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Pre-operative transfusions are associated with numerous post-operative complications in total hip arthroplasty

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ABSTRACT

Background: Primary total hip arthroplasty (THA) is among the most common surgical procedures and known to potentially cause significant blood loss. In total, 74,814 patients from the National Surgical Quality Improvement Project Database were studied. Complications were divided into post-operative and non-operative complications. Pre-operative transfusion in THA patients was found to be an independent predictor of infection (OR: 5.41), pneumonia (OR: 2.66), failure to wean (OR: 13.84), urinary tract infection (OR: 3.42), cardiac arrest (OR: 5.83), and transfusion post-operatively (OR: 5.94). Future medical decisions in primary THA cases should entail a careful risk-benefit and close monitoring in order to prevent complications.

1. Introduction

Based on current surgical trends, total hip arthroplasty (THA) is one of the five most common surgical procedures conducted in the United States.[1] Total hip arthroplasty is also known for causing significant intra-operative blood loss and is associated with a significant percentage of patients receiving allogeneic blood transfusions.[2–4] Despite the implementation of restrictive transfusion practices, studies have shown that the rate of post-operative transfusion for THA has gradually increased.[3,5] Post-operative blood transfusions have been shown to be associated with a myriad of adverse outcomes including increased risk of infection, immune system modulation, cardiac overload, lung injury, and blood type matching errors.[5]

Pre-operative anemia is pervasive among patients undergoing elective hip surgery, with an estimated prevalence of 12.9%, and of these patients, 17% developed severe anemia post-operatively.[2] Both pre-operative anemia and post-operative allogeneic transfusions have demonstrated increased complications, prolonged post-operative recovery, and increased morbidity and mortality.[2,5] Thus, the risks and benefits of transfusing and restricting transfusions must be carefully measured for every patient undergoing primary elective hip arthroplasty.

While several studies have investigated the effect of post-operative blood transfusion on adverse outcomes and overall morbidity and mortality, there is a scarcity of studies that have explored the effect of pre-operative blood transfusions on post-operative outcomes. In the present study, we aimed to examine the following: (1) What are the patient demographics and comorbidities associated with preoperative blood transfusion prior to THA? (2) Are patients with pre-operative blood transfusions at increased risk for postoperative complications after THA? (3) Do patients with pre-operative blood transfusions have an extended hospital stay or unplanned return to operating room? (4) Does a pre-operative blood transfusion act as an independent risk factor for development of a particular post-operative complication?

2. Methods

In total, 74,814 patients were included in the analysis to evaluate whether receiving a pre-operative blood transfusion contributes to the rates of post-operative complications after THA. Data was obtained from the National Surgical Quality Improvement Project Database years 2005–2014, with readmission/reoperation data beginning in 2011. Complications were broken down into operative complications, which are directly related to the surgical procedure, and non-operative complications, which are not directly connected to the operation.

Subjects were identified using Current Procedural Terminology

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(CPT) codes. Primary CPT code 27130 was used to identify patients receiving THA. Two patient cohorts were defined in this study: (1) patients that had received a pre-operative blood transfusion and (2) patients that did not receive pre-operative blood transfusion.

Baseline patient demographics and clinical characteristics included patient age, sex, race, and BMI, which was stratified according to the World Health Organization classification. Total length of stay (LOS), smoking status, absence or severity of dyspnea, preoperative functional status, type of anesthesia, and American Society of Anesthesiologists (ASA) class were also collected. Patient co-morbidities and operative features collected included diabetes mellitus status, pulmonary co-morbidity, cardiac comorbidity, renal failure, dialysis requirement, steroid use, history of recent weight loss, and bleeding disorder.

Recorded 30-day post-operative complications included death, cardiac complications (myocardial infarction or cardiac arrest requiring cardiopulmonary resuscitation), acute renal failure or progressive renal insufficiency, pulmonary complications (failure to wean from ventilator within 2 days postoperatively, unplanned reintubation, or pneumonia), deep vein thrombosis or pulmonary embolism, stroke, sepsis, deep surgical site infections (SSI), superficial SSI, wound dehiscence, and urinary tract infection. Return to operating room, readmission within 30 days and extended hospital LOS were also assessed.

2.1. Statistical analysis

Univariate analysis was performed using Pearson's Chi-square, Fisher's exact test, or ANOVA when appropriate. Variables with $p < 0.2$ were selected for multivariate analyses. For the multivariate analyses, a binary logistic linear regression analysis was performed to determine independent associations of risk factors for an extended hospital stay. To determine if blood transfusion was an independent risk factor for post-operative complications, a Poisson regression analysis was performed. The multivariate analysis results were reported as odds-ratios and 95% confidence intervals. A p-value of < 0.05 was used as the cutoff for significance. All statistical analyses were performed using SPSS V22 (IBM Pty Ltd; Armonk, NY).

3. Results

3.1. Demographics

Patients not receiving pre-operative transfusion compared to patients receiving a pre-operative transfusion demonstrated statistically significant differences in BMI ($p < 0.001$), race ($p = 0.002$), diabetes ($p = 0.034$), smoking status ($p = 0.043$), history of severe COPD ($p < 0.001$), hypertension on medication ($p < 0.001$), congestive heart failure ($p < 0.001$), steroid use for chronic condition (- < 0.001), disseminated cancer ($p < 0.001$), dyspnea ($p < 0.001$), functional status ($p < 0.001$), and ASA class ($p < 0.001$) (Table 1).

3.2. Complications

The amount of overall complications in primary total hip arthroplasty was 14,082 (19%). On univariate analysis of operative complications, organ space infection and wound disruption occurred at higher rates in preoperative transfusion patients ($p = 0.005$, $p < 0.001$). On univariate analysis of non-operative complications, pneumonia ($p < 0.001$), unplanned intubation ($p = 0.008$), failure to wean ($p < 0.001$), progressive renal insufficiency ($p = 0.047$), urinary tract infection ($p < 0.001$), needing a postoperative transfusion ($p < 0.001$), myocardial infarction ($p = 0.015$), cardiac arrest ($p < 0.001$), sepsis ($p = 0.001$), non-home discharge ($p < 0.001$), reoperation ($p < 0.001$), and readmission ($p = 0.009$) were shown to be higher in patients who required a pre-operative transfusion (Table 2).

On multivariate analysis and after controlling for contributing comorbidities, having had a pre-operative blood transfusion was found to be an independent predictor of organ space infection (OR: 5.41, 95% CI: 1.27–23.13, $p = 0.023$), pneumonia (OR: 2.66, 95% CI: 1.01–6.98, $p = 0.047$), failure to wean (OR: 13.84, 95% CI: 4.44–43.14, $p < 0.001$), urinary tract infection (OR: 3.42, 95% CI: 1.73–6.76, $p < 0.001$), cardiac arrest (OR: 5.83, 95% CI: 1.31–26.05, $p = 0.021$), transfusion post-operatively (OR: 5.94, 95% CI: 4.21–8.38, $p < 0.001$), and non-home discharge (OR: 3.18, 95% CI: 2.16–4.70, $p < 0.001$) (Table 3).

Table 1
Patient demographics and preoperative characteristics.

Variables	No Transfusion (n = 74,654)	Transfusion (n = 160)	P-Value
Demographics			
Age (years)	64.8	66.0	.207
BMI	30.0	26.6	< 0.001
Sex (female)	55.5	61.9	.107
Race			.002
American Indian or Alaskan Native	0.4	1.3	
Asian	1.5	2.6	
Black or African American	7.4	15.9	
Hispanic	0.1	0.0	
Native Hawaiian or Pacific Islander	0.2	0.0	
Unknown	2.5	1.3	
White	87.8	78.8	
Medical Comorbidities			
Diabetes	11.5	16.9	.034
Smoking (current or within 1 year)	13.3	18.8	.043
Alcohol Use	3.7	2.9	.789
Ascites	0.0	0.0	.840
History of Severe COPD	4.1	13.8	< 0.001
Hypertension on Medication	56.8	71.9	< 0.001
Congestive Heart Failure	0.4	3.8	< 0.001
History of MI	0.2	0.0	.816
History of PVD	0.0	0.8	.595
Renal Failure	0.1	0.0	.761
CVA	1.2	2.9	.349
Steroid Use for Chronic Condition	3.7	13.1	< 0.001
Disseminated Cancer	0.4	6.3	< 0.001
Chemotherapy for Malignancy	0.3	0.0	.750
Radiation for Malignancy	0.1	0.0	.845
ASA Class (%)			
1-No disturbance	4.3	0.6	< 0.001
2-Mild disturbance	54.5	15.6	
3-Severe disturbance	39.1	56.3	
4-Life threatening	2.0	26.9	
5-Moribund	0.0	0.6	
None Assigned	0.0	0.0	
Shortness of Breath			
At Rest	0.3	3.1	< 0.001
Moderate Exertion	4.8	5.6	
No	94.9	91.3	
Functional Status			
Independent	96.5	82.5	< 0.001
Partially Dependent	2.9	15.6	
Totally Dependent	0.2	0.6	
Unknown	0.5	1.3	

4. Discussion

In this large national, population-based retrospective study of primary THA patients, the findings of this study demonstrate that pre-transfused THA patients were at significantly increased risk of both operative and non-operative complications, compared to patients who were not transfused. This study sought to broaden the current

Table 2
Univariate analysis: Effect of transfusion on postoperative complications.

Complications	No Transfusion (n = 74654)	Transfusion (n = 160)	P-Value
Operative Complications (%)			
Total: 1204			
Superficial Surgical Site Infection	0.7 (553)	1.9 (3)	.095
Deep Surgical Site Infection	0.3 (220)	0 (0)	.492
Organ Space Infection	0.2 (161)	1.3 (2)	**.005**
Wound Disruption	0.1 (75)	1.3 (2)	**< 0.001**
Reoperation	2.1 (188)	0 (0)	.527
Non-Operative Complications	Total: 12,878		
Pneumonia	0.4 (299)	3.1 (5)	**< 0.001**
Pulmonary Embolism	0.3 (206)	0.6 (1)	.401
Unplanned Intubation	0.2 (174)	1.3 (2)	**.008**
Failure to wean	0.1 (76)	2.5 (4)	**< 0.001**
Progressive Renal Insufficiency	0.1 (80)	0.6 (1)	**.047**
Acute Renal Failure	0.1 (40)	0.0 (0)	.770
Urinary Tract Infection	1.2 (922)	6.9 (11)	**< 0.001**
Requiring Transfusion	13.3 (9962)	60.0 (96)	**< 0.001**
Stroke/CVA	0.1 (88)	0 (0)	.664
Myocardial Infarction	0.3 (196)	1.3 (2)	**.015**
Cardiac Arrest Requiring Resuscitation	0.1 (75)	1.3 (2)	**< 0.001**
DVT Requiring Therapy	0.4 (322)	0.6 (1)	.709
Sepsis	0.3 (249)	1.9 (3)	**.001**
Septic Shock	0.1 (60)	0.6 (1)	0.16
Non-Home Discharge	26.6 (17,743)	64.3 (93)	**< 0.001**
Length of Hospital Stay (days)	3.07	5.55	**< 0.001**
30-Day Readmission (%)	4.2 (350)	16.7 (3)	**.009**

Table 3
Multivariate analyses: Effect of Preoperative Blood Transfusion on Postoperative Complications in Patients Undergoing Primary THA.

Variables	Odds Ratio (95% CI)	P-Value
Superficial SSI	1.07 (.887, 1.29)	*.485*
Deep SSI	0.00	*.996*
Organ Space SSI	5.41 (1.27, 23.13)	***.023***
Wound Disruption	5.52 (.712, 42.79)	*.102*
Pneumonia	2.66 (1.01, 6.98)	***.047***
Re-intubation	0.00	*.996*
Pulmonary Embolism	1.88 (.251, 14.08)	*.539*
Failure to Wean > 48 Hours	13.84 (4.44, 43.14)	***< 0.001***
Progressive Renal Insufficiency	2.31 (.283, 18.90)	*.434*
Urinary Tract Infection	3.42 (1.73, 6.76)	***< 0.001***
Cardiac Arrest Requiring Resuscitation	5.83 (1.31, 26.05)	***.021***
Myocardial Infarction	1.66 (.359, 7.67)	*.517*
Transfusion	5.94 (4.21, 8.38)	***< 0.001***
Deep Vein Thrombosis	.984 (.134, 7.22)	*.987*
Sepsis	2.56 (.761, 8.59)	*.129*
Non-Home Discharge	3.18 (2.16, 4.70)	***< 0.001***
Reoperation	0.00	*.998*
Readmission	2.63 (.663, 10.44)	*.169*

*Comorbidities that were controlled for on regression include all comorbidities that had p-value of < 0.200 on analysis.

understanding of pre-operative transfusion complications in order to shape future medical decision making regarding pre-operative anemia in the context of primary total hip arthroplasty procedures and guide best practice for future management.

Pre-operative anemia is a fairly common diagnosis in the orthopedist setting with a prevalence of 52% of patients, attributed to the rising incidence with increasing age.[2,6,7] Managing pre-operative anemia is complex given that there are post-operative risks associated with both inadequate treatment as well as aggressive management. Failure to insufficiently treat pre-operative anemia is a major risk factor in perioperative and post-operative blood transfusion requirements, as well as higher post-operative complications such as lung injury and nosocomial infection.[2,7] However, aggressively correcting pre-operative anemia with allogeneic blood transfusions can have detrimental effects, as demonstrated by the findings of this study, which include increased infection risk, prolonged length of stay, prolonged intubation, discharge to a non-home facility, and cardiac arrest potential. This is congruent with studies done on post-operative transfusion studies, which have shown that, the increase in mortality in THA patients receiving transfusions post-operatively can last from 90 days to later.[8–10] Post-operative allogeneic blood transfusions were also associated with increased costs, longer hospital stay, and increased complications.[10,11]

The mortality of elective THA is generally low, however allogeneic transfusions in the pre- and post-operative context have shown increased risk and mortality.[9,10] Possible mechanisms for this mortality increase associated with transfusions includes adverse reactions such as transfusion associated cardiac overload (TACO), transfusion-related acute lung injury (TRALI), and increased infection risk secondary to transfusion related immune modulation (TRIM).[9] These mechanisms suggest that the transfused blood product could be the primary catalyst that results in inflammatory and immunological changes resulting in a delayed, complicated post operative recovery. Alternatively, elevated mortality risk related to blood transfusions could be secondary to severe anemia or major blood loss rather than the product of the transfusion itself.[9]

Given the complicated recovery course associated with patients receiving blood transfusions, focus should be placed on initiatives that treat anemia while avoiding transfusion. These include implementing restrictive transfusion practices, optimizing pre-operative hemoglobin using non-transfusion methods, and the use of tranexamic acid (TXA) to minimize blood loss. Restrictive transfusion practices have been applied in certain practices in order to minimize post-operative transfusion and have demonstrated 35% decrease in infection risk after implementation.[12] Previous literature suggested that blood transfusion was beneficial for increasing oxygen carrying capacity, but restrictive transfusion practice studies have shown that blood transfusions do not significantly increase oxygen carrying capacity or delivery in the perioperative context.[12] Restriction practices have not only decreased infection risk by removing the potential alteration in immune function but also decreased the cost from transfusion-associated infections, estimated to be approximately $14,000 per admission.[12] In addition to restrictive transfusion practices, optimizing pre-operative hemoglobin using non-transfusion methods such as iron supplementation as well as administration of synthetic erythropoietin (EPO) were also found to significantly reduce the need for post-operative allogeneic blood transfusion, thus decreasing the associated risks with transfusions.[6] However, the disadvantage of EPO is the financial burden it places on the US healthcare with an average of $380 per dose and an annual expenditure of 2 billion dollars.[6] Proponents argue that EPO administration could lead to savings through reduction in length of hospital stay, countering the initial costs.[6] While restrictive transfusion practices and non-transfusion methods such as iron and EPO administration methods have been practiced, the mainstay in blood loss reduction has been the use of tranexamic acid (TXA).[13–15] TXA has been shown to reduce post-operative bleeding, transfusion need, and the number of units transfused overall.[13–15] TXA is widely considered mainstay of treatment in blood loss reduction, but a major risk associated with its administration has been the possibility of venous thromboembolism (VTE) given its theoretic propensity to promote a hypercoagulable state.[15] This was studied in one particular meta-analysis, which demonstrated that there was no significant increase in the development of deep vein thrombosis (DVT) among patients who received TXA versus those who did not.[15] TXA is also more cost effective than blood transfusions, with an estimated savings of approximately $8370 per 100 patients, calculated only using the transfusion-associated costs.[15] These methods could be potential avenues for managing preoperative anemia in primary THA patients who would normally require transfusion and would possibly circumvent the post-operative complications and rise in mortality. Of the three

methods discussed, TXA is the most promising and has become part of routine standard of care. The extensive risks of transfusions evidenced through prior studies and the results of this paper, could potentially promote a paradigm shift in peri-operative anemia management among primary THA patients, in which transfusions are reserved for patients who require critical resuscitation.[14]

Finally, the results of this study also convey how complicated the post-operative recovery can be primary THA patients receiving pre-operative transfusions. Ultimately, patients who require a pre-operative transfusion will require more closely monitored care in order to anticipate for and prevent for possible post-operative complications. In the future, orthopedists should weigh the acute benefits of oxygen delivery from pre-operative transfusions with the chronic risks associated with post-operative recovery and increase in mortality when deciding to transfuse.

Limitations of this study include but are not limited to, the inability to abstract further clinical information including amount of intra-operative blood loss, the immediate pre- and post-operative hemoglobin values, and the threshold values to transfuse between hospital sites. Additionally, the number and volume of blood units used during each transfusion were not calculated, which could affect whether additional units of blood augment post-operative risks. Co-morbidities were accounted during regression analysis but certain co-morbidities could account for greater need for transfusion than others, which could affect how transfusions affect post-operative complications.

5. Conclusion

Overall, patients who were transfused with allogeneic blood products prior to a primary THA were at increased risk of operative and non-operative complications that encompassed increased infection risk (surgical site infections, pneumonia, and urinary tract infection), prolonged hospital stay, discharge to a non-home facility, and potential cardiac arrest leading to resuscitation. The risks are extensive and as a result, careful consideration must be taken when deciding whether to transfuse patients who are going to undergo an elective THA. Given these risks, management should focus on alternative methods to manage pre-operative anemia, namely the use of perioperative TXA as standard of care for preventing blood loss, and sparing pre-operative transfusions for those with critical anemia.

Conflict of interest statement

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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Appendix A. Supplementary data

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