Journal of Orthopaedics 16 (2019) 265–268

Contents lists available at ScienceDirect

Journal of Orthopaedics

journal homepage: www.elsevier.com/locate/jor

Preoperative blood transfusion associated with increased length of stay and increased postoperative complications after revision total knee arthroplasty

Alex Gu[a,b,*], Camilla M. Maybee[a], Chapman Wei[a], William V. Probasco[c], Michael P. Ast[d], Peter K. Sculco[b]

[a] George Washington School of Medicine and Health Sciences, 2300 Eye St, Washington, DC, 20037, USA
[b] Stavros Niarchos Foundation Complex Joint Reconstruction Center, Hospital for Special Surgery, 535 E 70th St, New York, NY, 10021, USA
[c] Department of Orthopedic Surgery, George Washington University, 2300 M St NW, Washington DC, 20037, USA
[d] Adult Reconstruction and Joint Replacement, Hospital for Special Surgery, 535 E 70th St, New York, NY, 10021, USA

ARTICLE INFO

Keywords:
Total knee arthroplasty
Revision TKA
Blood transfusions
Post-operative complications
Knee

ABSTRACT

Currently, the impact of preoperative transfusion on postoperative morbidity following revision total knee arthroplasty (TKA) is unknown. A retrospective cohort study using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was performed and included patients who underwent revision TKAs. Postoperative complications were analyzed. A total of 6,849 patients were included. Patients who received a preoperative blood transfusion were found to have an increased risk of developing 3 of 17 adverse events. Although overall complication rates remain relatively low, orthopedic surgeons should counsel their patients on the implications of preoperative blood transfusions on post-operative outcomes.

1. Introduction

As the demand for TKA continues to rise, projections show an increase of 673%—to 3.48 million—by 2030.[1] It is inevitable that the demand for revision TKA will also climb. The current cost of revision TKA in the US is $2.7 billion,[1] but the rising demand will result in an increased health care cost, projected to be approximately $13 billion.[2] Unfortunately, as demand continues to increase, the number of patients who suffer postoperative complications will rise as well, adding additional morbidity, mortality and cost. Therefore, analysis of risk factors for postoperative adverse events after revision surgery is critical in order to understand risk stratification, appropriately patient expectations, and create appropriate risk reduction programs.

Perioperative anemia exists in up to 80% of patients undergoing major orthopedic procedures,[3] and various strategies exist in current practice regarding peri-operative blood management. Pre-operative blood management strategies include supplementation with iron or Procrit, as well as the management of anti-platelet agents.[4] Intra-operative use of TXA has been shown to be successful in mitigating blood loss in several surgical disciplines,[3] though other strategies include the use of tourniquets to reduce blood flow to lower extremities, hypotensive epidural anesthesia, acute normovolemic hemodilution, antifibrinolytic agents, topical fibrin sealants, intraoperative cell salvage, epinephrine containing injections, platelet-rich plasma injections, and sealing the femoral tunnel.[4] As much as 50% of total blood loss in TKA occurs post-operatively, so post-operative strategies include joint compression, cryotherapy, post-operative cell saving, and drain clamping.[4]

While preoperative blood transfusion is a relatively infrequent intervention, it is currently part of the algorithm for refractory preoperative anemia. However, it is unclear what, if any, effect pre-operative blood transfusion has on postoperative complications after revision TKA. Extensive research has been done evaluating the impact of perioperative blood transfusions in the perioperative setting after primary joint replacement with studies reporting an increase incidence of infection, DVT requiring anticoagulation therapy, fluid overload, and longer duration of hospitalization.[5] In this study, we specifically focused the preoperative blood transfusions in patients undergoing revision TKA and examined the following: (1) Are their differences in patient demographics and comorbidities in patients undergoing revision TKA requiring a preoperative blood transfusion, (2) Is a preoperative blood transfusion an independent risk factor for development of postoperative complications? (3) Are revision TKA patients with blood transfusions more likely to require an extended hospital stay or

* Corresponding author. Stavros Niarchos Foundation Complex Joint Reconstruction Center, Hospital for Special Surgery, 535 E 70th St, New York, NY, 10021, USA.
E-mail addresses: algu@gwu.edu (A. Gu), Camilla.maybee@gmail.com (C.M. Maybee), cwei@gwu.edu (C. Wei), Probasco24@gmail.com (W.V. Probasco), astp@hss.edu (M.P. Ast), Sculcop@hss.edu (P.K. Sculco).

https://doi.org/10.1016/j.jor.2019.02.014
Received 15 August 2018; Accepted 17 February 2019
Available online 28 February 2019

unplanned return to operating room? We hypothesized that patients who received preoperative blood transfusions would be at increased risk for postoperative complications after controlling for comorbidities.

2. Methods

Data was collected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) for all revision TKAs from 2007 through 2014. ACS-NSQIP is a large multicenter registry that is prospectively collected by trained surgical clinical reviewers. Because ACS provides surgical clinical reviewer training for participating hospitals and auditing, the statistical reliability is adequate for assessing surgical quality and differentiating hospital performance.[6] Data collected include preoperative demographic information, perioperative events, and complications occurring within 30 days of initial surgical intervention.

Subjects were identified using Current Procedural Terminology (CPT) codes. CPT codes 27486 and 27487 were used to identify patients undergoing revision TKA. Two patient cohorts were defined in this study: (1) patients who received preoperative blood transfusions within 72 h of revision TKA, and (2) patients who did not receive preoperative blood transfusions.

Baseline patient demographics and clinical characteristics included patient age, sex, and BMI, which was stratified per the World Health Organization classification. Total length of stay after operation, presence and severity of dyspnea, SIRS/sepsis presence and severity and functional status were also collected. Patient comorbidities and operative features collected included diabetes mellitus status, pulmonary comorbidities, smoking status, cardiac comorbidites, renal failure, history of CVA, steroid use, bleeding disorders, and transfusion requirement.

Recorded operative complications included superficial surgical site infection, deep surgical site infection, organ space infection, wound disruption, and reoperation. Non-operative complications included pulmonary complications (pneumonia, pulmonary embolism, unplanned intubation, failure to wean), cardiac complications (myocardial infarction or cardiac arrest requiring cardiopulmonary resuscitation), acute renal failure or progressive renal insufficiency, urinary tract infection, deep vein thrombosis requiring therapy or pulmonary embolism, and stroke. Readmission within 30 days and extended hospital LOS were also assessed.

Data on patients' demographics, comorbidities, and postoperative complications were analyzed with SPSS software. Univariate analysis was performed using Chi-square and one-way ANOVA when appropriate. Linear regression analyses were performed with transfusion as a binary variable and all comorbidities with p-values less than 0.200 being controlled for. This was to determine the presence of independent predictors of surgical complications.

3. Results

A total of 6,849 subjects were included in this study after the inclusion criteria were applied. There were no significant differences noted based on sex or BMI class. However, comparing non-transfused to transfused groups, there were significantly more cases of dyspnea at rest ($p < 0.001$), significantly higher rates of SIRS or sepsis ($p < 0.001$), and significantly less functional independence ($p < 0.001$) in those that received a blood transfusion preoperatively (Table 1).

3.1. Comorbidities

In total, subjects that required preoperative transfusions were more likely to have 4 out of the 8 preoperative comorbidities examined than subjects that did not receive transfusions (Table 1). The transfused group had higher incidences of diabetes ($p = 0.008$), history of severe COPD ($p < 0.001$), congestive heart failure ($p = 0.007$), and bleeding disorders ($p < 0.001$).

Table 1
Patient demographics and preoperative characteristics.

Variables	No Transfusion	Transfusion	P-Value
Demographics			
Sex (Female)	57.3	67.3	.148
BMI	33.1	31.6	.194
Age	65.56	66.86	.395
Medical Comorbidities			
Diabetes	21.3	36.5	**.008**
Smoking (current or within 1 year)	11.2	9.6	.712
History of Severe COPD	5.1	17.3	< **0.001**
Hypertension on Medication	66.8	65.4	.828
Congestive Heart Failure	0.7	3.8	**.007**
Renal Failure	0.2	0.0	.762
Steroid Use for Chronic Condition	4.8	5.8	.756
Bleeding Disorder	5.1	26.9	< **0.001**
Sepsis Status			
SIRS	0.6 (44)	5.8 (3)	< **0.001**
Sepsis	1.9 (131)	9.6 (5)	
Septic Shock	0.1 (9)	1.9 (1)	
Shortness of Breath			
At Rest	0.2	3.8	< **0.001**
Moderate Exertion	7.4	3.8	
No	92.4	92.4	
Functional Status			
Independent	93.5	86.5	< 0.001
Partially Dependent	5.3	9.6	
Totally Dependent	0.3	3.8	

*Demographics and comorbidities with p-values less than 0.200 were included in multivariate analysis.

3.2. Length of stay from operation to discharge

There was a significant difference in length of stay between the preoperatively transfused group and non-transfused group. Patients requiring preoperative transfusions stayed in the hospital nearly twice as long after surgery. Patients in the preoperatively transfused group had an average length of hospital stay of 7.33 days, whereas those who did not receive transfusions had an average LOS of 3.98 days ($p < 0.001$) (Table 2).

3.3. Postoperative complications

In the non-transfused group, there were a total of 2012 postoperative complications out of 6797 patients—a complication rate of 29.6%. In the transfused group there were 49 total complications that occurred in 52 total patients and a complication rate of 94.2%. It should be noted, however, that the complication with the highest incidence was postoperative transfusions, which can be expected in patients who were transfused preoperatively. On univariate analysis, the transfused group had a significantly higher incidence than the non-transfused group of pneumonia ($p < 0.001$), failure to wean ($p < 0.001$), postoperative transfusion requirement (< 0.001), myocardial infarction ($p = 0.001$), deep venous thrombosis ($p = 0.047$), and sepsis ($p = 0.011$) (Table 2). Using multivariate analysis, preoperative transfusions were shown to be an independent predictor of 3 postoperative complications: failure to wean (OR: 12.56, 95% CI: 1.61–97.76 $p = 0.016$), myocardial infarction (OR: 12.35, 95% CI: 2.30–66.29, $p = 0.003$), and postoperative transfusion (OR: 5.12, 95% CI: 2.82–9.29, $p < 0.001$) (Table 3).

4. Discussion

While previous studies have looked at the risks associated with post-

Table 2
Complication and 30-day readmission rate for preoperative transfusion, univariate analysis.

Complications	No Transfusion (n = 6797)	Transfusion (n = 52)	P-Value
Operative Complications (%)			
Superficial Surgical Site Infection	0.8 (56)	0.0 (0)	.511
Deep Surgical Site Infection	1.0 (68)	0.0 (0)	.469
Organ Space Infection	1.5 (100)	3.8 (2)	.159
Wound Disruption	0.4 (30)	0.0 (0)	.631
Non-Operative Complications (%)			
Pneumonia	0.5 (34)	5.8 (3)	< 0.001
Unplanned Intubation	0.3 (23)	1.9 (1)	.054
Pulmonary Embolism	0.5 (33)	0.0 (0)	.614
Failure to wean	0.2 (12)	5.8 (3)	< 0.001
Progressive Renal Insufficiency	0.4 (24)	0.0 (0)	.668
Acute Renal Failure	0.3 (23)	0.0 (0)	.674
Urinary Tract Infection	1.1 (75)	0.0 (0)	.446
Requiring Transfusion	19.5 (1324)	61.5 (32)	< 0.001
Myocardial Infarction	0.3 (20)	3.8 (2)	< 0.001
Cardiac Arrest Requiring Resuscitation	0.1 (9)	0.0 (0)	.793
DVT Requiring Therapy	1.0 (70)	3.8 (2)	.047
Sepsis	1.4 (96)	5.8 (3)	.009
Septic Shock	0.2 (15)	1.9 (1)	.011
Length from operation until discharge (days)	3.98	7.33	< 0.001
30-Day Readmission (n = 711)	6.4 (45)	12.5 (1)	.486
Reoperation (n = 791)	3.8 (30)	0.0 (0)	.572

Table 3
Multivariate analysis of preoperative transfusion impact on postoperative complications.

Variables	Odds Ratio (95% CI)	P-Value
Organ Space Infection	2.79 (.627, 12.45)	.178
Pneumonia	4.31 (.690, 26.94)	.118
Unplanned Intubation	1.01 (.069, 14.662)	.996
Failure to Wean	12.56 (1.61, 97.76)	**.016**
Myocardial Infarction	12.35 (2.30, 66.29)	**.003**
Postoperative Transfusion	5.12 (2.82, 9.29)	< **0.001**
Sepsis	3.04 (.825, 11.22)	.095
Septic Shock	1.16 (.048, 28.17)	.926
DVT Requiring Therapy	3.66 (.787, 17.03)	.098
30-Day Readmission (n = 711)	2.67 (.302, 23.58)	.378

*Postoperative complications with negligible odds ratios were not included in Table 3.

operative transfusion, there is a paucity of data evaluating surgical outcomes and complications following preoperative blood transfusions in patients undergoing revision TKA.

To study the effect of preoperative blood transfusion on early postoperative complications, this study compared patients who either did or did not receive a preoperative blood transfusion within 72 h of revision TKA. The results of this study reveal that patients who received preoperative blood transfusions had an increased length of stay as well as an increased likelihood of postoperative complications versus those that did not receive a pre-operative blood transfusion even after controlling for comorbidities. A preoperative blood transfusion was associated with increased risk of failure to wean from a ventilator, postoperative MI, and postoperative transfusion. Interestingly, these patients were 12 times more likely to develop an MI or fail to wean. Given these findings, surgeons should carefully monitor patients in the postoperative period, consider standard protocols for postoperative rule out MI, and the use of neuraxial instead of general anesthesia. In addition, patients requiring preoperative transfusion should be counseled as to these increased risks.

In addition, careful consideration should be given to patients that initially present requiring a preoperative blood transfusion. Currently, there are viable alternatives to replenishing hemoglobin levels in a patient during the preoperative period, including iron treatments and erythropoietin therapy preoperatively. Recently, TXA has become an increasingly utilized which has dramatically decreased transfusion rates after TKA and may reduce the threshold for preoperative blood transfusion.[7] A 2009 study showed that, in patients undergoing total knee replacement, those who received 1 g of intravenous tranexamic acid at the induction of general anesthesia, there was a significant reduction in early-postoperative blood loss and total blood loss.[7] A more recent study of two consecutive cohorts of patients undergoing either TKA or total hip arthroplasty showed that an even higher pre-operative dose of TXA (up to 2.5 g) was associated with less blood loss than in lower doses with no apparent increase in risk for deep vein thrombosis, pulmonary embolism, GI bleed, MI, stroke, or death.[8]

There were some limitations to this study. One of the biggest limitations is that the study does not further stratify results based on the subjects' requirement for transfusion pre-operatively, intra-operatively, post-operatively, or all three. For example, it is certainly possible that a patient requiring a single transfusion is less likely to develop complications than a patient requiring more than one transfusion or requiring transfusion on more than one occasion. The transfused cohort could also be further stratified based on quantity of blood received—this could possibly shed more light on the demographics and comorbidities that not only pre-dispose a patient to needing a blood transfusion but also those who may be eligible for alternative therapy. A patient requiring only a single unit of blood, for example, could possibly be more successfully treated with an alternative therapy such as iron supplementation or EPO than a patient requiring several units. One final limitation is that we did not consider the type and severity of pre-existing bleeding and clotting disorders in patients undergoing revision TKA. There is certainly a difference in the treatment of a patient with mild anemia pre-operatively and a patient with a more severe and chronic condition such as von Willebrand disease or hemophilia. In addition, we do not know how many of these patients had anemia of chronic disease and the impact of the underlying disease state on postoperative outcomes. Whether preoperative transfusion still has a role in the management of preoperative anemia, particularly in the era of TXA, remains to be determined. Regardless, the results of this study provide additional information that patients who receive preoperative transfusions are at increased risk for extended stay, additional transfusions, and cardiac complications and this should be incorporated into any future risk adjusted payment models for revision TKA. In addition, the results of this study encourage close cardiac monitoring and perioperative interventions specifically targeted at reducing the specific complications associated with preoperative blood transfusions.

5. Conclusion

This study evaluated patients who underwent revision TKA to evaluate the impact of preoperative blood transfusions on perioperative outcomes and comorbidities. Patients who received blood transfusions were found to have longer lengths of stay and be at significantly higher risk for certain adverse events identified when compared to patients who were not transfused. Overall, there were significantly higher rates of postoperative complications in patients who received transfusion before surgery. Although there are clearly risks involved with blood transfusions, there is obviously still a need to replenish blood in those that have had significant blood loss. Physicians should be aware of risks associated with blood transfusions in these patients as well as ways to reduce the need for transfusions. This study provides important information for preoperative risk stratification, patient selection, and postoperative management of these complex patients.

Conflict of interest statement

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

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jor.2019.02.014.

References

1. Delanois RE, Mistry JB, Gwam CU, Mohamed NS, Choksi US, Mont MA. Current epidemiology of revision total knee arthroplasty in the United States. *J Arthroplasty.* 2017;32:2663–2668.
2. Bhandari M, Smith J, Miller L, Block J. Clinical and economic burden of revision knee arthroplasty. *Clin Med Insights Arthritis Musculoskelet Disord.* 2012;5:89–94.
3. Newman C, Tran P, McGregor S, Bramley D. Patient blood management strategies in total knee and hip arthroplasty. *Curr Orthop Pract.* 2018;29(1):31–36 January/February 2018.
4. Themistoklis T, Theodosia V, Konstantinos K, Georgios D. *World J Orthoped.* 2017;8(6):441–454.
5. Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB. An analysis of blood management in patients having a total hip or knee arthroplasty. *JBJS.* 1999;81(1):2–10.
6. Huffman KM, Cohen ME, Ko CY, Hall BL. A comprehensive evaluation of statistical reliability in ACS NSQIP profiling models. *Ann Surg.* 2015;261(6):1108–1113.
7. Rajesparan K, Biant LC, Ahmad M, Field RE. The effect of an intravenous bolus of tranexamic acid on blood loss in total hip replacement. *J Bone Joint Surg.* 2009;91(6):776–783 Jun.
8. Morrison RJM, Tsang B, Fishley W, Harper I, Joseph JC, Reed MR. Dose optimisation of intravenous tranexamic acid for elective hip and knee arthroplasty: the effectiveness of a single pre-operative dose. *Bone Joint Res.* 2017;6:499–505. https://doi.org/10.1302/2046-3758.68.BJR-2017-0005.R1.