Anemia at Presentation Predicts Acute Mortality and Need for Readmission Following Geriatric Hip Fracture

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Background: There is a paucity of research regarding the relationship between anemia and postoperative morbidity and mortality among geriatric patients presenting with hip fracture. The objective of this study was to determine the effect of anemia at presentation on 30-day morbidity and mortality among geriatric patients with hip fracture.

Methods: The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database was queried for all hip fracture patients ≥60 years old from 2011 to 2016. Included were all emergency unilateral, non-pathological hip fractures (femoral neck, intertrochanteric, or subtrochanteric) treated with arthroplasty, intramedullary nailing, or open reduction and internal fixation. Anemia was classified as a hematocrit (HCT) level of <0.41 and <0.36 for male and female patients, respectively. Age, body mass index (BMI), race, comorbidities, smoking status, American Society of Anesthesiologists (ASA) class, baseline functional status, time to surgery, operative time, anesthesia type, need for transfusion, fixation method, length of stay (LOS), and discharge destination were collected. Our primary outcome of interest was 30-day postoperative mortality, with all-cause readmission and any postoperative ischemic events (cerebrovascular accident [CVA] and myocardial infarction [MI]) analyzed as secondary outcomes. A multivariable regression analysis was performed and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated while controlling for confounding variables.

Results: Of 34,805 patients identified, 22,469 (65%) were anemic at presentation (63% female; mean age, 80 ± 8 years), while 12,336 (35%) were non-anemic (85% female; mean age, 79 ± 8 years). Anemia at presentation was independently associated with higher odds of mortality (OR,1.3 [95% CI, 1.1 to 1.5]) and readmission (OR, 1.2 [95% CI, 1.1 to 1.3]), while no relationship was observed for MI (OR, 1.1 [95% CI, 0.9 to 1.4]) or CVA (OR, 0.8 [95% CI, 0.6 to 1.1]).

Conclusions: Our findings suggest that anemia at presentation is associated with greater 30-day postoperative morbidity and mortality in geriatric hip fracture patients. Additional research should focus on elucidating this modifiable risk factor and advancing the preoperative optimization of hip fracture patients.

Level of Evidence: Prognostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

The rate of hip fracture is greater among geriatric patients than among younger patients, and older hip fracture patients often have more comorbidities[1]. The rate of mortality following hip fracture can be up to 5% in-hospital[2], 7% within 30 days[3], and as high as 24% within 1 year[3]. The preoperative optimization of modifiable risk factors has been

the focus of considerable research in an attempt to lower morbidity and mortality following hip fracture in geriatric patients[2,4-6].

Anemia is commonly encountered in geriatric hip fracture patients, with an estimated 40% of patients presenting with a hemoglobin level of <120 g/L or a hematocrit (HCT) level of <0.36 to <0.41[7]. Anemia at presentation can be due to hip fracture-associated blood loss or secondary to chronic comorbid conditions. The management of anemic patients may include preoperative fluid resuscitation, the administration of blood products or erythropoietin, and/or the minimization of further intraoperative losses. The evidence surrounding the effects of anemia at presentation on hip fracture outcomes is limited, but some studies have suggested a correlation with mortality, most notable among elderly and frail patients[8-12]. Our current understanding of the relationship between anemia at presentation in geriatric patients with hip fracture and postoperative morbidity and mortality is based largely on studies with relatively small sample sizes[7,8,12-18]. Furthermore, the variation in reporting standards and diagnostic criteria for anemia makes comparisons between studies difficult. A relationship between anemia and higher mortality rate among elective arthroplasty patients has also been reported[19].

The primary objective of the current study was to determine whether the mortality rate within 30 days was higher for geriatric patients who presented with anemia, using data from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).

Materials and Methods

Data Source

Data regarding >270 perioperative variables, from >700 hospitals, are recorded in the ACS-NSQIP database[19]. Data regarding these variables are collected from the time of admission to 30 days postoperatively. Data are extracted from patient charts by trained Surgical Clinical Reviewers and coded according to Current Procedural Terminology (CPT) codes[19,20]. The database is routinely audited by the ACS to ensure adherence to data-entry guidelines and accuracy[20]. The reliability of the ACS-NSQIP database and the reproducibility of its data have been widely reported in both orthopaedic and other surgical research[20-25].

Study Population

Inclusion criteria were geriatric patients (defined in this study as ≥60 years of age[5,16,18]) who presented with an emergency traumatic unilateral hip fracture (femoral neck, intertrochanteric, or subtrochanteric, as defined by CPT codes) and who underwent operative management with arthroplasty, intramedullary (IM) nailing, or open reduction and internal fixation (ORIF). Bilateral, periprosthetic, infectious, pathological, and open hip fractures were excluded. The ACS-NSQIP database was queried from 2011 to 2016, inclusive, using CPT codes 27236, 27244, and 27245 (Appendix A).

Data Acquisition

Patient demographics, comorbidities, and peri- and postoperative variables were gathered for each patient encounter. Demographic data included age, sex, race, body mass index (BMI), and baseline functional status (independent, partially dependent, or totally dependent)[19]. Comorbidities included congestive heart failure (CHF), hypertension, chronic obstructive pulmonary disease (COPD), diabetes, kidney disease requiring dialysis, and active smoking. American Society of Anesthesiologists (ASA) classification was also assessed. Peri- and postoperative variables included hip fracture fixation method, type of anesthesia used, the need for packed red blood-cell (pRBC) transfusion, discharge destination (skilled nursing facility/rehabilitation center or home), hospital length of stay (LOS, in days), and operative duration (in minutes). The primary independent variable of interest was preoperative HCT level (hemoglobin is not recorded by the ACS-NSQIP), which was used as a surrogate to identify anemic patients (HCT level of <0.41 and <0.36 for male and female patients, respectively)[19].

Provider factors collected included the time from hospital admission to the index surgery, classified as 0 to 23 hours ("day 0"), 24 to 47 hours ("day 1"), 48 to 71 hours ("day 2"), and ≥72 hours ("day 3 or greater"). Similarly, the time from preoperative HCT bloodwork to the index surgery was recorded.

The primary outcome of interest was 30-day mortality. Secondary outcomes included all-cause hospital readmission, myocardial infarction (MI), and cerebrovascular accident (CVA).

Research ethics board approval was obtained prior to study commencement.

Data Analysis

Descriptive statistics are presented as the mean and standard deviation or as the frequency and percentage, as appropriate. Missing values for age and sex were imputed using multiple imputation[26]. Patients who were missing the HCT value or missing the time from blood draw for HCT assessment to the index surgery were excluded. HCT was primarily analyzed as a categorical variable (anemic versus non-anemic). The analysis of HCT as a continuous variable is included in Appendix B, as such analysis may be of less clinical utility in terms of risk stratification compared with categorical analysis. In clinical settings, simple classification of patients as anemic or non-anemic may allow for earlier intervention.

All outcomes are expressed as proportions. Unadjusted associations between variables and outcomes were assessed using Mann-Whitney U, Pearson chi-square, and Fisher exact tests, as appropriate. Multivariable logistic-regression models were used to assess the influence of anemia on acute morbidity and mortality, while adjusting for age, race, sex, BMI, functional status, diabetes, smoking status, hypertension, COPD, CHF, kidney disease requiring dialysis, ASA class, the need for pRBC transfusion, fixation method, anesthesia type, time to surgery, and operative duration. These variables were selected because of their clinical relevance and known prognostic value[2,4,5,9,12,13,16,17]. Interaction terms between HCT and all covariates were examined. Model calibration was assessed using Pearson goodness-of-fit statistics. The predictive accuracy of the regression models was determined by plotting receiver operating characteristic (ROC) curves and calculating the

Harrell concordance statistic (C-statistic, equivalent to the area under the ROC curve: ≤0.5 = poor, ≥0.6 = moderate, ≥0.7 = good, and ≥0.8 = strong discriminative ability)[27]. The Youden J statistic (which maximizes sensitivity and specificity) was used to determine optimal cutoff points, i.e., the HCT threshold below which morbidity and mortality increased[28]. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated for each outcome. The Bonferroni multiple-comparisons correction was used to minimize the possibility of a type-1 error; therefore, significance was defined as $p \leq 0.0125$. All statistics were calculated using SAS software (version 9.4; SAS Institute).

Results

A total of 35,617 geriatric patients with a hip fracture were identified from 2011 to 2016. Of those patients, 254 were excluded because of an open, infected, or pathological hip fracture, 167 were excluded because they underwent non-emergency hip fracture fixation, 149 were excluded because of missing HCT values, and 242 were excluded because the time from HCT bloodwork to the index surgery was missing. This resulted in a study sample of 34,805 patients (98%). The time from presentation to the index surgery was available for all patients.

Patient demographics are presented in Table I. The non-anemic patients (n = 12,336, 35%) had a mean age of 79 ± 8 years and BMI of 25 ± 7 kg/m², and 85% were female, while the patients with anemia (n = 22,469, 65%) had a mean age of 80 ± 8 years and BMI of 24 ± 6 kg/m², and 63% were female. The most common comorbidities were hypertension (64%), diabetes (15%), active smoking (14%), bleeding disorder (14%), COPD (11%), CHF (2%), and kidney disease requiring dialysis (0.7%) in the non-anemic group, and in the anemic group, hypertension (71%), diabetes (23%), bleeding disorder (20%),

TABLE I Patient Demographics*			
	Total (N = 34,805)	Normal HCT (N = 12,336 [35.4%])	Low HCT (N = 22,469 [64.6%])
Age† (yr)	79.2 ± 7.8	78.6 ± 7.9	79.5 ± 7.7
Sex (no. [%])			
Male	10,294 (29.6)	1,878 (15.2)	8,416 (37.5)
Female	24,511 (70.4)	10,458 (84.8)	14,053 (62.5)
BMI† (kg/m²)	24.5 ± 6.4	24.9 ± 6.6	24.4 ± 6.3
Race (no. [%])			
White	25,958 (74.6)	9,375 (76.0)	16,583 (73.8)
Black	988 (2.8)	211 (1.7)	777 (3.5)
Asian	951 (2.7)	229 (1.9)	722 (3.2)
Hispanic	1,613 (4.6)	422 (3.4)	1,191 (5.3)
Other	5,295 (15.2)	2,099 (17.0)	3,196 (14.2)
Diabetes (no. [%])	6,990 (20.1)	1,877 (15.2)	5,113 (22.8)
Active smoker (no. [%])	4,338 (12.5)	1,685 (13.7)	2,653 (11.8)
COPD (no. [%])	4,443 (12.8)	1,399 (11.3)	3,044 (13.6)
CHF (no. [%])	1,150 (3.3)	263 (2.1)	887 (4.0)
Hypertension (no. [%])	23,821 (68.4)	7,900 (64.0)	15,921 (70.9)
Bleeding disorder (no. [%])	6,119 (17.6)	1,674 (13.6)	4,445 (19.8)
Kidney disease requiring dialysis (no. [%])	762 (2.2)	84 (0.7)	678 (3.0)
ASA class (no. [%])			
1	230 (0.7)	129 (1.1)	101 (0.5)
2	6,670 (19.2)	3,213 (26.1)	3,457 (15.4)
3	22,106 (63.5)	7,598 (61.6)	14,508 (64.6)
4	5,799 (16.7)	1,396 (11.3)	4,403 (19.6)
Functional status (no. [%])			
Independent	28,224 (81.1)	10,315 (83.6)	17,909 (79.7)
Partially dependent	5,593 (16.1)	1,740 (14.1)	3,853 (17.2)
Totally dependent	988 (2.8)	281 (2.3)	707 (3.2)

*HCT = hematocrit, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, and ASA = American Society of Anesthesiologists. †The values are given as the mean and standard deviation.

TABLE II Perioperative Variables*		
	Normal HCT (N = 12,336 [35.4%])	Low HCT (N = 22,469 [64.6%])
Time to surgery (no. [%])		
Day 0	3,923 (31.8)	4,399 (19.6)
Day 1	6,580 (53.3)	11,973 (53.3)
Day 2	1,410 (11.4)	4,086 (18.2)
Day ≥3	423 (3.4)	2,011 (9.0)
No. of days from HCT to index surgery†	0.5 ± 0.6	0.3 ± 0.6
Operative duration† (min)	64.9 ± 40.2	66.3 ± 42.3
Fixation method (no. [%])		
IM nail	4,853 (39.3)	11,211 (49.9)
Arthroplasty	5,562 (45.1)	7,333 (32.6)
ORIF	1,921 (15.6)	3,925 (17.5)
Anesthesia type (no. [%])		
Neuraxial	2,933 (23.8)	4,668 (20.8)
General	8,786 (71.2)	16,814 (74.8)
Other	617 (5.0)	987 (4.4)
Transfusion (no. [%])	1,639 (13.3)	8,711 (38.8)
LOS† (days)	5.7 ± 4.9	6.8 ± 6.5
Discharge destination (no. [%])		
Home	2,871 (23.3)	4,061 (18.1)
Skilled nursing facility/rehab.	9,013 (73.1)	17,306 (77.0)
Other	452 (3.7)	1,102 (4.9)

*HCT = hematocrit, IM = intramedullary, ORIF = open reduction and internal fixation, and LOS = length of stay. †The values are given as the mean and standard deviation.

COPD (14%), active smoking (12%), CHF (4%), and kidney disease requiring dialysis (3%).

Perioperative variables are summarized in Table II. The patients with anemia were more likely to undergo delayed surgery. These patients were also more likely to undergo IM nailing, while the non-anemic patients were more likely to undergo arthroplasty. ORIF was the least common operative technique in both groups. In both groups, the majority of patients received a general anesthetic. More anemic patients received pRBC transfusion (39% versus 13%). The group with anemia had an average LOS of 7 ± 7 days, compared with 6 ± 5 days for the non-anemic group, and the percentage of patients who were discharged to a skilled nursing facility/rehabilitation center rather than to home was greater for the anemic group.

Unadjusted rates of 30-day postoperative complications are summarized in Table III. The 30-day mortality rate was 5% in the anemic group and 2.5% in the non-anemic group (p < 0.001). The rate of all-cause readmission in the anemic

TABLE III Unadjusted Rates of 30-Day Postoperative Complications: Comparison of Non-Anemic and Anemic Groups*				
Complication	No. (%) of Total Cohort (N = 34,805)	No. (%) with Normal HCT (N = 12,336)	No. (%) with Low HCT (N = 22,469)	P Value†
Death	1,432 (4.1)	313 (2.5)	1,119 (5.0)	**<0.001**
Readmission	2,989 (8.6)	829 (6.7)	2,160 (9.6)	**<0.001**
MI	570 (1.6)	139 (1.1)	431 (1.9)	**<0.001**
CVA	246 (0.7)	83 (0.7)	163 (0.7)	0.6

*HCT = hematocrit, MI = myocardial infarction, and CVA = cerebrovascular accident. The values are given as the number, with the percentage in parentheses. The percentages in the Complication column are of the total cohort (n = 34,805). †Bold indicates a significant difference between the Normal HCT and Low HCT groups.

TABLE IV Multivariable Analysis for Mortality*			
Variable	Odds Ratio	95% CI	P Value†
Normal HCT	Ref.	Ref.	—
Low HCT	1.30	1.12-1.49	**0.004**
Age	1.04	1.03-1.05	**<0.001**
Female sex	0.58	0.52-0.65	**<0.001**
BMI	0.97	0.96-0.98	**<0.001**
Race			
White	Ref.	Ref.	—
Black	0.66	0.46-0.94	**0.005**
Asian	0.66	0.44-0.98	0.047
Hispanic	0.67	0.50-0.90	**<0.001**
Other	0.74	0.62-0.88	**0.005**
Diabetes	0.95	0.83-1.10	0.5
Active smoker	0.98	0.82-1.19	0.9
COPD	1.61	1.40-1.85	**<0.001**
CHF	1.68	1.37-2.05	**<0.001**
Hypertension	0.94	0.83-1.07	0.3
Kidney disease requiring dialysis	1.89	1.47-2.44	**<0.001**
ASA class			
1	Ref.	Ref.	—
2	1.33	0.18-9.68	0.2
3	3.81	0.53-27.34	0.1
4	8.34	1.16-59.97	**<0.001**
Functional Status			
Independent	Ref.	Ref.	—
Partially dependent	2.41	2.14-2.72	0.02
Totally dependent	4.14	3.36-5.10	**<0.001**
Time to surgery			
Day 0	Ref.	Ref.	—
Day 1	0.89	0.77-1.03	0.06
Day 2	1.09	0.92-1.30	0.5
Day ≥3	1.26	1.03-1.55	**0.001**
Operative duration	1.00	0.99-1.01	0.1
Fixation method			
IM nail	Ref.	Ref.	—
Arthroplasty	0.99	0.87-1.12	0.7
ORIF	1.02	0.87-1.19	0.8
Anesthesia type			
General	Ref.	Ref.	—
Neuraxial	0.87	0.75-1.01	0.1
Other	0.99	0.77-1.28	0.6
Discharge home	0.69	0.59-0.81	**<0.001**
Transfusion	1.10	0.97-1.24	0.1

*C = 0.812, Pearson goodness of fit = 1.00; C = C-statistic quantifying goodness of fit based on area under the receiver operating characteristic curve. HCT = hematocrit, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, ASA = American Society of Anesthesiologists, IM = intramedullary, and ORIF = open reduction and internal fixation. †Bold indicates a significant value.

group was 9.6% compared with 6.7% in the non-anemic group (p < 0.001). The rate of MI was 1.9% among the anemic patients and was 1.1% among the non-anemic patients (p < 0.001). Similar rates of CVA were observed between the groups (0.7% in each group; p = 0.6).

After multivariable logistic regression, anemia was associated with higher odds of 30-day mortality (OR, 1.3 [95% CI, 1.1 to 1.5]; p = 0.004; C = 0.8) and all-cause readmission (OR, 1.2 [95% CI, 1.1 to 1.3]; p = 0.005; C = 0.6) (Tables IV and Tables V). Transfusion status was not predictive of mortality or CVA (both p = 0.1), but it was a risk factor for MI (OR, 1.9 [95% CI, 1.6 to 2.3]; p < 0.001) and readmission (OR, 1.2 [95% CI, 1.1 to 1.3]; p = 0.001). No association was observed between anemia and MI or CVA (p = 0.3 and p = 0.2, respectively) (Tables VI and Tables VII).

Discussion

The findings of our study suggest that geriatric hip fracture patients who are anemic at presentation have greater odds of acute mortality and readmission. The 30-day mortality rate for all patients with hip fracture was 4.1%, with anemic patients overall having double the mortality rate of non-anemic patients (5% versus 2.5%; adjusted OR, 1.3). Anemia at presentation was also associated with higher odds of all-cause readmission (OR, 1.2). This is in keeping with previous studies[8,12,18,29-33]. Of note, these relationships persisted despite controlling for transfusion status.

To our knowledge, our study involves the largest cohort to date among studies evaluating geriatric patients presenting with anemia and hip fracture[8,12,16,18,29-34]. In the largest previous study (n = 8,787), the authors reported preoperative anemia for 38% of the patients and a mortality rate of 4.6%, with uncontrolled 30-day mortality risk ratios ranging from 1.7 to 2.5 as the severity of anemia increased[29]. However, that study is based on data that are >30 years old, did not examine outcomes other than mortality, and, according to the authors, was underpowered[29]. Reported rates of anemia on presentation in geriatric patients with hip fracture have varied, partly because of inconsistent definitions of anemia, with most studies reporting a rate of 30% to 75%[8,12,15,16,31-34].

Anemia-associated morbidity and mortality can stem from sequelae of anemia, such as hypoperfusion, increased cardiac demand, and transfusion-associated complications, but may also be due to the underlying chronic comorbid conditions causing the anemia itself[12,31,35-39]. The OR for 30-day mortality following preoperative blood transfusion has been reported to be as high as 2.4 for hip fracture patients[22]. Transfusion rates among anemic patients have ranged from 28%[12] to 43%[15,31]. In our study, 65% of the patients were anemic on admission, 39% of whom received a transfusion. Although our rate of anemia was on the upper end of that in previously reported studies, our transfusion and mortality rates are in keeping with those of other studies, perhaps supporting what has been suggested previously: that the HCT level has a similar reliability to hemoglobin in detecting clinically relevant anemia[8,12,30-33,40].

Some authors have suggested that risk factors for anemia are more prognostic of postoperative morbidity/mortality than

TABLE V Multivariable Analysis for Readmission*			
Variable	Odds Ratio	95% CI	P Value†
Normal HCT	Ref.	Ref.	—
Low HCT	1.18	1.08-1.30	**0.005**
Age	1.01	1.00-1.02	**<0.001**
Female sex	0.81	0.75-0.88	**<0.001**
BMI	1.00	0.99-1.01	0.8
Race			
White	Ref.	Ref.	—
Black	1.10	0.90-1.36	0.1
Asian	0.87	0.68-1.12	0.9
Hispanic	1.01	0.85-1.20	0.1
Other	0.55	0.48-0.63	**<0.001**
Diabetes	1.11	1.01-1.22	0.03
Active smoker	1.16	1.03-1.31	0.01
COPD	1.48	1.33-1.64	**<0.001**
CHF	1.32	1.12-1.57	**0.001**
Hypertension	1.16	1.06-1.27	**0.001**
Kidney disease requiring dialysis	1.54	1.26-1.89	**<0.001**
ASA Class			
1	Ref.	Ref.	—
2	1.23	0.58-2.65	0.4
3	1.82	0.85-3.89	0.08
4	2.40	1.12-5.16	**<0.001**
Functional status			
Independent	Ref.	Ref.	—
Partially dependent	1.23	1.12-1.36	**0.008**
Totally dependent	1.46	1.20-1.78	**0.007**
Time to surgery			
Day 0	Ref.	Ref.	—
Day 1	1.06	0.96-1.17	0.5
Day 2	1.11	0.98-1.25	0.6
Day ≥3	1.17	1.00-1.37	0.1
Operative duration	1.001	1.000-1.002	0.07
Fixation method			
IM nail	Ref.	Ref.	—
Arthroplasty	1.15	1.05-1.25	**0.002**
ORIF	1.00	0.90-1.12	0.2
Anesthesia type			
General	Ref.	Ref.	—
Neuraxial	0.95	0.86-1.05	0.5
Other	0.99	0.82-1.19	0.9
Discharge home	0.98	0.90-1.07	0.7
Transfusion	1.16	1.06-1.26	**0.001**

*C = 0.639, Pearson goodness of fit = 0.5649; C = C-statistic quantifying goodness of fit based on area under the receiver operating characteristic curve. HCT = hematocrit, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, ASA = American Society of Anesthesiologists, IM = intramedullary, and ORIF = open reduction and internal fixation. †Bold indicates a significant value.

TABLE VI Multivariable Analysis for Myocardial Infarction*			
Variable	Odds Ratio	95% CI	P Value†
Normal HCT	Ref.	Ref.	—
Low HCT	1.11	0.90-1.38	0.3
Age	1.03	1.02-1.05	**<0.001**
Female sex	0.73	0.61-0.88	**<0.001**
BMI	1.00	0.98-1.01	0.4
Race			
White	Ref.	Ref.	—
Black	0.80	0.47-1.36	0.6
Asian	0.83	0.47-1.45	0.7
Hispanic	0.65	0.40-1.05	0.1
Other	1.35	1.07-1.71	**0.001**
Diabetes	1.43	1.17-1.74	**<0.001**
Active smoker	1.30	1.00-1.70	0.05
COPD	1.14	0.90-1.44	0.3
CHF	1.49	1.07-2.09	0.02
Hypertension	1.43	1.15-1.77	**0.001**
Kidney disease requiring dialysis	1.66	1.11-2.48	**0.01**
ASA class			
1	Ref.	Ref.	—
2	0.88	0.12-6.49	0.1
3	1.59	0.22-11.50	0.5
4	2.19	0.30-15.94	0.06
Functional status			
Independent	Ref.	Ref.	—
Partially dependent	1.14	0.92-1.41	0.4
Totally dependent	0.99	0.60-1.63	0.8
Time to surgery			
Day 0	Ref.	Ref.	—
Day 1	1.00	0.81-1.24	0.06
Day 2	0.79	0.59-1.04	0.2
Day ≥3	0.77	0.54-1.00	0.3
Operative duration	1.002	1.001-1.003	0.11
Fixation method			
IM nail	Ref.	Ref.	—
Arthroplasty	1.03	0.85-1.25	0.3
ORIF	0.85	0.66-1.08	0.1
Anesthesia type			
General	Ref.	Ref.	—
Neuraxial	0.98	0.79-1.22	0.9
Other	1.00	0.67-1.50	0.95
Discharge home	2.62	2.17-3.16	**<0.001**
Transfusion	1.93	1.61-2.32	**<0.001**

*C = 0.720, Pearson goodness of fit = 0.1387; C = C-statistic quantifying goodness of fit based on area under the receiver operating characteristic curve. HCT = hematocrit, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, ASA = American Society of Anesthesiologists, IM = intramedullary, and ORIF = open reduction and internal fixation. †Bold indicates a significant value.

the anemia itself[31,35]. Common risk factors for anemia include male sex, an age of >80 years, the number of comorbidities, and higher ASA class[2,4,5,9,12,13,16,17,31,33]. The authors of a meta-analysis published in 2015[11] reported an overall relative risk of 1.6 for mortality within 1 year of surgery in anemic hip fracture patients; however, after controlling for confounding variables, this association persisted in only 3 of 8 studies[7,8,30]. Likewise, Vochteloo et al.[31] reported no relationship between anemia and mortality after controlling for transfusion status. Conversely, several other studies have reported greater short-term and long-term mortality among patients who were anemic at presentation after controlling for confounding variables[7,8,18,29,30,32,40], which is consistent with our findings.

The importance of urgent surgical management of hip fracture and efficient preoperative optimization has been the focus of considerable research[2-5]. The recent HIP ATTACK (Hip Fracture Accelerated Surgical Treatment and Care Track)[6] trial found that surgery within 6 hours of diagnosis resulted in lower rates of postoperative delirium and urinary tract infections, faster time to mobilization, and shorter LOS compared with the standard of care (<24 hours); however, there were no overall differences in major postoperative complication or mortality rates. In patients with elevated troponins, however, accelerated surgery was associated with a considerable reduction in mortality[6]. Although there may be minimal benefit of emergency versus urgent hip fracture fixation, time to surgery has been reported to be one of the most influential modifiable risk factors for postoperative complications[4]. Time to surgery is strongly associated with patients' preoperative comorbidities, stability, and overall general health[4]. In our study, anemic patients were more likely to undergo delayed surgery, which was associated with a 30-day mortality OR of 1.3 when surgery was performed on day 3 or greater.

Despite considerable evidence supporting the association between anemia at admission and postoperative morbidity and mortality, a systematic review by Rocos et al.[37] found no published prospective studies comparing the utilization of blood products versus fluid resuscitation in preoperative optimization of hip fracture patients. Fluid resuscitation with 1 L of normal saline solution over 8 hours was demonstrated to reduce the hemoglobin level by 7, 11, and 22 g/L for intracapsular, intertrochanteric, and subtrochanteric hip fractures, respectively[14]. Anemia on presentation, combined with the dilutional effect of resuscitation and estimated operative blood loss of 500 to 1,500 mL[34], has led some authors to suggest a repeat complete blood-cell count immediately preoperatively for all hip fracture patients with a hemoglobin level of <120 g/L on admission[14]. In our study, patients had a mean interval of 0.4 day from HCT bloodwork to index surgery (0.3 and 0.5 day for anemic and non-anemic HCT patients, respectively). Additionally, the value of serum lactate has been suggested as a measure of occult hypoperfusion given its strong prognostic utility for 30-day mortality (OR of 5 when >3 mmol/L)[38].

The use of tranexamic acid (TXA) has gained increasing popularity recently in both elective and traumatic orthopaedic procedures[41-47]. There is compelling evidence suggesting that

TABLE VII Multivariable Analysis for Cerebrovascular Accident*			
	Odds Ratio	95% CI	P Value†
Normal HCT	Ref.	Ref.	—
Low HCT	0.81	0.60-1.09	0.2
Age	1.01	0.99-1.02	0.6
Female sex	0.86	0.65-1.15	0.2
BMI	0.99	0.97-1.01	0.2
Race			
White	Ref.	Ref.	—
Black	0.83	0.39-1.79	0.6
Asian	1.35	0.69-2.67	0.3
Hispanic	0.89	0.48-1.66	0.98
Other	0.91	0.69-1.47	0.7
Diabetes	1.18	0.87-1.60	0.3
Active smoker	1.22	0.82-1.84	0.3
COPD	0.62	0.40-0.95	0.03
CHF	1.68	1.00-2.81	0.049
Hypertension	1.30	0.96-1.77	**0.01**
Kidney disease requiring dialysis	1.30	0.65-2.59	0.5
ASA Class 3 or 4	1.56	1.02-2.39	0.04
Functional status			
Independent	Ref.	Ref.	—
Partially dependent	1.46	1.08-1.99	0.03
Totally dependent	1.36	0.69-2.69	0.7
Time to surgery			
Day 0	Ref.	Ref.	—
Day 1	0.92	0.67-1.27	0.2
Day 2	1.15	0.77-1.71	0.5
Day ≥3	1.15	0.69-1.90	0.6
Operative duration	1.002	1.000-1.005	0.04
Fixation method			
IM nail	Ref.	Ref.	—
Arthroplasty	0.93	0.70-1.23	0.9
ORIF	0.82	0.63-1.20	0.4
Anesthesia type			
General	Ref.	Ref.	—
Neuraxial	0.89	0.63-1.24	0.3
Other	1.18	0.67-2.09	0.4
Discharge home	3.12	2.34-4.16	**<0.001**
Transfusion	1.26	0.95-1.58	0.1

*C = 0.673, Pearson goodness of fit = 0.0661; C = C-statistic quantifying goodness of fit based on area under the receiver operating characteristic curve. HCT = hematocrit, BMI = body mass index, COPD = chronic obstructive pulmonary disease, CHF = congestive heart failure, ASA = American Society of Anesthesiologists, IM = intramedullary, and ORIF = open reduction and internal fixation. †Bold indicates a significant value.

the intraoperative administration of TXA reduces transfusion rates and bleeding complications in arthroplasty patients[44,45]. The benefit of TXA appears to also apply to hip fracture patients[41,42,46,47]; however, additional research is required to fully elucidate this with respect to preoperative anemia and is outside the scope of this study.

This study had several limitations. As >700 hospitals contribute to the ACS-NSQIP database, we were unable to comment on data integrity; however, routine standardized audits of the database have consistently shown excellent reliability and accuracy, especially for orthopaedic procedures[20-25,48]. Because the ACS-NSQIP collects data for only 30 days following surgery, we did not have access to longer-term morbidity and mortality data. We were therefore only able to analyze acute postoperative complications. Furthermore, the retrospective nature of our study limited our analysis to pre-existing ACS-NSQIP variables collected. Despite hemoglobin level being a more common marker of anemia, it is not collected by the ACS-NSQIP, and we had to rely on HCT as a surrogate marker of anemia, which has been commonly done[49-52]. The difference in reliability between hemoglobin and HCT in quantifying anemia is, however, minimal[53]. Furthermore, HCT level may also be less susceptible to the dilutional effect of fluid resuscitation[54,55]. Similarly, we were unable to gather data to calculate a comorbidity index such as the Charlson Comorbidity Index; however, recent data suggest that ASA class (as used in our study) may better predict 1-year mortality following hip fracture[56]. Additionally, we were unable to differentiate primary blood-loss-associated anemia from anemia secondary to chronic underlying conditions. As such, preexisting anemia due to chronic comorbid conditions may be a confounder. Time from admission to the index surgery and time from HCT bloodwork to the index surgery are inputted as calendar days rather than hours in the ACS-NSQIP database, which, given recent evidence supporting rapid fixation of hip fractures[4], limits the degree to which these variables could be analyzed as we could only categorize in gross time frames. Because of registry limitations, we were also unable to comment on preoperative anticoagulant use, the value of HCT used to trigger transfusions, how MI and CVA were diagnosed and treated, resuscitation protocols used, and use of TXA and postoperative venous thromboprophylaxis. Likewise, we did not have access to radiographs and were therefore unable to comment on fracture pattern and quality of reduction/fixation postoperatively.

To the best of our knowledge, this study involves the largest cohort for examining the effects of preoperative anemia on morbidity and mortality among geriatric patients with hip fracture. Our analysis of 34,805 patients suggests that anemia at presentation is independently associated with higher rates of acute postoperative mortality and readmission. Additional research should focus on elucidating this modifiable risk factor and advancing the preoperative optimization of hip fracture patients.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/A208). ∎

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