Preoperative Hypoalbuminemia Is Associated With Early Morbidity and Mortality After Revision Total Hip Arthroplasty

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abstract

Hypoalbuminemia is associated with early morbidity and mortality in revision total knee arthroplasty. We evaluated the effect of preoperative hypoalbuminemia on 30-day morbidity and mortality in revision total hip arthroplasty (THA). The National Surgical Quality Improvement Program (NSQIP) database was queried from 2015 to 2018 to identify patients who underwent revision THA. Patients were stratified based on the presence or absence of preoperative hypoalbuminemia and their odds of a major complication or death within 30 days of revision THA with multivariate logistic regression. After Bonferroni correction for these 2 primary outcomes, statistical significance was defined as $P<.025$. A total of 2492 revision THAs with complete data were identified, of which 486 (20%) had preoperative hypoalbuminemia. Preoperative hypoalbuminemia increased the absolute risk of a major complication by 15.3% compared with patients with revision THA without hypoalbuminemia (30% vs 14.7%, $P<.001$). Patients with preoperative hypoalbuminemia also had nearly a 7-fold higher incidence of death (3.3%) compared with those with revision THA without preoperative hypoalbuminemia (0.5%, $P<.001$). After logistic regression, the odds of having a major complication after revision THA with preoperative hypoalbuminemia within 30 days were increased by 80% (odds ratio, 1.8; 95% CI, 1.4-2.3; $P<.001$), and the odds of death within 30 days were increased by 210% (odds ratio, 3.1; 95% CI, 1.2-7.8; $P=.020$). Hypoalbuminemia is associated with early morbidity and mortality after revision THA. [*Orthopedics*. 20XX;XX(X):xx-xx.]

Total hip arthroplasty (THA) effectively treats the pain and disability associated with end-stage degeneration of the hip. Despite the robust long-term survival of THA, the burden of revision THA is expected to increase 137% by 2030, with aseptic indications becoming increasingly common.[1-3]

Revision THA is associated with increased length of hospital stay and resource use compared with primary THA.[2] Compared with revision total knee arthroplasty (TKA), revision THA is also associated with an almost 2-fold increase in 30-day morbidity and a 10-fold increase in 30-day mortality.[4,5] Factors associated with these adverse outcomes after revi-

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Table 1

Revision Total Hip Arthroplasty Procedures Identified From the NSQIP Database

Characteristic	Value
Age, mean±SD, y	66.9±12.6
Female, No.	1354 (54.3%)
Body mass index, mean±SD, kg/m^2	29.9±7.0
Normal (<25 kg/m^2), No.	1370 (55.0%)
Class I obesity (≥25 and <35 kg/m^2), No.	609 (24.4%)
Class II/III obesity (≥35 kg/m^2), No.	513 (20.6%)
Medical comorbidity, No.	
Hypoalbuminemia	486 (19.5%)
Congestive heart failure	38 (1.5%)
Pulmonary disease	258 (10.4%)
End-stage renal disease	24 (1.0%)
Anemia	449 (18.0%)
Dependence	186 (7.5%)
Tobacco use within 1 year	415 (16.7%)
Diabetes mellitus	130 (5.2%)
Septic revision	216 (8.7%)

Abbreviation: NSQIP, National Surgical Quality Improvement Program.

sion THA include preoperative anemia, chronic obstructive pulmonary disease, and 2-component revision.[4] Given the increased burden of morbidity and mortality for revision THA compared with revision TKA, it is critical to understand the risk factors associated with adverse outcomes in revision THA.

Albumin is a protein that is widely used as an indicator of overall nutritional status.[6] The association between serum hypoalbuminemia and poor perioperative outcomes, including increased morbidity and mortality in primary total joint arthroplasty, is well established.[7] The relationship of hypoalbuminemia and morbidity or mortality in revision THA is less well defined. To date, preoperative hypoalbuminemia is associated with increased surgical site infections after revision total joint arthroplasty and major medical complications after revision TKA.[8,9] Hence, we sought to characterize the effect of preoperative hypoalbuminemia on the early postoperative outcomes of patients undergoing revision THA. We hypothesized that preoperative hypoalbuminemia would be associated with an increase in major complications and mortality within 30 days of revision THA.

Materials and Methods

The National Surgical Quality Improvement Program (NSQIP) database is composed of deidentified preoperative characteristics and 30-day outcomes for patients undergoing surgery.[10] The data at each institution are entered by trained specialists, and the interrater reliability is greater than 98%.[11] Patients admitted to NSQIP-participating institutions from 2015 to 2018 and undergoing revision THA were identified as eligible patients with *Current Procedural Terminology* codes 27134, 27137, and 27138. Septic revision THA was defined with *International Classification of Diseases* (*ICD*), 9th edition, code 996.6x and *ICD,* 10th edition, code T84.5x. A total of 9266 patients who underwent additional procedures or had incomplete data were excluded from our analysis with listwise deletion to create a complete case data set.[12] A comparison of multiple imputation and listwise deletion (ie, complete case analysis) sets to deal with incomplete data within NSQIP showed that listwise deletion is more accurate.[13]

The primary end point of this study was a major complication or death within 30 days. A 30-day major complication was defined as surgical site infection, wound dehiscence, pulmonary embolism, pneumonia, reintubation, requirement for more than 48 hours of ventilation, acute renal failure, cerebrovascular accident, myocardial infarction, reoperation, or readmission within 30 days of the procedure.

Hypoalbuminemia was defined as serum albumin level of less than 3.5 g/dL.[14] Information on patients undergoing revision THA with and without preoperative hypoalbuminemia was stratified and compared. Continuous data were reported as mean and SD. Categorical data were reported as number and percentage. Significant covariates were identified with Fisher's exact test and were included in a multivariate bivariate logistic regression along with clinically significant risk factors to determine the odds ratio (OR) and 95% CI of a 30-day major complication or death. Variables included in the logistic regression included age, insulin-dependent diabetes, body mass index, smoking history, operative time, dependent functional status, preoperative anemia, end-stage renal disease, congestive heart failure, pulmonary disease, and revision for infection. After Bonferroni correction, statistical significance was set at $P<.025$. All statistical analyses were performed with Stata, version 14.0, software (StataCorp LP).

Results

We identified 2492 patients who underwent revision THA. Of the 2492 patients, 486 had preoperative hypoalbuminemia (**Table 1**). The patients who underwent revision THA with preoperative hypoalbuminemia were older (age >80 years, 27.8% vs 14.1%; $P<.0001$), varied in severity of obesity (Class I, 33.3% vs 22.3%, $P<.001$; Class II/III, 17.3% vs 21.4%, $P<.001$), and had higher rates of congestive heart failure (4.3% vs 0.9%, $P<.001$), pulmonary disease (14.4% vs 9.4%, $P<.001$), end-stage renal disease (2.9% vs 0.5%, $P<.001$), preoperative anemia (36% vs 13.7%, $P<.001$), dependent functional status (19.1% vs 4.6%, $P<.001$), tobacco use (21.6% vs 15.5%, $P<.001$), insulin-dependent diabetes mellitus (10.1% vs 3.9%, $P<.001$), and septic revision THA (18.3% vs 6.3%, $P<.001$) compared with

those undergoing THA without preoperative hypoalbuminemia (**Table 2**).

Patients undergoing revision THA with preoperative hypoalbuminemia had a 15.3% increase in the absolute risk of a major complication within 30 days of revision compared with patients undergoing THA without preoperative hypoalbuminemia (30% vs 14.7%, *P*<.001). Those undergoing revision THA with preoperative hypoalbuminemia had a 2.8% increase in 30-day mortality compared with patients without preoperative hypoalbuminemia (3.3% vs 0.5%, *P*<.001) (**Table 3**).

Patients undergoing revision THA with preoperative hypoalbuminemia had a 4.4% increase in the absolute risk of a periprosthetic joint infection within 30 days of revision compared with those undergoing THA without preoperative hypoalbuminemia (6.6% vs 2.2%, *P*<.001).

Multivariable logistic regression showed that preoperative hypoalbuminemia in revision THA was associated with an 80% increase in the odds of having a major complication (OR, 1.8; 95% CI, 1.4-2.3; *P*<.001) and a 210% increase in the odds of death (OR, 3.1; 95% CI, 1.2-7.8; *P*=.020) within 30 days.

Table 2

Characteristics of Patients Undergoing Total Hip Arthroplasty With and Without Hypoalbuminemia

Characteristic	No. (%) Albumin ≥3.5 g/dL (n=2006)[a]	Albumin <3.5 g/dL (n=486)[a]	*P*
Age			
<65 y	878 (43.8)	146 (30)	
65-80 y	846 (42.2)	205 (42.2)	<.001
>80 y	282 (14.1)	135 (27.8)	
Body mass index			
Normal, <25 kg/m^2	1130 (56.3)	240 (49.4)	
Class I obesity, 25-35 kg/m^2	447 (22.3)	162 (33.3)	<.001
Class II/III obesity, >35 kg/m^2	429 (21.4)	84 (17.3)	
Female sex	1088 (54.2)	266 (54.7)	.879
Comorbidity			
Congestive heart failure	17 (0.9)	21 (4.3)	<.001
Pulmonary disease[b]	188 (9.4)	70 (14.4)	<.001
End-stage renal disease	10 (0.5)	14 (2.9)	<.001
Anemia[c]	274 (13.7)	175 (36)	<.001
Dependent functional status[d]	93 (4.6)	93 (19.1)	<.001
Tobacco use[e]	310 (15.5)	105 (21.6)	<.001
Insulin-dependent diabetes mellitus	81 (3.9)	49 (10.1)	<.001
Septic revision[f]	127 (6.3)	89 (18.3)	<.001

[a]Operative time (mean±SD), albumin ≥3.5 g/dL 141.2±68.7 minutes vs albumin <3.5 g/dL 140.0±72.7 minutes, P=.74.
[b]Chronic obstructive pulmonary disease or dyspnea on exertion.
[c]Hematocrit value <36% for women or <39% for men.
[d]Not independent for all activities of daily living.
[e]Current smoker within 1 year.
[f]Revision total hip arthroplasty for a septic indication.

Discussion

Understanding the risk factors for adverse outcomes after revision THA is critical for optimizing patient care. Our study showed that preoperative hypoalbuminemia is associated with double the rate of a major complication within 30 days of revision THA compared with revision THA among patients without preoperative hypoalbuminemia. We also found that preoperative hypoalbuminemia was associated with a 7-fold increase in 30-day mortality compared with patients without preoperative hypoalbuminemia. We would like to highlight the use of a homogenous revision THA population because we believe it is critical to reducing confounders.[5] Bozic et al[5] showed that the most common etiologies for revision in TKA (infection) and THA (dislocation) differ substantially. Compared with patients undergoing revision TKA, those undergoing revision THA are sicker, as shown by the major severity of illness score, and undergo more full-component revisions. All-encompassing, revision THA is associated with a 52% greater resource burden than revision TKA. Thus, aggregate analysis of revision knee and hip arthroplasty introduces the potential for misleading results. Further, we expand on the observations made by Rynecki et al[15] by noting the association of preoperative hypoalbuminemia and mortality within 30 days of revision THA.

In both arthroplasty- and non-arthroplasty–related hip surgery, preoperative hypoalbuminemia is associated with adverse outcomes. Kishawi et al[16] showed that a low serum albumin value is associated with 30-day major postoperative complications in knee, hip, and shoulder revision arthroplasty. Our study expands on these findings by also showing an association with mortality in a more homogenous revision THA population.[16] Ryan et al[14] evaluated patients with hip fracture

Table 3

Comparison of 30-Day Major Medical Events Versus Albumin Level Across the Study Population

	No. (%)		
Major medical event	Albumin ≥3.5 g/dL (n=2006)	Albumin <3.5 g/dL (n=486)	*P*
30-day mortality	10 (0.5)	16 (3.3)	<.001
30-day morbidity	294 (14.7)	146 (30)	<.001
Surgical site infection	44 (2.2)	32 (6.6)	<.001
Dehiscence	8 (0.4)	6 (1.2)	.039
Pneumonia	13 (0.7)	12 (2.5)	.001
Pulmonary embolism	6 (0.3)	7 (1.4)	.006
Reintubation	6 (0.3)	5 (1)	.045
Failure to wean from ventilator within 48 h	3 (0.1)	0 (0)	1
Renal failure	2 (0.1)	1 (0.2)	.479
Cerebrovascular accident	3 (0.1)	0 (0)	1
Cardiac arrest	3 (0.1)	4 (0.8)	.03
Myocardial infarction	15 (0.8)	5 (1)	.569
Reoperation related to procedure	158 (7.9)	70 (14.4)	<.001
Readmission related to procedure	242 (12.1)	114 (23.5)	<.001

and reported that preoperative hypoalbuminemia predicted readmission, length of hospital stay, and mortality. Using the NSQIP data set, Bohl et al[17] found that preoperative hypoalbuminemia among geriatric patients with hip fracture was associated with sepsis, unplanned intubation, and mortality. In primary arthroplasty, the effect of preoperative hypoalbuminemia is associated with increased 30-day major complications, 30-day mortality, and 90-day cost of care.[7,12,18-22] For patients undergoing revision TKA, preoperative hypoalbuminemia was associated with major complications, including surgical site infection, urinary tract infection, sepsis, prolonged ventilator status, renal failure, and death.[23] Rudasill et al[24] evaluated the effect of preoperative hypoalbuminemia for patients undergoing primary and revision arthroplasty at a single tertiary care hospital. This study showed an association with hypoalbuminemia and increased care costs for all primary and revision arthroplasty procedures.[24] Their subgroup analysis of 10 patients undergoing revision THA showed that hypoalbuminemia significantly increased length of stay and total cost of care.[24]

A previous study using the NSQIP database to study the effect of hypoalbuminemia in revision THA did not control for septic and aseptic etiologies when reporting their outcomes.[25] This is critical because septic revision THA is independently associated with increased morbidity and mortality compared with aseptic revision THA.[26] Thus, interpretation of previous studies of preoperative hypoalbuminemia in revision THA is limited by this confounding covariate. Bohl et al[12] evaluated the incidence of hypoalbuminemia among 4517 patients undergoing revision arthroplasty for septic and aseptic etiologies. They found that the prevalence of hypoalbuminemia is substantially higher during septic revision THA.[12] This finding was mirrored in our study because the incidence of hypoalbuminemia was 18.3% for septic revision THA and 6.3% for aseptic revision THA (*P*<.001). Bohl et al[8] also observed that preoperative hypoalbuminemia in revision total joint arthroplasty was associated with early prosthetic joint infection. We also found this correlation because patients undergoing revision THA with hypoalbuminemia had a 6.6% incidence of prosthetic joint infection, whereas those without hypoalbuminemia had an incidence of 2.2% (*P*<.001).

Our data show that albumin status is a crucial modulator of postoperative outcomes for patients undergoing revision THA. These findings suggest that albumin status should be noted ahead of revision THA. The reasons for the increase in adverse outcomes associated with hypoalbuminemia include impaired (1) innate and humoral immune system function, (2) endothelial wall stability, and (3) intravascular fluid retention.[27] Ryan et al[14] showed that hypoalbuminemia correlates with the incidence of periprosthetic joint infection after primary THA better than American Society of Anesthesiologists score while having an equivalent association with major medical complications compared with American Society of Anesthesiologists score. Hypoalbuminemia was associated with renal failure and congestive heart failure in our study and in previous publications.[28,29] Revision THA in the setting of multiple medical comorbidities may provide a systemic second hit to patients, contributing to our observation of increased morbidity and mortality. Therefore, given the association of hypoalbuminemia with other substantial medical comorbidities, hypoalbuminemia may be a marker of medical frailty, and modification may not substantially address the underlying causal medical comorbidities. We speculate that preoperative hypoalbuminemia may be a marker of the severity of medical comorbidity that is not considered in

other measures, such as the Charlson and Elixhauser comorbidity indexes, given its strong independent association with mortality in our study.[30,31] Previous findings suggested that correction of albumin status for patients undergoing arthroplasty may reduce hospital stay and overall 90-day charges.[32] However, whether correction is possible for medically frail patients undergoing revision arthroplasty remains unknown and warrants further study. Thus, given the tremendous increase in resource use associated with hypoalbuminemia and its corresponding medical comorbidities, patients undergoing revision THA with preoperative hypoalbuminemia should be excluded from current and future bundled payment models.[25]

There are limitations to our study. Although the data were prospectively collected, our study is retrospective and is unable to report causality. Additionally, we report only early postoperative outcomes, and a data set that collects longer-term outcomes is necessary to evaluate the relationship between hypoalbuminemia and outcomes in revision THA after 30 days. Although the NSQIP data set has been widely used to report the outcomes of both primary and revision arthroplasty, it is subject to coding error and data entry inaccuracies.[12] Additionally, missing data may influence the final outcome, although our excluded number of patients mirrors that of other work assessing revision arthroplasty.[12] Our use of listwise deletion sought to mitigate this limitation because this is the most accurate method of associating risk in NSQIP, which strengthens the associations we found with preoperative hypoalbuminemia and revision THA.[13] Multiple imputation increases the ability to detect differences by increasing sample size when listwise deletion is unsuccessful. Our finding of an association between our dependent variable and both study end points precludes the need for multiple imputation simply to increase the sample size.[33] Multiple imputation should also be interpreted with caution when it detects a difference that is not seen with listwise deletion because this could indicate a type II error.[34]

Conclusion

For patients undergoing revision THA, preoperative hypoalbuminemia is associated with morbidity and mortality before 30 days. Consideration should be given to assessing preoperative albumin status ahead of revision THA. Further prospective study is necessary to characterize these outcomes beyond 30 days and to determine whether correction is possible and improves perioperative outcomes.

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