21	0.548
Hypoalbuminemia (<3.5 g/dL)	3.17	1.46	6.90	0.004

[a] Each line represents a separate multivariable logistic regression to give an adjusted odds ratio and p value while controlling for patient characteristics and propensity score. Odds ratios for the obesity classes were adjusted for hypoalbminemia, and odds ratios for hypoalbuminemia were adjusted for BMI

observed not only with wound complications, but complications in other organ systems as well. Most prior studies, however, classify obese patients as those merely with BMI ≥30 kg/m^2; rarely have subgroup analyses been performed on cohort of the morbidly obese with BMI ≥40 kg/m^2. One of the strengths of the current study is the statistical power to further stratify obese patients given the large study population. As demonstrated in this study, obese I and obese II classes with BMI between 30 and 40 kg/m^2 did not confer additional risk for adverse outcomes relative to non-obese patients. As the prevalence of obesity increases and patients with BMI greater than 30 kg/m^2 become more common, additional stratification is important for more accurate preoperative risk prediction and targeted strategies for risk reduction. For example, resources for preoperative weight optimization, such as bariatric surgery, may be better allocated only to patients with BMI ≥40 kg/m^2.

Preoperative malnutrition has also been shown to be a predictor of postoperative complications after TKA. However, the overall incidence of malnutrition in patients undergoing TKA is unknown due to an inconsistent definition of malnourished. In a consecutive series of 217 patients undergoing primary TKA or THA, Greene et al. [19] found four patients (1.8%) with hypoalbuminemia, and 57 patients had a lymphocyte count of less than 1500 cells/mm^3 (another commonly used marker of malnutrition). Similarly, in a prospective study of 2161 patients undergoing TKA or THA, Huang et al. [20] found that 8.5% of their cohort was malnourished, defined as either serum albumin <3.5 g/dL or serum transferrin <200 mg/dL. Of their malnourished cohort, however, 72.8% of patients had a normal albumin and low transferrin. While albumin, lymphocyte count, and transferrin are all useful markers of nutritional status [9], it is difficult to compare prevalence rates between studies with different definitions of malnutrition. However, despite varying definitions in the orthopedic literature, malnutrition has been associated with prosthetic joint infections as well as persistent wound drainage, hematoma formation, infection, renal complications, and cardiac complications postoperatively [19, 20]. Consistent with prior published literature, our multivariable regression models found preoperative

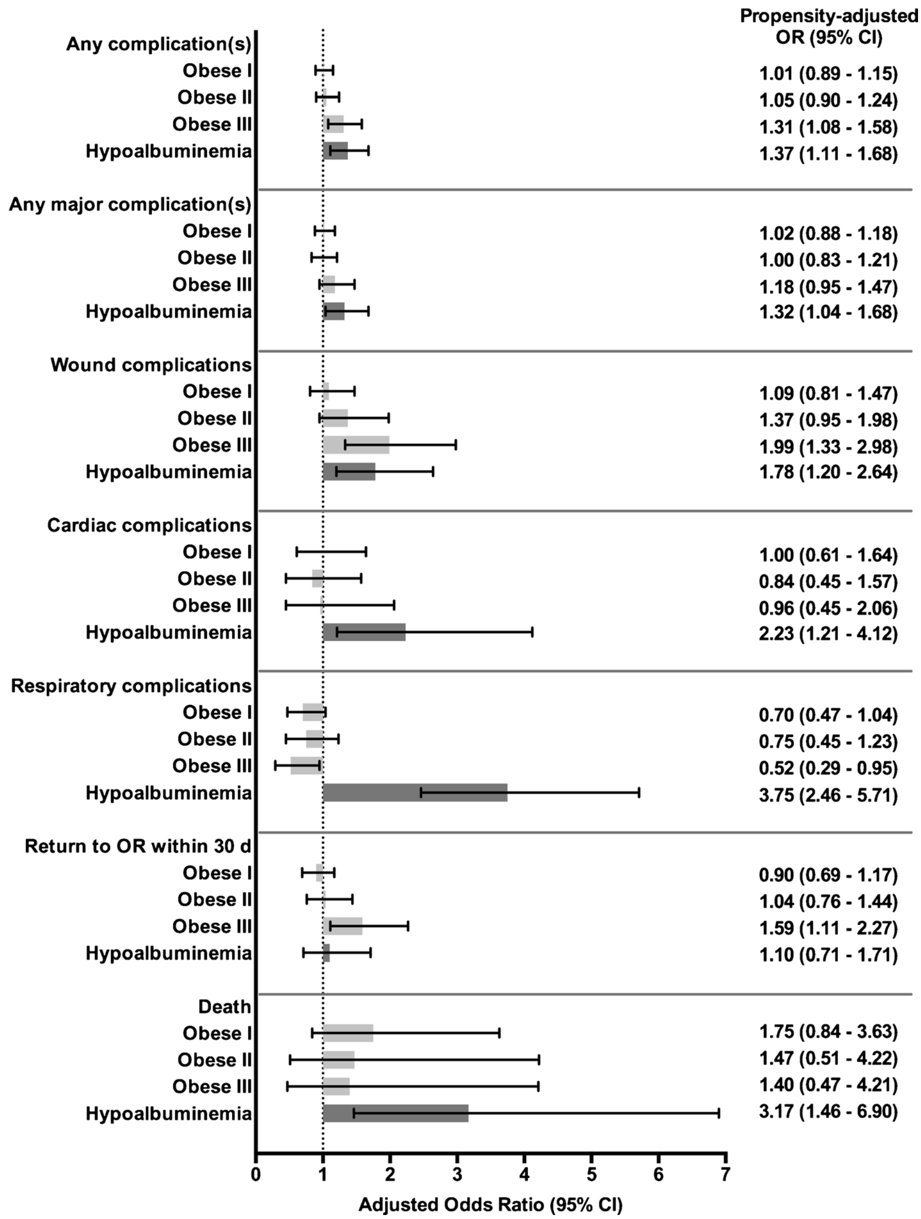

Fig. 1. Forest plot of propensity-adjusted odds ratios for developing select postoperative complications based on preoperative obesity class: obese I (30–34.9 kg/m^2), obese II (35–49.9 kg/m^2), or obese III (≥40 kg/m^2), as well as preoperative hypoalbuminemia (<3.5 g/dL). *Error bars* indicated 95% confidence intervals (CI), and *vertical dotted line* represents adjusted odds ratio of one. A 95% CI that does not include odds ratio of one indicates $p < 0.05$ and statistical significance.

hypoalbuminemia to be a significant predictor of wound complications, as well as any postoperative complication(s), major complications, cardiac complications, respiratory complications, and death. While adjusting for BMI, the independent predictive strength of hypoalbuminemia was stronger and more consistent than that of obesity.

In this study population, the prevalence of preoperative malnutrition as measured by hypoalbuminemia increased significantly from the non-obese (3.7%) to obese III (6.1%). There is a paucity of studies that have examined nutritional status and obesity concurrently in TKA patients. In the study by Huang et al. [20], the authors found that 9% of patients with BMI 20 to 29.9 kg/m^2 were malnourished, 7.7% were malnourished in the BMI 30 to 39.9 kg/m^2 group, and 7.8% in the BMI ≥40 kg/m^2 group. They did not find any statistically significant differences in the distribution of various BMI classes between malnourished and non-malnourished patients, though their BMI groups were defined differently than our current study. In a retrospective review of 6489 TKA cases from a single institution, Peersman et al. [25] showed that poor nutrition, obesity, and diabetes were associated with subsequent joint infections. Unfortunately, they did not provide their definition for poor nutrition, nor was the prevalence of malnutrition or obesity available. Nonetheless, our results show a strong trend of increasing prevalence of malnutrition with obesity, a somewhat paradoxical and likely underappreciated finding in the orthopedic realm. In the bariatric surgery literature, however, preoperative albumin deficiency rates of up to 15.6% in morbidly obese patients have been reported [3].

Recent studies by Nelson et al. [22] and Bohl et al. [5] have similarly used the NSQIP database to investigate the effects of malnutrition on complications following joint arthroplasty. In the study by Nelson et al. [22], they concluded that while hypoalbuminemia was associated with increased mortality and major complications, morbid obesity was not independently associated with the majority of postoperative complications. However, in their study, obesity and malnutrition were analyzed in separate cohorts, as preoperative albumin measurements were not available for half of their study sample. Similarly, the study by Bohl et al. [5] concluded that hypoalbuminemia was independently associated with increased postoperative morbidity, while excluding the patients that did not have albumin measurements. This is a major shortcoming of these aforementioned studies, as a selection bias clearly exists between those patients who have preoperative albumin measurements and those that did not, as was demonstrated in Table 1 of our results; this potential selection bias was not addressed with propensity score adjustment or matching in these studies, which undoubtedly influenced their results. Furthermore, Nelson et al. [22] only classified patients as being non-obese and obese based on a threshold BMI of 40 kg/m^2, rather than performing a more detailed sub-class analysis. We believe as the prevalence of obesity continues to rise in the US population, determining relative risk among class I to III obesity will be paramount in risk stratifying obese patients undergoing TKA. In our study, when we sub-classified obese patients, we did find that obese III did increase the risk of complications after TKA.

In conclusion, the prevalence of malnutrition as defined by a serum albumin level <3.5 g/dL increases with obesity class. Further, after adjusting for medical comorbidities and BMI, preoperative hypoalbuminemia was a strong predictor of postoperative complications and was in fact stronger than class III obesity. Preoperative malnutrition and obesity are potentially modifiable risk factors; thus, we believe patients should be screened for preoperative malnutrition prior to TKA, especially in those who are underweight or obese III and surgeons should counsel patients on the strong increased risk that malnutrition carries for 30-day complications after TKA. Additionally, as risk-adjustment models for bundled reimbursements for joint replacement are developed, the current results suggest that obese III and hypoalbuminemia may be relevant variables to take into consideration.

Compliance with Ethical Standards

Conflict of Interest: Michael C. Fu, MD, MHS and Alexander S. McLawhorn, MD, MBA have declared that they have no conflict of interest. Michael B. Cross, MD reports grants and personal fees from Smith and Nephew; personal fees from Link, Acelity, Exactech, Intellijoint; other from Journal of Orthopaedics and Traumatology and Bone Joint Journal 360; grants from Michael Price Family Foundation, outside the work. Douglas E. Padgett, MD reports personal fees from Stryker and Mako and other from Journal of Arthroplasty, outside the work.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was waived from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

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