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Original Research

Preoperative Malnutrition and Metabolic Markers May Predict Periprosthetic Fractures in Total Hip Arthroplasty

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ABSTRACT

Background: Periprosthetic fractures are a devastating complication of total hip arthroplasty (THA) and are associated with significantly higher mortality rates in the postoperative period. Given the strain that periprosthetic fractures place on the patient as well as the healthcare system, identifying and optimizing medical comorbidities is essential in reducing complications and improving outcomes.

Methods: All THA with primary indications of osteoarthritis from 2007 to 2020 were queried from the National Surgical Quality Improvement Program database. Demographic data, preoperative laboratory values, medical comorbidities, hospital course, and acute complications were collected and compared between patients with and without readmission for a periprosthetic fracture. A multivariate logistic regression analysis was performed to determine associated independent risk factors for periprosthetic fractures after index THA.

Results: The analysis included 275,107 patients, of which 2539 patients were readmitted for periprosthetic fractures. Patients with postoperative fractures were more likely to be older (>65 years), females, BMI >40, and increased medical comorbidities. Preoperative hypoalbuminemia, hyponatremia, and abnormal estimated glomerular filtration rates were independent risk factors for sustaining a periprosthetic fracture and readmission within 30 days. Modifiable patient-related factors of concurrent smoking and chronic steroid use at the time of index THA were also independent risk factors for periprosthetic fractures. Inpatient metrics of longer length of stay, operative time, and discharge to rehab predicted postarthroplasty fracture risk. Readmitted fracture patients subsequently had increased risks of developing a surgical site infection, urinary tract infection, and requiring blood transfusions.

Conclusions: Patients with hypoalbuminemia, hyponatremia, and abnormal estimated glomerular filtration rate are at increased risk for sustaining periprosthetic fractures after THA. Preoperative optimization with close monitoring of metabolic markers and modifiable risk factors may help not only prevent acute periprosthetic fractures but also associated infection and bleeding risk with fracture readmission.

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Introduction

Total hip arthroplasty (THA) is a common and incredibly effective treatment option for advanced osteoarthritis of the hip. Each year in the United States, approximately 300,000 primary THAs are

performed [1] in order to reduce pain and improve overall function and quality of life after conservative medical therapy has failed [2]. With rising demands from an aging population [3], by the year 2030, the estimated number of primary THAs is expected to increase by 174% [4]. Unfortunately, as older patients often have worse bone quality and younger patients have greater activity demands [4], it is expected that the number of periprosthetic fractures will also increase during this time [5].

Periprosthetic fractures are a devastating complication of THA and are associated with significantly higher mortality rates in the postoperative period [6]. As the second most common indication

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for revision THA, periprosthetic fractures often occur in acutely ill patients who require urgent surgery [7]. Surgery is unfortunately challenging in this patient population but must be performed to alleviate pain and prevent impaired mobility as well as to decrease the risk of complications brought on by prolonged bed rest [7]. Given the substantial strain that periprosthetic fractures place on the patient as well as the healthcare system as a whole, identifying, and addressing patient-, surgical- and prosthesis-related risk factors for this particular complication is vital [8].

To date, a variety of risk factors for periprosthetic fractures following THA have been identified, including sex, age >70 years [9], prosthesis design as well as cemented vs uncemented prosthesis, [10] implant stability and loosening of the femoral stem, [11] osteoporosis, [10] bisphosphonate use [12] as well as many others. Interestingly, despite being prevalent in around 20% of the elderly population [13], malnutrition and its association with periprosthetic fractures after THA have not been well studied. Further investigation into this topic is warranted given the fact that certain nutrients have been proven essential for bone metabolism homeostasis [14] and have been associated with decreased bone loss even in postmenopausal women [15]. Furthermore, insufficient intake of certain nutrients has even been implicated in impaired fracture healing [15]. The purpose of this study, therefore, is to investigate which risk factors, with an emphasis on malnutrition and modifiable risk factors, predict periprosthetic fracture in THA patients. Our hypothesis is that elderly patients with hypoalbuminemia, hyponatremia, and increased medical comorbidities are at an increased risk for sustaining acute periprosthetic fractures after elective THAs compared to younger, well-nourished patients.

Material and methods

This retrospective, deidentified database study was accepted under exempt status by the institutional review board. As such, no informed consent was obtained. The National Surgical Quality Improvement Program (NSQIP) database was queried using Current Procedural Terminology code 27130 for all primary THA performed during the years 2007 to 2020. The NSQIP database is a commonly utilized resource in the field of orthopedics and has been employed many times in general orthopedics as well as in the hip arthroplasty literature [16–19]. The database contains well-organized patient information gathered from over 600 hospitals from across the United States. Data are uploaded and maintained by healthcare professionals and is accumulated from outpatient visits, patient interviews, and postoperative records [20]. The database is also regularly audited to help guarantee its accuracy [21].

All adult patients (aged ≥ 18 years) who underwent THA during the years 2007 to 2020 with preoperative medical history and laboratory values as well as postoperative outcomes and complications documented in the database were included. Patients <18 years of age or those with missing postoperative outcomes and complication data were not included. Information on demographics, preoperative laboratory results, American Society of Anesthesiologists (ASA) classification, and a patient's past medical history were extracted and further categorized as given in Table 1. THA operative details, anesthesia type, postoperative outcomes, length of stay, discharge disposition, and postoperative complications were also collected and compared between groups. Postoperative complications, including 30-day superficial wound infection, deep incision surgical site infection, pulmonary embolism, acute renal failure, urinary tract infection, myocardial infarction, bleeding requiring blood transfusion, deep vein thrombosis/thrombophlebitis, sepsis, ventilator requirement, reoperation rate, and readmission rate were included in the analysis. Patients with periprosthetic hip fracture were identified using the International

Classification of Disease, Ninth 996 as well as the Tenth M97, T84, and S72 Revisions, Clinical Modification codes. To evaluate risk factors for periprosthetic hip fracture, the subjects were categorized as periprosthetic fracture patients and nonperiprosthetic fracture patients.

Preoperative laboratory values included in this study were sodium level (normal range 135–147 mmol/L), estimated glomerular filtration rate (eGFR) (normal range ≥ 90 ml/min/1.73 m², mild-to-moderate range 30–89 ml/min/1.73 m², severe range <30 ml/min/1.73 m²), white blood cell count (low-to-normal range 0–11 $\times 10^9$ /l, high range 12+ $\times 10^9$ /l), serum glutamic oxaloacetic transaminase (SGOT) IU/L, alkaline phosphatase (low range < 44 IU/L, normal range 44–147 IU/L, and high range >147 IU/L), and platelet level (low range thrombocytopenia 0–139 $\times 10^9$ /l). Patients were determined to have no anemia (hematocrit >36% for women, >39% for men), mild anemia (hematocrit 33%–36% for women, 33%–39% for men) or moderate-to-severe anemia (hematocrit <33% for either women or men) based on serum hematocrit. The blood urea nitrogen (BUN)–to–creatinine (Cr) ratio was used as a marker for dehydration, with nondehydrated subjects defined as those with a BUN/Cr < 20, moderately dehydrated patients defined as those with a BUN/Cr of 20 to 25, and severely dehydrated subjects defined as those with a BUN/Cr > 25 [19]. Body mass index (BMI) was separated into kg/m² ranges (<18.5, 18.5–24.9, 25–29.9, 30–39.9, and >40). Albumin levels were utilized as a marker for malnutrition, with hypoalbuminemia defined as <3.5 g/dl [19].

Preoperative medical comorbidities, such as diabetes, severe chronic obstructive pulmonary disease (COPD), smoking, ascites, hypertension requiring medications, renal failure, cancer, blood disorders, anemia requiring preoperative blood transfusions, systemic sepsis, and >10% weight loss prior to surgery were recorded to account for independent risk factors. The level of frailty was calculated using an index score based on the presence of the 5 comorbidities: congestive heart failure within 30 days prior to surgery, insulin-dependent or noninsulin-dependent diabetes mellitus, COPD or pneumonia, partially dependent or totally dependent functional health status at time of surgery, and hypertension requiring medication.

To analyze the risk factors for periprosthetic hip fracture following THA, multiple bivariate and multivariate analyses were performed. Categorical variables were analyzed using Chi-squared or Fischer's exact test, whereas categorical variables were analyzed using student's t-test. Bivariate logistic regressions were employed to determine the significance of preoperative laboratory values with regards to periprosthetic fractures. Multivariate models were then built using forward stepwise logistic regression as well as with clinical judgment. These models included aspects of subject demographics, laboratory results, medical comorbidities, and operative information. Multivariate stepwise logistic regression was also utilized to build models for postoperative complications in order to identify confounding variables for periprosthetic hip fracture. Statistics were performed on IBM SPSS Statistics, version 26 (IBM Corp., Armonk, NY). Significance was defined as $\alpha < 0.05$.

Results

Baseline characteristics

In the years 2007 to 2020, there were 275,107 patients who underwent primary THA in the United States with data recorded in the NSQIP database. Within this study population, 0.9% or 2539 individuals had their recovery complicated by periprosthetic hip fracture. Within the periprosthetic fracture cohort, there was a greater proportion of female subjects (all patients: 55.0% female, periprosthetic fracture patients: 62.4% female, $P < .001$). There were

Table 1
Descriptive statistics

Variable	All patients	Periprosthetic fracture	P
n, %	275,107 (100.0)	2539 (0.9)	–
Demographics			
Sex, n (%)			<.001
Male	123,829 (45.0)	955 (37.6)	
Female	151,194 (55.0)	1584 (62.4)	
Nonbinary	4 (0.0)	0 (0.0)	
Race, n (%)			.058
White	200,305 (72.9)	1862 (73.3)	
Black/African American	21,242 (7.7)	183 (7.2)	
Asian	4099 (1.5)	23 (0.9)	
Native Hawaiian/Pacific Islander	651 (0.2)	6 (0.2)	
American Indian/Alaska Native	1090 (0.4)	18 (0.7)	
Unknown/Not reported	47,454 (17.3)	447 (17.6)	
Other race	32 (0.0)	0 (0.0)	
Race combinations with low frequency	1 (0.0)	0 (0.0)	
Ethnicity, n (%)			.795
Non-Hispanic	216,932 (96.2)	1994 (96.3)	
Hispanic	8632 (3.8)	77 (3.7)	
Age, mean ± SD	65.4 ± 11.4	67.6 ± 11.8	<.001
Height, mean ± SD	66.2 ± 4.2	65.7 ± 4.3	<.001
Weight, mean ± SD	188.7 ± 46.0	192.4 ± 51.1	<.001
BMI, mean ± SD	30.2 ± 6.3	31.2 ± 7.3	<.001
BMI categories			<.001
BMI <18.5	2429 (0.9)	33 (1.3)	
18.5-24.9	52,023 (19.1)	459 (18.3)	
25-29.9	91,011 (33.3)	704 (28.0)	
30-39.9	108,163 (39.6)	1016 (40.4)	
>40	19,458 (7.1)	300 (11.9)	
Preoperative laboratory values			
eGFR levels, n (%)			.001
Normal	93,162 (36.2)	786 (32.8)	
Mild-to-moderate	162,008 (63.0)	1584 (66.1)	
Severe	2121 (0.8)	26 (1.1)	
Sodium levels, n (%)			<.001
Low	12,214 (4.8)	190 (7.9)	
Normal	242,366 (95.1)	2198 (91.8)	
High	352 (0.1)	6 (0.3)	
BUN, mean ± SD	17.9 ± 7.3	18.3 ± 7.7	.008
Serum creatinine, mean ± SD	0.9 ± 0.4	0.9 ± 0.4	.360
BUN/Cr Level, n (%)			.017
<20	125,362 (52.7)	1143 (51.7)	
20-25	62,776 (26.4)	552 (25.0)	
25+	49,952 (21.0)	517 (23.3)	
BUN/Cr > 10, n (%)	112,728 (47.3)	1069 (48.3)	.353
Hypoalbuminemia, n (%)	7580 (5.3)	138 (9.5)	<.001
Total bilirubin, mean ± SD	0.6 ± 0.4	0.6 ± 0.4	.366
SGOT, mean ± SD	24.0 ± 15.8	25.3 ± 16.6	.005
Alkaline phosphatase levels, n (%)			<.001
<44	3670 (2.8)	15 (1.1)	
44-147	123,068 (94.6)	1256 (94.6)	
148+	3377 (2.6)	57 (4.3)	
WBC level, n (%)			<.001
Low/Normal	253,832 (97.3)	2334 (95.9)	
High	6929 (2.7)	100 (4.1)	
Anemia severity, n (%)			<.001
Nonanemia	225,007 (85.8)	1954 (79.8)	
Mild Anemia	28,657 (10.9)	353 (14.4)	
Moderate-to-severe anemia	8595 (3.3)	141 (5.8)	
Low platelet, n (%)	7855 (3.0)	100 (4.1)	.001
PTT, mean ± SD	29.4 ± 5.0	29.7 ± 5.0	.075
INR, mean ± SD	1.0 ± 0.3	1.0 ± 0.2	.166
PT, mean ± SD	11.9 ± 2.5	11.6 ± 2.2	.711
Past medical history			
Diabetes, n (%)			<.001
Not diabetic	241,555 (87.8)	2180 (85.9)	
Insulin dependent	8063 (2.9)	107 (4.2)	
Noninsulin dependent	25,116 (9.1)	252 (9.9)	
Oral medication	373 (0.1)	0 (0.0)	
Smoking status, n (%)			<.001
Nonsmoker	240,774 (87.5)	2115 (83.3)	
Smoker	34,333 (12.5)	424 (16.7)	
Dyspnea, n (%)			<.001
None	262,265 (95.3)	2347 (92.4)	
At rest	546 (0.2)	9 (0.4)	
Moderate exertion	12,296 (4.5)	183 (7.2)	

(continued on next page)

Table 1 (continued)

Variable	All patients	Periprosthetic fracture	P
History of severe COPD, n (%)	10,897 (4.0)	187 (7.4)	<.001
Ascites, n (%)	73 (0.0)	0 (0.0)	1.000
CHF (in 30 d before surgery), n (%)	1108 (0.4)	16 (0.6)	.080
Hypertension requiring medication, n (%)	152,514 (55.4)	1590 (62.6)	<.001
Renal failure, n (%)	186 (0.1)	3 (0.1)	.247
Currently on dialysis (preoperative), n (%)	697 (0.3)	10 (0.4)	.160
Disseminated cancer, n (%)	1170 (0.4)	16 (0.6)	.122
Steroid use for chronic condition, n (%)	10,225 (3.7)	168 (6.6)	<.001
>10% loss body weight in last 6 mo, n (%)	683 (0.2)	9 (0.4)	.309
Bleeding disorders, n (%)	6221 (2.3)	84 (3.3)	<.001
Transfusion >4 units PRBCs in 72 h before surgery, n (%)	481 (0.2)	12 (0.5)	.002
Preoperative systemic sepsis, n (%)			.743
None	273,344 (99.4)	2523 (99.4)	
SIRS	1526 (0.6)	16 (0.6)	
Sepsis	95 (0.0)	0 (0.0)	
Septic shock	10 (0.0)	0 (0.0)	
Operative details			
Location, n (%)			.001
Outpatient	18,000 (6.5)	126 (5.0)	
Inpatient	257,107 (93.5)	2413 (95.0)	
Anesthesia, n (%)			.001
Epidural	1656 (0.6)	12 (0.5)	
General	130,519 (47.4)	1318 (51.9)	
Local	65 (0.0)	1 (0.0)	
None	40 (0.0)	0 (0.0)	
Other	147 (0.1)	1 (0.0)	
Regional	5186 (1.9)	32 (1.3)	
Spinal	99,084 (36.0)	828 (32.6)	
MAC/IV sedation	38,360 (13.9)	347 (13.7)	
Unknown	35 (0.0)	0 (0.0)	
ASA class, n (%)			<.001
0 = None assigned	24 (0.0)	0 (0.0)	
1 = No disturb	9859 (3.6)	41 (1.6)	
2 = Mild disturb	142,500 (51.8)	992(39.1)	
3 = Severe disturb	116,506 (42.4)	1409 (55.5)	
4 = Life threat	5925 (2.2)	96 (3.8)	
Operative time, mean \pm SD	91.9 \pm 39.1	99.4 \pm 49.5	<.001

ASA, American Society of Anesthesiologists; BMI, body mass index; BUN, blood urea nitrogen; Cr, creatinine; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; PRBC, packed red blood cell; SGOT, serum glutamic oxaloacetic transaminase; WBC, white blood cells.

Bold values indicate $P < .05$.

no significant differences in the distribution of races and ethnicities within the periprosthetic fracture and non-periprosthetic fracture groups (all $P > .05$). Average age (all patients: 65.4 ± 11.4 years, periprosthetic fracture patients: 67.6 ± 11.8 years, $P < .001$), weight (all patients: 188.7 ± 46.0 pounds, periprosthetic fracture patients: 192.4 ± 51.1 , $P < .001$), and BMI (all patients: 30.2 ± 6.3 , periprosthetic fracture patients: 31.2 ± 7.3 , $P < .001$) were greater in the periprosthetic fracture cohort. There was also a greater proportion of periprosthetic fracture patients who were categorized in obesity classes I and II, with a BMI from 30 to 39.9 (all patients: 39.6%, periprosthetic fracture patients: 40.4%) as well as in obesity class III, with a BMI >40 (all patients: 7.1%, periprosthetic fracture patients: 11.9%) ($P < .001$) (Table 1).

Regarding preoperative laboratory values, the periprosthetic fracture group had a greater proportion of mild-to-moderate (all patients: 63.0% mild-to-moderate, periprosthetic fracture patients: 66.1% mild-to-moderate) as well as severe range eGFR values (all patients: 0.8% severe, periprosthetic fracture patients: 1.1% severe, $P = .001$). Similarly, periprosthetic fracture patients were more likely to be hyponatremic (all patients: 4.8% low sodium, periprosthetic fracture patients: 7.9% low sodium, $P < .001$) and severely dehydrated (all patients: 21.0% BUN/Cr 25+, periprosthetic fracture patients: 23.3% BUN/Cr 25+, $P = .017$). Similarly, periprosthetic fracture patients were more likely to have hypoalbuminemia (all patients: 5.3% low albumin, periprosthetic fracture patients: 9.5% low albumin, $P < .001$). Average BUN (all patients: 17.9 ± 7.3 BUN, periprosthetic fracture patients: 18.3 ± 7.7

BUN, $P = .008$) and SGOT (all patients: 24.0 ± 15.8 SGOT, periprosthetic fracture patients: 25.3 ± 16.6 SGOT, $P = .005$) were greater amongst the periprosthetic fracture cohort. A larger proportion of periprosthetic fracture patients had alkaline phosphatase levels over 148 (all patients: 2.6%, periprosthetic fracture patients: 4.3%, $P < .001$) as well as moderate-to-severe anemia (all patients: 3.3% anemic, periprosthetic fracture patients: 5.8% anemic, $P < .001$) and low platelet levels (all patients: 3.0% thrombocytopenic, periprosthetic fracture patients: 4.1% thrombocytopenic, $P = .001$) (Table 1).

In the analysis of subject past medical history, it was found that a larger number of periprosthetic fracture patients were diabetic (all patients: 12.2% diabetic, periprosthetic fracture patients: 14.1% diabetic, $P < .001$) and current smokers (all patients: 12.5% smokers, periprosthetic fracture patients: 16.7% smokers, $P < .001$). Periprosthetic fracture patients also had a greater proportion of moderate exertion dyspnea patients as well as patients with a history of severe COPD, with hypertension requiring medication, with steroid use for a chronic condition, with bleeding disorders or with a transfusion of >4 units packed red blood cells received within the 72 hours before surgery (all $P < .05$). Periprosthetic fracture patients were also more likely to have a frailty score of ≥ 2 (all patients: 13.7% frail, periprosthetic fracture patients: 18.8% frail, $P < .001$) (Table 1).

Regarding THA operative details, a larger number of periprosthetic fracture patients required an inpatient procedure (all patients: 93.5% inpatient, periprosthetic fracture patients: 95.0%

inpatient, $P = .001$) as well as general anesthesia (all patients: 47.4% general anesthesia, periprosthetic fracture patients: 51.9% general anesthesia, $P = .001$). Patients from the periprosthetic fracture group were more likely to be declared an ASA class of 3 (all patients: 42.4% ASA 3, periprosthetic fracture patients: 55.5% ASA 3) or an ASA class of 4 (all patients: 2.2%, periprosthetic fracture patients: 3.8%) ($P < .001$). Finally, mean operative time, in minutes, was significantly longer for periprosthetic fracture subjects (all patients: 91.9 ± 39.1 minutes, periprosthetic fracture patients: 99.4 ± 49.5 minutes, $P < .001$) (Table 1).

Postoperative outcomes & complications

Mean length of hospital stay (all patients: 2.4 ± 3.1 days, periprosthetic fracture patients: 3.3 ± 4.2 days, $P < .001$) was longer for periprosthetic fracture patients. A significantly smaller number of periprosthetic fracture patients were able to be discharged to home after the procedure (all patients: 83.3% home, periprosthetic fracture patients: 70.4% home, $P < .001$). There were more superficial wound infections, deep incision surgical site infection, pulmonary embolism complications, acute renal failure complications, urinary tract infection complications, myocardial infarction complications, bleeding transfusion complications, deep vein thrombosis /thrombophlebitis complications, and sepsis and septic shock complications in the periprosthetic fracture group (all $P < .05$). There was also an increased ventilator requirement in the periprosthetic fracture group >48 hours after surgery (all patients: 0.1% on ventilators, periprosthetic fracture patients: 0.2% on ventilators, $P = .006$). Periprosthetic fracture patients were significantly more likely to require reoperation/readmission (all patients: 3.8%, periprosthetic fracture patients: 97.4%, $P < .001$). There was also a

higher occurrence of *Clostridioides difficile* (*C. diff*) infection in the periprosthetic fracture group (all patients: 0.1% with *C. diff*, periprosthetic fracture patients: 0.8% with *C. diff*, $P < .001$) (Table 2).

Bivariate and multivariate regression models

In the first bivariate logistic regression model, mild-to-moderate eGFR (odds ratio [OR]: 1.160, 95% confidence interval [CI]: 1.065-1.265, $P = .001$), low sodium (OR: 1.727, 95% CI: 1.487-2.005, $P < .001$), higher preoperative BUN (OR: 1.007, 95% CI: 1.002-1.012, $P = .005$), hypoalbuminemia (OR: 1.894, 95% CI: 1.587-2.260, $P < .001$), higher preoperative SGOT (OR: 1.003, 95% CI: 1.001-1.005, $P = .003$), an alkaline phosphatase of greater than 148 (OR: 1.665, 95% CI: 1.274-2.176, $P < .001$), higher white blood cell count (OR: 1.578, 95% CI: 1.290-1.930, $P < .001$), mild anemia (OR: 1.424, 95% CI: 1.270-1.596, $P < .001$), moderate-to-severe anemia (OR: 1.904, 95% CI: 1.603, 2.262, $P < .001$), and low platelet level (OR: 1.385, 95% CI: 1.132-1.694, $P = .002$) were all individually associated with a greater risk for periprosthetic hip fracture. Contrarily, an alkaline phosphatase level of less than 44 (OR: 0.398, 95% CI: 0.239-0.663, $P < .001$) was associated with a lesser risk of fracture (Table 3).

In a multivariate logistic regression model examining the correlation between BMI categories and risk of periprosthetic fracture, being underweight (OR: 1.547, 95% CI: 1.084-2.208, $P = .016$) and being obese ($P < .001$) were associated with greater fracture risk. Patients in the overweight BMI >40 category were at an increased risk for periprosthetic fracture (OR: 1.759, 95% CI: 1.519, 2.037, $P < .001$) (Table 4).

In another multivariate logistic regression built to identify risk factors for periprosthetic hip fractures, demographic variables such as older age (OR: 1.008, 95% CI: 1.002-1.014, $P = .006$) and obesity

Table 2
Additional complications.

Outcomes	All patients (n = 275,107)	Periprosthetic fracture (n = 2539)	P
Length of stay, mean \pm SD	2.4 \pm 3.1	3.3 \pm 4.2	<.001
Discharge destination, n (%)			<.001
Skilled care, not home	26,796 (10.0)	434 (17.1)	
Unskilled facility not home	368 (0.1)	12 (0.5)	
Facility which was home	941 (0.4)	17 (0.7)	
Home	222,185 (83.3)	1785 (70.4)	
Separate acute care	778 (0.3)	22 (0.9)	
Rehab	15,315 (5.7)	261 (10.3)	
Expired	199 (0.1)	1 (0.0)	
Against medical advice	58 (0.0)	1 (0.0)	
Hospice	47 (0.0)	0 (0.0)	
Unknown	61 (0.0)	1 (0.0)	
Multilevel senior community	32 (0.0)	0 (0.0)	
Superficial wound infections, n (%)	1931 (0.7)	98 (3.9)	<.001
Deep incisional SSI complications, n (%)	583 (0.2)	147 (5.8)	<.001
Organ/Space SSI complications, n (%)	846 (0.3)	405 (16.0)	<.001
Unplanned intubation complications, n (%)	430 (0.2)	7 (0.3)	.125
Pulmonary embolism complications, n (%)	719 (0.3)	18 (0.7)	<.001
On ventilator >48 h complications, n (%)	172 (0.1)	6 (0.2)	.006
Progressive renal insufficiency complications, n (%)	256 (0.1)	3 (0.1)	.514
Acute renal failure complications, n (%)	141 (0.1)	8 (0.3)	<.001
Urinary tract infection complications, n (%)	2522 (0.9)	73 (2.9)	<.001
Stroke/CVA complications, n (%)	278 (0.1)	2 (0.1)	1.000
Coma >24 h complications, n (%)	2 (0.0)	0 (0.0)	1.000
Peripheral nerve injury complications, n (%)	24 (0.0)	0 (0.0)	1.000
Cardiac arrest requiring CPR complications, n (%)	243 (0.1)	4 (0.2)	.293
Myocardial infarction complications, n (%)	663 (0.2)	16 (0.6)	.001
Bleeding transfusions complications, n (%)	16,828 (6.1)	317 (12.5)	<.001
DVT/Thrombophlebitis complications, n (%)	1019 (0.4)	31 (1.2)	<.001
Sepsis complications, n (%)	706 (0.3)	131 (5.2)	<.001
Septic shock complications, n (%)	173 (0.1)	17 (0.7)	<.001
Reop/Read, n (%)	10,536 (3.8)	2474 (97.4)	<.001
<i>Clostridioides difficile</i> occurrences, n (%)	240 (0.1)	19 (0.8)	<.001

DVT, deep vein thrombosis; SSI, surgical site infection.
Bold values indicate $P < .05$.

Table 3
Laboratory values and periprosthetic fractures.

Laboratory values	OR	95% CI	P
eGFR (ref = normal)			
Mild-to-moderate eGFR	1.160	(1.065, 1.265)	.001
Severe eGFR	1.459	(0.984, 2.161)	.060
Sodium (ref = normal)			
Low sodium	1.727	(1.487, 2.005)	<.001
High sodium	1.895	(0.844, 4.251)	.121
Preoperative BUN	1.007	(1.002, 1.012)	.005
Preoperative serum creatinine	1.038	(0.958, 1.125)	.360
BUN/Cr (ref = less than 20)			
BUN/Cr 20-25	0.964	(0.871, 1.068)	.483
BUN/Cr 25+	1.137	(1.024, 1.262)	.016
Hypoalbuminemia (ref = normal)	1.894	(1.587, 2.260)	<.001
Preoperative total bilirubin	0.935	(0.808, 1.081)	.364
Preoperative SGOT	1.003	(1.001, 1.005)	.003
Alkaline phosphatase (ref = 44-147)			
Less than 44	0.398	(0.239, 0.663)	<.001
Greater than 148	1.665	(1.274, 2.176)	<.001
WBC level	1.578	(1.290, 1.930)	<.001
Anemia (ref = normal)			
Mild anemia	1.424	(1.270, 1.596)	<.001
Moderate-to-severe anemia	1.904	(1.603, 2.262)	<.001
Low platelet level (ref = normal)	1.385	(1.132, 1.694)	.002
Preoperative PTT	1.010	(0.999, 1.022)	.074
Preoperative INR	1.109	(0.957, 1.285)	.169
Preoperative PT	0.939	(0.674, 1.307)	.708

BUN, blood urea nitrogen; CI, confidence interval; Cr, creatinine; eGFR, estimated glomerular filtration rate; OR, odds ratio; SGOT, serum glutamic oxaloacetic transaminase; WBC, white blood cells.

Bold values indicate $P < .05$.

class III or BMI >40 (OR: 1.576, 95% CI: 1.315-1.890, $P < .001$) were found to be associated with greater risk of fracture. With regards to preoperative laboratory values, mild-to-moderate eGFR (OR: 1.168, 95% CI: 1.029-1.324, $P = .016$) and low sodium (OR: 1.570, 95% CI: 1.284-1.922, $P < .001$) were also associated with periprosthetic fracture. Moreover, being a current smoker (OR: 1.536, 95% CI: 1.320-1.787, $P < .001$) was correlated with increased fracture risk. Finally, with regards to operative details, longer operative time (OR: 1.003, 95% CI: 1.002-1.004, $P < .001$) and longer length of hospital stay (OR: 1.015, 95% CI: 1.008-1.023, $P < .001$) were associated with periprosthetic fracture following THA. Contrarily, discharge home (OR: 0.598, 95% CI: 0.525-0.681, $P < .001$) was associated with decreased fracture risk (Table 5).

Then, in the final multivariate logistic regression model, organ/space surgical site infection, urinary tract infection, and bleeding transfusion complications were all significantly associated with periprosthetic fracture (all $P < .05$) (Table 6).

Discussion

With the emphasis on value-based healthcare models, it is important for surgeons to adequately optimize patients prior to surgery to reduce hospital readmissions and costs, facilitate early functional rehabilitation, and decrease LOS [22]. Preoperative recognition and management of modifiable risk factors for THA periprosthetic fractures are important components of

Table 4
BMI and periprosthetic fracture.

BMI	OR	95% CI	P
<18.5	1.547	(1.084, 2.208)	.016
25-29.9	0.876	(0.778, 0.986)	.028
30-39.9	1.065	(0.954, 1.190)	.263
>40	1.759	(1.519, 2.037)	<.001

BMI, body mass index; CI, confidence interval; OR, odds ratio.

Bold values indicate $P < .05$.

Table 5
Risk factors for periprosthetic fracture.

Risk factor assessed	OR	95% CI	P
Female	1.003	(0.891, 1.129)	.962
Asian	0.607	(0.324, 1.137)	.119
Age	1.008	(1.002, 1.014)	.006
BMI 25-29.9	0.881	(0.776, 1.001)	.052
BMI >40	1.576	(1.315, 1.890)	<.001
Mild-to-moderate eGFR	1.168	(1.029, 1.324)	.016
Low sodium	1.570	(1.284, 1.922)	<.001
Preoperative creatinine	0.906	(0.791, 1.036)	.149
Hypoalbuminemia	1.250	(1.021, 1.532)	.031
Alkaline phosphatase >148	1.274	(0.962, 1.689)	.092
WBC level	1.153	(0.881, 1.508)	.300
Mild anemia	1.069	(0.909, 1.259)	.420
Moderate-to-severe anemia	1.144	(0.895, 1.463)	.282
Non-insulin-dependent diabetes	0.841	(0.673, 1.052)	.129
Smoking status	1.536	(1.320, 1.787)	<.001
Hypertension requiring medication	1.026	(0.901, 1.169)	.697
Steroid use for chronic condition	1.320	(1.056, 1.651)	.015
Bleeding disorders	1.112	(0.838, 1.477)	.462
Transfusion >4 units PRBCs in 72 h before surgery	1.091	(0.501, 2.374)	.827
Frailty ≥ 2	1.154	(0.958, 1.391)	.131
Mild disturb ASA	0.907	(0.696, 1.182)	.470
Severe disturb ASA	1.111	(0.861, 1.433)	.417
Operative time	1.003	(1.002, 1.004)	<.001
Length of total hospital stay	1.015	(1.008, 1.023)	<.001
Discharge, home	0.598	(0.525, 0.681)	<.001

ASA, American Society of Anesthesiologists; BMI, body mass index; CI, confidence interval; eGFR, estimated glomerular filtration rate; OR, odds ratio; PRBC, packed red blood cell; WBC, white blood cell.

Bold values indicate $P < .05$.

interdisciplinary surgical planning and physician-patient communication on expected outcomes [23-25]. While the surgical techniques and implants have advanced to decrease periprosthetic fracture rates in susceptible elderly patients, there is still a component of preoperative laboratory values, medical history, and perioperative care that needs to be further explored and standardized. Elderly, osteoporotic patients undergoing arthroplasty are susceptible to periprosthetic fracture complications due to relative medical frailty, and they are prone to underlying disabilities and fatigue limiting their ability to return to functional independence [26]. This study found older age, hypoalbuminemia, hyponatremia, abnormal eGFR, smoking, chronic steroid use, and longer inpatient hospital stay to be independent risk factors for post-operative periprosthetic fracture propagation within 30 days. Risk stratification and medical clearance are essential components of surgical planning and optimization surgeons can take to prevent periprosthetic fracture rates and reduce overall healthcare costs.

Among baseline demographics, patients with 30-day post-operative periprosthetic fractures were more likely to be females, older age, higher ASA classification, obese, smokers, and have a history of hypertension, diabetes, bleeding disorders, and COPD. Similar to prior studies, older age, higher ASA classification, dyspnea, and COPD predict overall medical frailty which may contribute to underlying risk for fragility fractures and falls [27,28]. Smokers, diabetics, and patients with COPD have previously been shown to have increased prosthesis-related complications and high revision rates, which may stem from poor circulatory function and bone-implant integration leading to increased fracture risk [29]. While a low BMI, especially <18.5 is likely to predict muscle weakness and overall nutritional deficiency, obesity may also contribute to increased risk for periprosthetic fractures through prosthesis failure and overall fall risk [30,31]. Previous studies have suggested the interaction of microtrauma due to the impact of excessive body weight on the surgical site, increased distribution of load on the joint, and replacement of muscle mass by fat may

Table 6
Risk of postoperative complications with periprosthetic fracture.

Complication	OR	95% CI	P
Organ/Space SSI	115.318	(99.988, 132.998)	<.001
Urinary tract infection	3.058	(2.381, 3.929)	<.001
Bleeding transfusions	2.074	(1.828, 2.353)	<.001

CI, confidence interval; OR, odds ratio; SSI, surgical site infection white blood cell. Bold values indicate $P < .05$.

heighten risk of implant failure leading to periprosthetic fractures [32]. It may be prudent for surgeons to consider a preoperative nutrition evaluation for both underweight and overweight patients who may benefit from further medical workup and delay of surgery to prevent complications.

Hypoalbuminemia has been regularly used in the orthopedic trauma literature to reflect malnutrition and fragility [33]. Serum albumin levels <3.5 are considered to represent inadequate nutritional status, and have been shown to be associated with chronic inflammation, delayed bone healing, decreased strength, and impaired collagen synthesis [34,35]. The decreased strength and muscle weakness combined with slow osseous integration of implants likely contribute to increased risk of periprosthetic fractures and falls due to poor lower chain mobility and inability to comply with activity restrictions [36]. Malnourished patients required prolonged hospitalization stay and higher rates of discharge to acute rehabilitation possibly due to dependent gait assistance and increased safety precaution. Implementation of a postoperative protein-based diet after hip fracture surgery have previously been associated with lower complication rates, and surgeons should consider nutrition consultation, vitamin supplementation, and emphasis on a high-protein diet to decrease periprosthetic fracture risk, improve muscular strength, and reduce overall medical complications [37].

Hyponatremia is one of the most common electrolyte abnormalities measured in clinic, and prior studies have corroborated the relationship between hyponatremia and risk of fractures, especially in the geriatric population [38–42]. Recent studies have suggested hyponatremia to be associated with loss of osmolytes and neurotransmitters involved with gait function and neuromuscular coordination, thus leading to gait disturbances and risk of falls and fractures [43,44]. While low sodium levels may compromise nerve-muscle conduction and balance, chronic mild hyponatremia has also been shown to decrease overall hip bone mineral density scores [45]. Low extracellular sodium directly stimulates bone resorptive activity and causes subsequent bone demineralization in the hip, which may further slow femoral stem osseous integration after THA and increase the risk of acute periprosthetic fractures [46]. Although hyponatremia is associated with bone loss and gait disturbances, low serum sodium is a modifiable risk factor that when corrected can reverse the demineralization and gait disorders leading to postoperative complications [47]. It is important for healthcare providers to recognize perioperative hyponatremia as a risk factor for periprosthetic fractures as preoperative serum sodium levels are reproducible, affordable, and readily obtainable measurements in the clinic [47]. Preoperative medical optimization of hyponatremia, whether due to endocrine, medication side effects, or dietary imbalances, should be corrected prior to elective THA even in asymptomatic elderly individuals to improve outcomes, decrease LOS, and reduce healthcare costs.

Further preoperative modifiable laboratory values, such as eGFR, have been previously investigated and validated as a marker for severity of chronic kidney disease, which is a risk factor for periprosthetic fractures [48]. In our study, abnormal preoperative eGFR predicted higher rate of fracture risk requiring further surgical

intervention and longer hospital stay. Renal complications lead to poor bone mineralization and high rates of fracture risk due to abnormal bone remodeling potential and underlying osteoporosis [49]. Other modifiable risk factors, such as active smoking and chronic steroid use, were also independent risk factors for sustaining periprosthetic fractures due to underlying bone metabolic changes [50]. Cigarette smoking is known to increase the risk of hip fractures by impairing the absorption of calcium and reducing overall bone mass through increase in osteoclast proliferation [51]. Smoking cessation programs are useful resources surgeons should incorporate when discussing modifiable habits that can be addressed to avoid complications. Furthermore, a growing percentage of patients with joint disease also present with chronic steroid use, and our study suggests these patients have increased risk of sustaining acute periprosthetic fractures. While adjusting steroid intake for chronic inflammatory conditions may be limited, surgeons may consider modifying weight bearing status, implant type, cementation, and surgical technique in patients with chronic steroid use to prevent periprosthetic fractures [52].

In addition to the modifiable preoperative risk stratification of patients who may be susceptible to periprosthetic fractures, it is important for surgeons to identify perioperative factors, such as LOS and operative time, as variables that may increase risk of complications. In our multivariate logistic regression, LOS and increased operative time were significantly associated with periprosthetic fractures. Overall increased time under anesthesia not only predicts increased surgical complexity, but also has been shown to increase thromboembolic events, blood loss, pulmonary complications, and transfusion requirements [53]. Elderly patients requiring increased inpatient stay are at risk for hospital acquired delirium and cognitive impairment, further increasing the risk of gait imbalance and low velocity falls leading to fracture risk. Patients with multiple comorbidities are at increased risk of periprosthetic fractures, and it is important that an interdisciplinary team of rehabilitation physicians, social workers, and therapists are working together to ensure proper gait training, safety assessment, and discharge planning in high fall-risk and cognitively impaired postoperative patients [54].

Not only are readmissions and reoperation rates for THA periprosthetic fractures costly and increase morbidity, but this study found readmitted fracture patients are subsequently at increased risk for sustaining surgical site infections, bleeding requiring transfusion requirements, and urinary tract infections. Periprosthetic fractures cause increased periosteal bleeding and soft tissue disruption which may lead to hemorrhage and deep hematoma formation [55]. The deep hematoma and underlying bleeding may cause acute blood loss anemia requiring postoperative transfusions, which are known to increase overall morbidity, outcomes, and infections in THA [56]. Stasis of the hematoma in combination with allogenic transfusions may lead to infections of the hip and further site infections if not addressed immediately and carefully monitored. Furthermore, perioperative immobilization post fracture fixation combined with increased hospital stay may lead to higher risks of contracting urinary tract infection's, which have been further increase hospital costs and patient morbidity [57].

Despite the large number of patients included, there are limitations to consider when utilizing the NSQIP database, including selection bias. While we were able to analyze all primary THA using Current Procedural Terminology codes, there was unfortunately no ability to assess anterior vs posterior approach, conventional vs navigation assisted techniques, Dorr classification, and type of implants, such as cemented vs press-fit stems. While previous studies have correlated femoral morphology and type of taper stems to increased periprosthetic fracture risks, the NSQIP database only reports patient related characteristics, which was the focus of

this study [58,59]. While the data comprised a heterogeneous population nationwide at different ambulatory settings, the wide variety of in-patient hospitals and surgeon expertise and experience may confound outcomes. Although various institutions may implement different preoperative optimization pathways for THA, the inclusion of patients from both academic and private practice settings in rural and urban centers alike reflect the generalizability of our results. Furthermore, it is possible that we were not able to record all cases of postoperative periprosthetic fractures as the database is limited to short 30-day complication rates.

Conclusions

Patients with hypoalbuminemia, hyponatremia, and abnormal eGFR are at increased risk for sustaining periprosthetic fractures after THA. Preoperative optimization with close monitoring of metabolic markers and modifiable risk factors may help not only prevent acute periprosthetic fractures but also associated infection and bleeding risk with fracture readmission. An interdisciplinary team of primary care physicians, nutritionists, and social workers may help identify which patients may benefit from further medical workup, smoking cessation programs, and delay of surgery to prevent complications.

Conflicts of interest

The authors declare there are no conflicts of interest.

For full disclosure statements refer to <https://doi.org/10.1016/j.artd.2022.101093>.

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