ORIGINAL ARTICLE

Blood Management May Have an Impact on Length of Stay After Total Hip Arthroplasty

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Abstract *Background:* The steady rise in demand for total hip arthroplasty constitutes a significant and increasing burden on health care resources. The biggest contributors to the total cost of hip replacement procedures other than the price of the implant are hospital stay and postoperative rehabilitation. Blood management is one of the most adjustable factors that can impact length of stay and cost-efficiency while improving patient safety. Questions/Purposes: The primary purpose of this retrospective study was to assess the potential impact of blood management interventions on length of hospital stay after primary unilateral total hip arthroplasty. This was achieved by first identifying which patient and surgical factors are associated with an increased risk of prolonged hospital stay. Subsequently, the significant factors were controlled for through a multivariate regression analysis to quantify the association between blood transfusions and increased hospital stay. Methods: Retrospectively, the study included 2,104 primary total hip replacements. Eight hundred eighty-eight procedures were performed on males and 1,216 on females, with a mean age of 64 years at the time of the surgery (range 18-94 years) and BMI of 28.6 kg/m² (range 12-51.5 kg/m²). The correlation between each factor and length of stay was analyzed separately using univariate regression analysis. Those variables with $p \le 0.05$ in the univariate model were selected for inclusion in the multivariate logistic regressions. Multiple linear regression was used to analyze the effect of each significant factor and derive odds ratios with adjustment for the other variables.

Level of Evidence: Therapeutic Study Level IV: Retrospective case series. See Levels of Evidence for a complete description.

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J. Bou Monsef, MD · F. Boettner, MD (⊠) Hospital for Special Surgery, 535 East 70th Street, New York, NY 10021, USA e-mail: boettnerf@hss.edu *Results:* Multivariate Poisson regression revealed that increased length of stay was significantly correlated to patient age (p=0.05), the use of coumadin (p=0.02) or lovenox/ heparin (p=0.007) as opposed to aspirin for anticoagulation, and allogeneic blood transfusion (p<0.0001). The data shows that allogeneic blood transfusion is associated with a longer hospital stay regardless of absolute drop in hemoglobin level postoperatively or at discharge or the number of units transfused (OR=1.18, 95% CI=1.09 to 1.28, p<0.001). *Conclusion:* Transfusion of allogeneic blood is independently associated with increased hospital stay after total hip arthroplasty. Blood management modalities that can significantly reduce transfusion risk could impact length of stay as well as the total cost of hip replacement procedures.

Keywords total hip arthroplasty length of stay blood management · allogeneic blood · autologous blood transfusion · anemia

Introduction

The established success of total hip arthroplasty (THA) in restoring mobility makes it one of the most effective interventions in medicine. The clinical course of patients undergoing such procedures has changed significantly in the last decade. Minimally invasive surgical approaches in addition to optimized anesthesia and pain management protocols have allowed earlier and more aggressive mobilization and rehabilitation [28, 35]. Such streamlining of clinical practice aims to reduce preoperative morbidity while increasing cost-efficiency.

The rising demand for hip replacement surgery constitutes a significant and increasing burden upon health care resources [22, 25]. Despite advances in operative technique and clinical management, postoperative hospital stay remains one of the most significant contributors to the total cost of THA procedures [37]. Reducing hospital length of stay (LOS) after hip replacement improves patient satisfaction as well as cost-efficiency [17–20]. Multimodal clinical "fast-track" pathways attempt to reduce length of stay in elective procedures without increasing complications by targeting patient education, preoperative discharge planning, preemptive pain and nausea management, and accelerated rehabilitation [21, 9]. Increased postoperative stay following primary THA has been attributed to several variables, namely older age, female gender, comorbidities, obesity, smoking, low preoperative hip scores, incision length, operative time, and incidence of blood transfusion [6, 8, 10, 12, 16, 18–20, 31, 43].

Preoperative anemia and allogeneic transfusions are both independently associated with increased overall morbidity and adverse outcomes such as prolonged hospitalization, suboptimal rehabilitation, and infections [4, 13, 32, 36, 43]. Blood management protocols aim to reduce exposure to allogeneic blood based on the individualized risk assessment and preoperative hemoglobin (Hb), the time available before surgery, the expected blood loss for the procedure, the strict transfusion thresholds, and the suitable modality for the given setting [2, 7]. Preoperative strategies rely on optimization of preoperative hemoglobin levels through preoperative work-up, iron supplementation and/or erythropoietin, as well as preoperative autologous blood donation. Intraoperative modalities such as hypotensive anesthesia, blood salvage, hemodilution, as well as intravenous or topical pharmacologic agents such as tranexamic acid or fibrin sealants aim to reduce blood loss and transfusion requirements. The potential of such interventions to reduce exposure to allogeneic blood makes blood management one of the most modifiable factors that might significantly impact length of stay [5, 14, 23].

The primary purpose of this retrospective study was to assess the potential impact of blood management interventions on length of hospital stay after primary unilateral total hip arthroplasty. This was achieved by first identifying which patient and surgical factors are associated with an increased risk of prolonged hospital stay. Subsequently, the significant factors were controlled for through a multivariate regression analysis to quantify the association between blood transfusions and increased hospital stay.

Patients and Methods

A retrospective analysis was conducted on 2,104 primary unilateral total hip replacement procedures performed between 2009 and 2012 by one of 13 surgeons at the authors' institution. All patients underwent a preoperative work-up and given oral iron supplementation. Patients who were considered anemic (hemoglobin level below 12.5 g/dL) were advised to donate one unit of autologous blood 7 to 15 days prior to the date of surgery. No patient was allowed to donate less than 7 days prior to the procedure. Preoperatively, 343 patients (16.3%) were anemic among which 256 chose to donate autologous blood and 87 opted not to. The 1,761 non-anemic patients (83.7%) did not donate autologous units. This protocol was based on previous data from our institution showing no benefit and higher wastage rates for autologous blood donation in non-anemic patients undergoing total hip arthroplasty [3]. Patients received allogeneic transfusions if their hemoglobin (Hb) level dropped below 8.0 g/dL, and they displayed clinical symptoms of anemia (tachycardia and/or hypotension) despite an intravenous fluid bolus. The decision to transfuse autologous blood was made at the discretion of the anesthesiologist and medical attending, and strict transfusion guidelines were not enforced for autologous blood.

Gender, age, body mass index (BMI), preoperative Hb, autologous blood donation, number of autologous transfusions, number of allogeneic transfusions, postoperative Hb levels until date of discharge, and in-house complications were recorded. Length of stay was calculated as the number of days in hospital from the day of surgery to the day of discharge, with day of surgery being day 0. Patients who underwent revision THA, simultaneous bilateral THA, and patients with bleeding disorders were excluded. The study was approved by the institutional review board at the authors' institution.

All procedures were performed under hypotensive spinal–epidural anesthesia using a standardized posterior approach. During the study period, 888 procedures were performed on males and 1,216 on females, with a mean age of 64 years at the time of the surgery (range 18–94 years) and BMI of 28.6 kg/m² (range 12–51.5 kg/m²). Patients were divided by BMI into groups according to the World Health Organization (WHO) criteria; underweight (<18.5 kg/m²), normal weight (18.5 to 24.9 kg/m²), overweight (25 to 29.9 kg/m²), and obese (>30 kg/m²). Patients with BMI greater than 30 kg/m² were further subdivided into three groups, 30 to 34.9 kg/m², 35 to 39.9 kg/m², and 40 kg/m² or more (Table 1).

Descriptive statistics were used to illustrate patient demographics and health characteristics. Medians and the 25th and the 75th percentiles were calculated for length of stay; means and standard deviations were calculated for continuous variables, namely age, BMI, preoperative and postoperative hemoglobin levels, and hemoglobin drop directly postoperatively and at discharge. Frequency distributions were used for categorical variables, including gender, laterality, surgeon, day of the procedure, preoperative or postoperative anemia, type of anticoagulant, preoperative autologous blood donation, and blood transfusion, whether autologous, allogeneic, or both. The correlation between each factor and length of stay was analyzed separately using Kruskal–Wallis test, Wilcoxon rank-sum, or Pearson's chi-square as appropriate. Those variables with $p \le 0.05$ in the univariate model were selected for inclusion in the multivariate logistic regressions. Multiple linear regression was used to analyze the effect of each significant factor and derive odds ratios with adjustment for the other variables. Regression employed the length of stay as the dependent variable and the preselected risk factors as the independent variables. All analyses were conducted using SAS for Windows 9.2 (SAS Institute Inc., Cary, NC, USA). All tests were two-sided and a critical p value of 0.05 was set for all comparisons (Fig. 1).

Results

The mean duration of hospital stay for all the patients was 3.4 days with a range of 1 to 18 days. The median LOS was 3 days with an inter-quartile range (i.e., 25th and 75th

Table 1 Demographic factors of patients in the study

Factor	Number	Mean LOS	<i>p</i> value
Age (years)			
<60	704 (33.5%)	$3.2{\pm}1.2$	<0.0001 ^a
60–69	729 (34.6%)	3.3 ± 1.2	
70–79	488 (23.2%)	3.5 ± 1.2	
>80	183 (8.7%)	3.8 ± 1.6	
Gender			
Male	888 (42.2%)	3.3 ± 1.3	<0.0001 ^b
Female	1,216 (57.8%)	3.5±1.2	
Laterality	1,210 (071070)	010 - 112	
Left	951 (45.2%)	$3.4{\pm}1.3$	0.4747 ^b
Right	1,153 (54.8%)	3.4 ± 1.2	011717
BMI $(kg/m^2)^c$	-,		
<18.5	25 (1.2%)	$3.2{\pm}1.0$	$< 0.0001^{a}$
18.5–24.9	588 (28.0%)	3.4 ± 1.3	0.0001
25–29.9	761 (36.4%)	3.3 ± 1.2	
30-34.9	435 (20.7%)	3.4 ± 1.2	
35–39.9	183 (8.7%)	3.5 ± 1.3	
≥40	107 (5.1%)	3.8±1.5	

^a Obtained from Kruskal-Wallis test

^b Obtained from Wilcoxon rank-sum test

^c Some missing data

percentile) of 3 to 4 days. Tables 1, 2, and 3 display the individual categories for each factor, the number of cases in each category, and the mean length of stay. Older age, female gender, higher BMI, and lower hemoglobin levels were associated with longer hospital stay. The vast majority of patients (91%) were discharged within 4 days, and 70% of the patients were actually able to leave the hospital after 3 days (Tables 1, 2, and 3).

A number of preoperative factors were found to be significant predictors of length of stay when subjected to univariate analysis but not significant after multivariate analysis. These variables included female gender, higher BMI, lower preoperative and postoperative hemoglobin levels until postoperative day 2 and on discharge, autologous blood donation, and the surgeon performing the procedure. Multivariate Poisson regression revealed that longer length of stay was significantly associated with older patient age (p=0.05), the use of coumadin (p=0.02) or lovenox/heparin (p=0.007)

as opposed to aspirin for anticoagulation, and allogeneic blood transfusion (p<0.0001). However, after accounting for confounding factors, prolonged hospital stay was not associated with the absolute drop in hemoglobin level (p=0.63), the number of allogeneic units transfused, or autologous blood donation (p=0.61) or transfusion (p=0.65). In addition, having surgery on Monday was associated with decreased hospital stay (p=0.005) (Table 4).

Discussion

This study aims to evaluate the effect of allogeneic transfusions and potential impact of blood management on duration of hospitalization after primary hip arthroplasty. In accordance with previous data in the literature, the results confirm that there are a number of independent preoperative factors that can be used to predict the length of stay. However, this

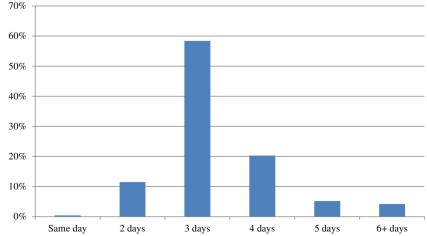


Fig. 1. Patient distribution by length of stay following primary THA.

Table 2	The effect of hemoglobin	level and bl	lood transfusions	on LOS
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Factor	Number	Mean LOS	p value
Preop Hb (g/dL)			
<12	190 (9.0%)	$3.7{\pm}1.6$	0.002^{a}
12-12.9	403 (19.2%)	$3.5{\pm}1.2$	
13–13.9	637 (30.3%)	3.4 ± 1.1	
>14	874 (41.5%)	3.3 ± 1.3	
Autologous blood			
Did not donate	1,848 (87.8%)	$3.4{\pm}1.2$	<0.0001 ^b
Donate	256 (12.2%)	3.6 ± 1.4	
Blood transfusion	200 (1212/0)		
None	1,792 (85.2%)	3.3 ± 1.2	< 0.0001 ^a
Autologous only	96 (4.6%)	3.5 ± 1.1	0.0001
Allogeneic only	182 (8.7%)	4.0 ± 1.8	
Autologous + allogeneic	34 (1.6%)	4.2 ± 1.3	
No. of allogeneic units received	51 (1.070)	1.2=1.0	
	1,888 (89.7%)	3.3 ± 1.2	<0.0001 ^a
1	173 (8.2%)	4.0 ± 1.6	
2	32 (1.5%)	4.1 ± 1.8	
3	7 (0.3%)	4.9 ± 3.6	
4	3 (0.1%)	5.7±0.6	
7	1	5	

^a Obtained from Kruskal-Wallis test

^b Obtained from Wilcoxon rank-sum test

study adds the association between heparin, lovenox, or warfarin and length of stay as compared to aspirin, as well as lack of association between LOS and autologous blood donation or transfusion. In addition, our data shows that allogeneic blood transfusion is associated with a longer hospital stay regardless of absolute drop in hemoglobin level

Table 3 Surgical factors of patients in the study

Factor	Number	Mean LOS	p value
Surgeon (TKA)			
1	59 (2.8%)	2.9 ± 1.1	< 0.0001 ^a
	36 (1.7%)	2.8 ± 0.7	
2 3	512 (24.3%)	$3.4{\pm}1.4$	
4	7 (0.3%)	3.1 ± 0.4	
5	51 (2.4%)	3.2 ± 0.8	
6	185 (8.8%)	$3.4{\pm}1.1$	
7	19 (0.9%)	3.6 ± 1.1	
8	421 (20.0%)	$3.4{\pm}1.4$	
9	301 (14.3%)	3.3 ± 1.2	
10	136 (6.5%)	$3.4{\pm}1.2$	
11	71 (3.4%)	3.5 ± 1.4	
12	239 (11.4%)	3.5 ± 1.2	
13	67 (3.2%)	3.7 ± 1.2	
Day of operation	· · · · · · · · · · · · · · · · · · ·		
Monday	461 (21.9%)	3.2 ± 0.9	< 0.0001 ^a
Tuesday	93 (4.4%)	$3.2{\pm}1.0$	
Wednesday	543 (25.8%)	3.6 ± 1.5	
Thursday	271 (12.9%)	3.5 ± 1.4	
Friday	554 (26.3%)	$3.4{\pm}1.2$	
Saturday	182 (8.7%)	3.1 ± 1.3	
Anticoagulation			
None	29 (1.4%)	$3.4{\pm}1.0$	< 0.0001 ^a
Aspirin	1,573 (74.8%)	3.3 ± 1.1	
Aspirin + coumadin	200 (9.5%)	3.6 ± 1.4	
Aspirin + coumadin + lovenox/heparin	21 (1.0%)	4.7±2.3	
Aspirin + lovenox/heparin	26 (1.2%)	4.0 ± 3.2	
Coumadin	215 (10.2%)	3.6 ± 1.1	
Coumadin + lovenox/heparin	34 (1.6%)	$4.4{\pm}2.1$	
lovenox	6 (0.3%)	3.8 ± 1.6	

*obtained from Kruskal-Wallis test

 Table 4
 Multivariate regression analysis to adjust for confounding factors

Variable	OR (95% CI)	$\Pr \ge t $
Age (in years)	1.00 (1.00, 1.00)	$0.05^{\rm a}$
Sex (female vs. male)	1.05 (0.99, 1.11)	0.09
$BMI (kg/m^2)$	1.00 (1.00, 1.01)	0.12
Preop Hb (g/dL)	0.99 (0.96, 1.03)	0.74
Postop Hb (g/dL)	1.01 (0.98, 1.05)	0.53
Hb drop (g/dL)	0.99 (0.96, 1.01)	0.33
Day of operation (Friday (reference))		
Monday	0.91 (0.82, 0.998)	0.05^{a}
Tuesday	0.93 (0.80, 1.08)	0.35
Wednesday	1.04 (0.96, 1.13)	0.29
Thursday	1.00 (0.92, 1.09)	0.97
Saturday	0.92 (0.84, 1.02)	0.10
Blood thinner use		
Aspirin	1.02 (0.93, 1.12)	0.65
Coumadin	1.09 (1.01, 1.18)	0.02^{a}
Lovenox/Heparin	1.17 (1.05, 1.31)	0.006^{a}
Preop autologous blood		
Donation vs No donation	1.03 (0.92, 1.15)	0.61
Blood transfusion		
Autologous (yes vs no)	1.03 (0.90, 1.18)	0.64
Allogeneic (yes vs no)	1.18 (1.09, 1.28)	<.0001 ^a

^a Significant association with longer length of stay

postoperatively or at discharge or the number of units transfused (OR=1.18, 95% CI=1.09 to 1.28, p<0.001).

Some of the results that were only significant in the univariate analysis might be accounted for by different medical comorbidities of the patients, and the lack of American Society of Anesthesiologists (ASA) grading for our cohort is a limitation of this study. Medical comorbidities clearly correlate with prolonged course of hospitalization [6, 8, 42], especially with the ASA scores of 3 and 4 [12]. In addition, univariate analysis involves measurement of one variable at a time, while multivariate analysis involves multiple variable and accounts for confounding effect. Thus, univariate analysis served to determine which factors would be significant enough to be considered in the multivariate regression model. Another limitation is the retrospective nature of the data, as well as the lack of reported outcome scores, blood loss, and operative times. Although the participation of different surgeons in the study precluded the standardization of incision length or implant type, the inclusion of multiple surgeons with differing experience contributes to providing results that are reproducible in highvolume orthopedic practices. No other blood management modalities were employed in this study.

Understanding the patient and surgical factors that might serve as predictors of longer hospital stay is essential for better planning and cost-efficacy of total hip replacement procedures. Patient demographic factors that correlate with increased LOS have been reported in the literature, namely older age, female gender, medical comorbidities, poor preoperative mobility, and higher BMI. However, our data adds to other studies that failed to establish a relation between BMI and LOS after adjusting for other factors [20]. It could be explained by the fact that slimmer and frailer elderly patients who have low BMI are likely to stay in the hospital for a longer period of time. Female patients tended to stay longer in hospital than males undergoing joint replacement procedures, although this effect did not remain significant after conducting multivariate analysis. Our data showed a significant correlation between age and length of stay and confirms the current literature [8, 12, 33, 41, 43]. In addition, the data revealed that anticoagulation with heparin and/ or warfarin were associated with longer hospital stay than with aspirin. Although this might be due to the fact that aspirin is easily administered orally and does not require blood testing, this is an interesting finding that warrants further investigation. Some of the results that were only significant in the univariate analysis might be accounted for by different medical comorbidities of the patients, and the lack of the American Society of Anesthesiologists (ASA) grading for our cohort is a limitation of this study. Medical comorbidities clearly correlate with prolonged course of hospitalization [6, 8, 42], especially with the ASA scores of 3 and 4 [12]. Another limitation is the retrospective nature of the data, as well as the lack of reported outcome scores and operative times.

Allogeneic blood transfusion has been associated with an increased length of stay after elective hip replacement surgery [43]. Although in some cases it might reflect complicated procedures with more blood loss and longer recovery, we failed to detect a significant association between the increased length of stay and hemoglobin drop, the number of units, or the transfusion of autologous blood. In addition, recent data suggests that the transfusion of allogeneic blood is also independently associated with significantly increased rates of upper and lower respiratory tract infections as well as wound infections [13, 32]. The association of allogeneic blood with longer hospital stay and increased complications has been attributed to immunomodulation, where allogeneic red blood cells may result in cytoskeletal changes in host red blood cells and alteration of host T cell regulation even if

white blood cells are filtered out [1, 11, 39]. In addition, inherent risks of infection transmission and febrile reactions among other transfusion-related complications persist despite advances in blood safety. The elective nature of joint replacement procedures and the efficacy and safety of various available blood management modalities allow the optimization of factors that determine allogeneic transfusion risk. Preoperative hemoglobin level has been shown to be the only variable to independently predict the need for blood transfusion after primary hip or knee arthroplasty [15]. Interestingly, there was no association between the hemoglobin levels or postoperative drop in hemoglobin and LOS in our multivariate analysis. The significant association detected in this study was the transfusion of any allogeneic blood regardless of the number of units transfused. Allogeneic blood transfusion is a major predictor of a longer LOS, and it has been reported to be the best predictor of discharge around the third postoperative day. Transfusion of one or more allogeneic blood units increases the risk of staying more than 3 days after joint arthroplasty by 3-fold [20]. Implementing a blood management protocol was shown to reduce the length of stay from 6 (5-8) days to 5 (3-7) and 4 (3-6) days for total hip replacement and total knee replacement respectively (p < 0.001) [24]. The algorithm relied on preoperative optimization of Hb level with oral iron supplementation with or without erythropoietin, adhering to a transfusion threshold, and employing modalities such as tranexamic acid, hypotensive anesthesia, or cell salvage in anemic patients. In addition, the protocol decreased the rate of readmission within 90 days from 13.5 to 8.2% (p=0.02) [24]. Since significant blood loss in joint replacement surgery can be anticipated, blood management modalities such as hypotensive anesthesia, preoperative blood salvage, and autologous blood donation in anemic patients decrease transfusion risk as well as LOS and total cost [20, 30, 36, 38].

Studies have suggested that the posterior approach in total hip is associated with longer postoperative hospitalization than the anterior approach [29]. Other data comparing the use of short versus standard femoral stems in patients less than 70 years old has reported significantly shorter mean postoperative stay for the short stem group by 2 days, resulting in 10% cost-saving per patient [40]. In addition, shorter incision lengths have shown to contribute to earlier discharge [34]. Some authors have reported increased length of stay for procedures done at the end of the week. This was attributed to the lack of physiotherapy and rehabilitation during the weekend in several institutions [8, 20]. The day of surgery did not influence the length of stay in this study except for a significant reduction when the procedure was performed on Monday. The association between poorer preoperative mobility and increased LOS stresses the importance of early and aggressive postoperative mobilization and rehabilitation. Although early aggressive rehabilitation protocols have proven effective [26, 27, 34], more research is needed to clarify this association.

The current data reveals a significant association between allogeneic blood transfusions and prolonged hospital stay after accounting for potential confounders and regardless of the number of units transfused. Although the immunomodulatory effects of allogeneic blood are not fully understood, it has been shown to independently correlate with a higher risk of postoperative infections and complications [32, 13]. Although the difference in the mean length of stay between categories of significant variables is sometimes less than half a day and may not be significant in an individual patient, it would give rise to a significant cost-saving over time. Blood management strategies such as preoperative hemoglobin optimization, selecting anemic patients for management options like preoperative autologous blood donation, and enforcing strict transfusion criteria can significantly reduce allogeneic transfusion requirements and the associated increased risk of increased hospital stay and cost of total hip arthroplasty procedures.

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Disclosures

Conflict of Interest: Friedrich Boettner, MD reports personal fees from Ethicon, Ortho Development, DJ Ortho and Smith and Nephew, grants from Smith and Nephew, outside the submitted work. Jad Bou Monsef, MD has declared that he has no conflict of interest.

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

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

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

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