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The hidden blood loss in proximal femur fractures is sizeable and significant

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ABSTRACT

Background: Patients sustaining hip fractures experience blood loss as a direct result the fracture independent of surgery. The objective of this study was to quantify the expected non-surgical blood loss for proximal femur fractures using hemoglobin values.

Methods: A retrospective chart review of patients at a level 1 trauma center sustaining proximal femur fractures between October 2015 and January 2018 was performed. Patients were ≥30 years of age, had sustained intertrochanteric, subtrochanteric, or femoral neck fractures and had hemoglobin values documented at admission and after 12 h but before surgery. Patients with concomitant fractures, other hemorrhagic injuries, or blood transfusions before their second hemoglobin result were excluded. A multivariate linear regression model was constructed to evaluate the predictive ability of age, sex, BMI, number of comorbidities, fracture type, anticoagulation/antiplatelet therapy, admission hemoglobin, timing of surgical intervention and changes in electrolyte levels on subsequent hemoglobin values. Hemoglobin changes were compared between intertrochanteric, subtrochanteric, and femoral neck fractures and anticoagulant therapy types with Welch's tests.

Results: 119 patients were included. The mean age was 80.9 ± 10.81 years. Nearly 53% of subjects were using anticoagulation therapy. The mean drop in hemoglobin was 1.4 ± 1.03 g/dL. The multivariate linear regression model had statistically significant predictive ability ($R = 0.91$, $p < 0.001$). Independent predictors of hemoglobin decrease were number of comorbid conditions ($p = 0.02$), admission hemoglobin reading ($p < 0.001$), fracture type ($p = 0.02$), and time from admission to surgery ($p = 0.03$). Intertrochanteric fractures demonstrated the largest hemoglobin drops. Anticoagulation therapy had no effect on subsequent hemoglobin.

Conclusion: Proximal femur fractures cause a significant amount of blood loss prior to surgical intervention. Patients at particular risk include those with comorbidities, intertrochanteric fractures, low admission hemoglobin values, and increased time to surgery. The identification of demographic, fracture type, and treatment characteristics may help surgeons identify patients at the greatest risk for blood loss, and provide more effective perioperative care.

1. Introduction

Hip fractures are a common orthopedic injury typically treated with surgery. Although patients presenting with hip fractures may display relatively benign-appearing deformities, hemorrhagic internal lesions are present, causing often unappreciated blood loss. Hemoglobin levels can give clinicians an approximation of a patient's intravascular red blood cell content. Although several factors can affect the hemoglobin lab value, it is still widely used as a surrogate measure of blood loss.[1–4] Drops in hemoglobin are expected after hip fracture surgery, and post-operative drops of up to four points have been documented in the literature.[5–8] However, the portion of blood loss that is attributable to fracture bleeding only remains ill-defined.

Anecdotal experience has revealed a substantial drop in Hemoglobin without surgery, subsequently termed hidden blood loss.[9–11] This phenomenon has been explored as it relates to other orthopedic procedures such as total joint arthroplasty,[3,12,13] but is less well developed for hip fractures. A previous study from the United Kingdom sought to quantify blood loss attributable to the

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fracture only, but did not include patients on blood thinners, effectively eliminating a large portion of patients with proximal femur fractures.[14] Another study analyzed blood loss in patients with proximal femur fractures whose surgery was delayed greater than 48 h. However, the study's primary focus was on hemoglobin values after surgery, which precluded the ability to quantify blood loss not attributable to surgery.[11] Liu et al. conducted a similar study but evaluated only patients with intertrochanteric fractures.[15]

A well-designed retrospective study to quantify the expected blood loss prior to surgery may help surgeons more adequately plan for surgery, and likewise, attain more accurate feedback on intraoperative blood loss. The primary objective of this study was to identify risk factors predictive of higher blood loss. Secondary objectives were to quantify the expected bloos loss for various proximal femur fractures, independent of surgery (hidden blood loss).

2. Methods

A sample size calculation was performed a priori. In order to achieve 80% power with an effect size (f^2) of 0.15 and alpha of 0.05, a sample of 108 subjects would be required. Following review and approval by our Institutional Review Board, we performed a retrospective chart review of patients sustaining proximal femur fractures who were treated at a single level I trauma center between October 2015 and January 2018. The electronic medical record was queried for qualifying patient charts using ICD 10 codes corresponding to femoral neck fractures (S72.00), intertrochanteric fractures (S72.10), and subtrochanteric fractures (S72.2). These included OTA fracture classification types 31A1.2-3, 31A2.2-3, and 31A3.1-3, 31B1.1-3, 31B2.1-3, and 31B3.[16]

Patients were eligible for inclusion if they were at least 30 years of age, sustained a proximal femur fracture, and had hemoglobin values documented both upon admission and at least 12 h after admission but prior to surgery. Patients with concomitant long bone fractures, hemorrhagic injuries, or blood transfusions prior to their second Hgb value were excluded. Charts were manually reviewed for demographic data, patient health status, lab values, and timing of surgery.

A multivariate linear regression model was constructed to evaluate the predictive ability of age, sex, BMI, number of comorbidities (chronic kidney disease, diabetes mellitus, congestive heart failure, anemia), fracture type (intertrochanteric, subtrochanteric, femoral neck), anticoagulation/antiplatelet therapy, admission hemoglobin value, and change in electrolyte levels (sodium, potassium, chlorine), and time from admission to surgery on the subsequent hemoglobin value. Changes in electrolyte levels were used as surrogate measures of dehydration and taken at the same time as each hemoglobin measure if available.

Additionally, changes in hemoglobin were compared between fracture types post-hoc comparisons in hemoglobin changes were performed between fracture types (femoral neck, intertrochanteric, and subtrochanteric) and between anticoagulation therapies with Welch's tests. Anticoagulation therapies were classified into antiplatelets, Vitamin K antagonists, factor Xa inhibitors, direct thrombin inhibitors, and low molecular weight heparins (LMWH), or none.

3. Results

119 patients (32 males, 87 females) were eligible for inclusion in the study. The mean age was 80.9 ± 10.81 years (range 49–104 years). The mean BMI was 25.0 ± 6.37 (range 10–51). Seventy-six patients (63.9%) sustained femoral neck fractures, 36 (30.3%) had intertrochanteric fractures, and 7 (5.9%) had subtrochanteric fractures. Over half of subjects (63 of 120) were using anticoagulation or antiplatelet therapy prior to admission. All demographics are displayed in Table 1.

Table 1
Demographics among included patients.

Factor	Value	Percentage/Range
Age	80.9 ± 10.8	49–104
Sex	32	26.9%
Male	87	73.1%
Female		
BMI	25.0 ± 6.4	10–51
Fracture Type	76	63.9%
Femoral Neck	36	30.3%
Intertrochanteric	7	5.9%
Subtrochanteric		
Comorbidities	10	8.4%
Anemia		
CHF	19	16.0%
CKD	22	18.5%
DM	24	20.2%
Anticoagulation Use	56	47.1%
None	32	26.9%
Antiplatelet	13	10.9%
Factor Xa Inhibitors	11	9.2%
Vitamin K Antagonists	4	3.4%
Direct Thrombin Inhibitors	3	2.5%
LMWH		
Electrolyte levels	−0.1 ± 3.01	N/A
Sodium	136 ± 6.0	117–171
#1	136 ± 5.1	125–168
#2	0.11 ± 0.518	N/A
Potassium	4.1 ± 0.63	2.4–5.9
#1	4.0 ± 0.45	3.0–5.2
#2	−1.9 ± 3.72	N/A
Chloride	101 ± 6.0	84–135
#1	103 ± 5.2	89–137
#2		

The average number of comorbidities per patient was 0.6 ± 0.91 (range 0–4, Table 1). Most patients ultimately underwent surgical intervention, with only 14 patients managed nonoperatively. Collectively, patients experienced a mean drop in hemoglobin of 1.4 ± 1.03 g/dL (range −1.3-5.2 g/dL). Five patients experienced a non-transfusion-related increase in hemoglobin. Patients requiring operative intervention experienced an additional mean Hgb drop of 1.6 g/dL for a mean post-operative Hgb level of 9.6 g/dL (Table 2). Twenty-five patients (21.0%) required a blood transfusion, all of whom were operatively managed (Table 2).[1]

The multivariate linear regression model appeared to have statistically significant predictive ability overall with an $R = 0.91$ and $p < 0.001$. Individual variables that had statistically significant predictive ability on subsequent hemoglobin values were number of comorbid conditions ($p = 0.02$), admission hemoglobin reading ($p < 0.001$), fracture type ($p = 0.02$), and time from admission to surgery ($p = 0.03$). Age, sex, BMI, number of comorbidities, changes in electrolyte levels, and anticoagulation did not appear to be predictive of subsequent hemoglobin values (Table 3).

A post-hoc test of hemoglobin decrease by fracture type revealed decreases of 1.6 ± 0.25 g/dL, 1.76 ± 1.14 g/dL, and 1.1 ± 0.96 g/dL for subtrochanteric, intertrochanteric, and femoral neck fractures respectively. Heterogeneity of variances secondary to unequal sample sizes between fracture types required utilization of a Welch's test in place of a one-way ANOVA test. The difference in hemoglobin drop was statistically significant ($F[2,38.4] = 5.9$, $p = 0.006$). A post-hoc Tukey test revealed that the mean

[1] Our institution uses hemoglobin values < 8 g/dL as a general indication for transfusion, though exceptions are granted as appropriate based on clinical judgement.

Table 2
Patient outcomes.

	Mean	Range
Nonoperatively treated		
Hgb #1 (g/dL)	11.9 ± 2.10	7.5–15.2
Hgb #2 (g/dL)	11.0 ± 1.79	7.0–13.4
Surgically treated		
Hgb #1 (g/dL)	12.6 ± 1.75	9.0–17.3
Hgb #2 (g/dL)	11.2 ± 1.91	6.7 ± 1.91
Hgb Post Op (g/dL)	9.6 ± 1.71	5.7–13.1
EBL (mL)	141 ± 120.5	5–650
Surgery Time (hrs)	1.5 ± 0.67	0.3–3.5
Admit to Surgery (hrs)	29.7 ± 17.47	13–138
Transfusion	25 (23.8%)	N/A
Postop Hgb (g/dL)[a]	7.9 ± 1.24	5.5–11.0

EBL: estimated blood loss.
[a] Mean postoperative hemoglobin for transfused patients only.

Table 3
Results of multivariate linear regression model.

Variables in Model	B	Significance
Constant	0.065	0.95
Age	0.001	0.95
Sex	0.28	0.24
BMI	0.01	0.57
Comorbidities	0.28	0.02[a]
Fracture Type	−0.41	0.02[a]
Anticoagulation	−0.024	0.75
Admission Hemoglobin	0.90	<0.001[a]
Time (Admit to OR)	−0.013	0.03
Change in sodium	−0.018	0.70
Change in potassium	−0.28	0.19
Change in Chloride	0.06	0.09
Overall model	R = 0.91	<0.001[a]

[a] Indicates statistical significance.

hemoglobin drop was statistically significant only between intertrochanteric fractures and femoral neck fractures ($p = 0.006$), where intertrochanteric fractures had a larger drop in hemoglobin than femoral neck fractures from admission (mean difference 0.6 g/dL, 95% CI [0.13–1.08]) (Table 4).

A Welch's test was also performed to evaluate changes in Hgb between patients utilizing anticoagulation/antiplatelet therapies and patients that did not. There was no statistically significant difference in mean Hgb drops between patients taking Vitamin K antagonists, factor Xa inhibitors, direct thrombin inhibitors, LMWH, antiplatelet therapies, and patients not taking any anticoagulation or antiplatelet therapies ($F[5,14.2] = 0.6$, $p = 0.73$). Mean Hgb drops for each group are shown in Table 5.

Table 5
Difference in hemoglobin readings between anticoagulation therapies.

	N (%)	Mean ± SD
Therapy Type		
None	56 (47.1)	1.5 ± 1.01
Antiplatelet	32 (26.9)	1.2 ± 0.90
Factor Xa Inhibitors	13 (10.9)	1.3 ± 1.04
Vitamin K Antagonists	11 (9.2)	1.4 ± 1.58
Direct Thrombin Inhibitors	4 (3.4)	1.5 ± 0.26
LMWH	3 (2.5)	1.7 ± 1.07
Overall Comparison	F(5,14.2) = 0.6	p = 0.73

4. Discussion

Although blood loss following hip fracture surgery is expected, the hidden blood loss resulting from the fracture can be substantial and often goes unrecognized. This retrospective analysis indicates that non-surgical drops in hemoglobin are occurring in patients sustaining proximal femur fractures. Furthermore, there are patient characteristics associated with greater drops in hemoglobin. Recognition of these characteristics in patients may help clinicians more effectively manage blood loss in the perioperative period.

The present results indicate that patients sustaining intertrochanteric fractures experienced the greatest drops in hemoglobin (1.74 g/dL ± 1.13), followed by subtrochanteric (1.59 g/dL ± 0.25), and then femoral neck fractures (1.1 g/dL ± 0.96). These values are similar to those obtained by Smith et al., who reported on 118 patients sustaining proximal femur fractures with a delay to surgery greater than 48 h. Though Smith et al. did not differentiate between intertrochanteric and subtrochanteric fractures or include anemic patients, they found an average Hgb drop of 2.02 for intracapsular fractures and 1.5 for extracapsular fractures.[11] Similarly, Kumar et al. reviewed 127 patients with proximal femur fractures and reported preoperative drops in Hgb of 1.1 g/dL for intertrochanteric, 2.2 g/dL for subtrochanteric, and 0.7 g/dL for femoral neck fractures.[14] The present study expands upon the results of these studies, as both excluded patients with preexisting anemia or anticoagulation treatments.

It is interesting to note that admission hemoglobin levels are a risk factor for hidden blood loss. This may be partially attributed to our inclusion of patients with preexisting anemia, as those patients are likely to have lower admission hemoglobin levels, potentially indicating medical frailty and subsequently decreased physical

Table 4
Relevant comparisons by fracture type. Both demographic characteristics and outcomes were compared.

Fracture Type N (%)	Age	Sex	BMI	Blood Thinners	Anemia	CHF	CKD	DM
Femoral Neck 76 (63.9%)	81 ± 10.6	55 F (72.4)	24 ± 5.3	42 (55.3)	6 (7.9)	9 (11.8)	15 (19.7)	13 (17.1)
Intertrochanteric 36 (30.3%)	80 ± 11.3	25 F (69.4)	26 ± 7.5	17 (47.2)	4 (11.1)	8 (22.2)	7 (19.4)	8 (22.2)
Subtrochanteric 7 (5.9%)	83 ± 11.0	7 (100)	27 ± 9.6	4 (57.1)	0 (0)	2 (28.6)	0 (0)	3 (42.9)
p-values	0.81	0.24	0.17	0.71	0.60	0.24	0.43	0.25

	Hgb 1	**Hgb 2**	**Hgb Change**	**EBL**	**Surgery Length**	**Hgb Postop**
Femoral Neck	12.8 ± 1.78	11.7 ± 1.83	1.1 ± 0.96	148 ± 135.0	1.6 ± 0.69	10.1 ± 1.64
Intertrochanteric	12.2 ± 1.78	10.5 ± 1.71	1.8 ± 1.14	119 ± 76.2	1.2 ± 0.53	8.8 ± 1.53
Subtrochanteric	11.3 ± 1.60	9.7 ± 1.69	1.6 ± 0.25	175.0 ± 140.7	1.2 ± 1.00	8.8 ± 1.57
p-values	0.04[a]	<0.001[a]	0.006[a]	0.32	0.025[a]	0.001[a]

EBL: estimated blood loss.
[a] Indicates statistical significance.

reserve to produce hemoglobin following injury. Clinicians may need to pay particular attention to these patients in the perioperative setting, as their ability to withstand and recover from major surgical insult is compromised.

Increased time from admission to surgery was also predictive of an increased drop in hemoglobin ($p = 0.01$). This is expected, as a fracture represents active blood loss until the fracture is reduced and stabilized. This information lends new perspective to the debate of timing of hip fracture surgery and if earlier intervention is beneficial. Several studies have found decreased mortality for patients undergoing surgery within 12 and 24 h[17,18,21] and fewer complications such as pressure sores and length of hospital stay. Furthermore, Want et al. found that increased time from admission to surgery resulted in larger postoperative hemoglobin drops in intertrochanteric fractures treated with cephalomedullary nailing.[21] Still, other studies have concluded that delaying surgery up to 48 h has no effect on patient outcomes.[19,20] Our results support earlier operative intervention.

It is interesting to note the statistically significant post-operative Hgb values between fracture types, specifically the lower post-operative hemoglobin values associated with femoral neck fractures. At this institution, femoral neck fractures are repaired almost exclusively with anterior-approach hemiarthroplasty, as opposed to intertrochanteric and subtrochanteric fractures which are repaired with cephalomedullary nail placement. Because hemiarthroplasty is generally more costly with respect blood loss than cephalomedullary nailing, it stands to reason that there is another significant source of blood loss associated with these fractures. Because patients did not differ with respect to any other demographic characteristics (Table 4), hidden blood loss is a probable explanation for this observation.

Contrary to our initial predictions, anticoagulation/antiplatelet therapy was not an independent predictor of preoperative blood loss. This has been absent from previous studies seeking to quantify the hidden blood loss associated with proximal femur fractures.[7,11,14,15] Of note, five patients experienced non-transfusion-related hemoglobin increases. Four of these patients were using antiplatelet or anticoagulation medications prior to admission. The observed increase in hemoglobin may be a result of holding anticoagulation/antiplatelet therapies during preoperative optimization. The other patient was volume overloaded on admission, which may explain the subsequent hemoglobin increase.

This study has several strengths, most notably the inclusion of populations previously excluded from prior works such as those taking anticoagulation/antiplatelet medications and patients treated nonoperatively. Though previous studies have evaluated the safety and blood loss associated with anticoagulant/antiplatelet therapies in patients sustaining proximal femur fractures, these studies focused primarily on post-operative outcomes such as transfusions, complications, and time from admission t surgery.[5,6,10,15,21] An additional strength is the simplicity and validity of hemoglobin values as a surrogate measure of blood loss. Morbidity and mortality associated with decreased Hgb values in patients has been well established.[22,23,24] Thus, closely monitoring Hgb values facilitates improved patient outcomes, and provides a reliable estimation of blood loss without complex calculations.[2,4,10,15,25]

The present study does have limitations. We recognize the limitations and potential for selection bias inherent with a retrospective study. Also, patients with higher acuity typically require more time to optimize for surgery, potentially selecting higher acuity patients to be included in this study. However, we feel this bias to be minimal. Included patients with admission to surgery times greater than 12 h were overwhelmingly a result of logistical delays (i.e. operating room space and personnel limitations). Likewise, several patients included in this study initially presented in the evening but did not undergo surgery until the following morning, effectively satisfying the 12-h hemoglobin value requirement without constituting a true medical delay.

This study was also limited by the uneven distribution between proximal hip fracture types; there were substantially fewer intertrochanteric and subtrochanteric fractures than femoral neck fractures. Having a more even distribution of fracture type may have identified other outcomes of clinical and statistical significance. Similarly, future studies may also explore further subclassifying proximal femoral fractures. For example, in our study all femoral neck fractures were grouped, regardless of degree of displacement or location. Future studies may find that a complete femoral neck fracture may cause more hidden blood loss than a simpler valgus impacted fracture.

Finally, we were unable to control for how much of the hemoglobin drop may have been caused by hemodilution secondary to IV fluids. This is because exact volumes of IV fluids were unable to be extracted from the Electronic Medical Record (EMR). We feel this effect to be minimal, as only patients requiring maintenance IV fluids were included in our study. Furthermore, we utilized changes in electrolyte levels as surrogate measures of dehydration. Because our results did not indicate changes in sodium, potassium, or chloride to be risk factors for increased blood loss, we suspect that dehydration and hemodilution were not significant factors contributing to the hemoglobin drops observed. Future studies may focus on assessing patient hydration status upon admission and its effect on hidden blood loss. Similarly, pre-injury hemoglobin values would have been an ideal baseline from which to base further hemoglobin drops. However, the retrospective study design and large proportion of patients without regular outpatient laboratory draws at this institution precluded accessibility to this data.

5. Conclusion

Proximal femur fractures are traumatic events resulting in immediate and significant blood loss. The blood loss secondary to the fracture itself cannot be overlooked, as theses fractures may occur in older persons with decreased vital reserves. We have shown the amount of blood loss in proximal femur fractures to be statistically significant. In addition, the identification of demographic, fracture, and treatment characteristics may help surgeons identify patients at the greatest risk for blood loss, and consequently, provide more effective perioperative care.

CRediT authorship contribution statement

John Stacey: Conceptualization, Methodology, Data curation, Writing - original draft, Writing - review & editing. **Thomas DiPasquale:** Conceptualization, Writing - review & editing, Supervision.

Declaration of competing interest

None.

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