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Risk Factors for Transfusions Following Total Joint Arthroplasty in Patients with Rheumatoid Arthritis

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Abstract

Background/Objective—Despite effective therapies, rheumatoid arthritis (RA) can result in joint destruction requiring total joint arthroplasty to maintain patient function. An estimated 16% to 70% of those undergoing total joint arthroplasty of the hip or knee will receive a blood transfusion. Few studies have described risk factors for blood transfusion following total joint arthroplasty in patients with RA. To identify demographic and clinical risk factors associated with receiving a blood transfusion following total joint arthroplasty among patients with RA.

Methods—A retrospective study ($N = 3,270$) was conducted using de-identified patient health claims information from a commercially-insured, U.S. dataset (2007–2009). Data analysis included descriptive statistics and multivariate logistic regression.

Results—Females were more likely to receive a blood transfusion (Odds ratio [OR]=1.48; 95% Confidence Interval [CI]: 1.16–1.87; $p=.001$). When compared to those in the South, patients residing the Midwest were less likely to receive a blood transfusion following total joint arthroplasty (OR=0.56, 95% CI: 0.44–0.71). Relative to those receiving total knee arthroplasty, patients who underwent total hip arthroplasty were more likely to receive a blood transfusion (OR=1.39, 95% CI: 1.14–1.70), and patients who underwent a total shoulder arthroplasty were less likely to receive a blood transfusion (OR=0.14 and 95% CI: 0.05–0.38; $p<.001$). Patients with a history of anemia were more likely to receive a blood transfusion compared to those who did not have this diagnosis (OR=3.30, 95% CI: 2.62–4.14; $p<.001$).

Conclusion—Risk factors for the receipt of blood transfusions among RA patients who have undergone total joint arthroplasty were identified.

Keywords

rheumatoid arthritis; transfusions; total joint arthroplasty; risk factors; anemia

Introduction

Rheumatoid arthritis (RA), a systemic autoimmune disease affecting 1% of the U.S. population, is characterized by symmetric joint inflammation which, if left untreated, results in joint destruction.[1] Despite the effective immunosuppressive therapies used to treat this condition, joint destruction requiring orthopedic surgery, such as total joint arthroplasty, is often needed to maintain patient function.[2]

There has been a negligible decline in the rate of total joint arthroplasty among RA patients (4.6 in 100,000 in 1991 to 4.5 in 100,000 in 2005) especially for older patients who suffered from the disease when fewer effective treatments were available (0–44 year age group: 3.2 % decrease; 45–65 year group: 0.6% decrease; and > 65 year age group: 0.8% decrease). [3] Thus, for many RA patients total joint arthroplasty remains a necessary medical treatment.

Prior research suggests that persons with RA who have undergone total joint arthroplasty are at increased risk of requiring a blood transfusion.[4] Stundner and colleagues found that of patients undergoing total knee arthroplasty, patients with RA are at a 50% higher risk of requiring a blood transfusion.[4] In one of the few studies investigating the risks of blood transfusion following total joint arthroplasty in patients with RA, Ogbemudia et al. reported that 21% of patients at one institution received a blood transfusion.[5] In the general population, 16% to 70% of persons undergoing total joint arthroplasty require a blood transfusion.[6]

Blood transfusions expose patients to increased risks including allergic reactions, viruses and infectious diseases, fever, iron overload, lung injury, hemolytic reactions, and Graft–Versus-Host Disease and persons who have received blood transfusions are more likely to have adverse health outcomes such as increased mortality;[7–9] thus, identifying risk factors for receipt of a blood transfusion following total joint arthroplasty in patients with RA is important.

Patients with RA have clinical and demographic factors which could affect surgical outcomes, such as the receipt of a blood transfusion, following total joint arthroplasty.[4] For example, patients with RA are typically younger and more are female when compared to patients with osteoarthritis.[4] As another example, the location of the joint replaced has been identified as a risk factor for receipt of a blood transfusion following total joint arthroplasty.[4, 10, 11] This increased requirement for blood transfusions does not, at least in the case of total knee arthroplasty, appear to be related to an increased number of bleeding episodes for RA patients.[12]

Anemia is a co-morbid condition that has been a focus of prior research in patients with RA undergoing total joint arthroplasty because of its association with clinical factors such as prosthetic joint infections, increased health costs, and longer lengths of hospitalization.[2, 4, 5, 13] The prevalence of anemia among RA patients ranges from 33–59%, and anemia has a multifactorial etiology in this population (i.e., direct inflammatory effects, bone marrow suppression secondary to medications, impairment in the synthesis of erythropoietin due to a functional iron deficiency with high iron stores but low availability).[14–16] A low

preoperative hemoglobin has been identified to significantly increase the risk of requiring a blood transfusion in patients with RA (odds ratio [OR] 14.4–21.9, $p < .001$).[5]

Because of the dearth of studies investigating risk factors for blood transfusions in RA patients specifically, research conducted in the general population provided guidance for our more population-targeted approach. In the general population, anemia has been found to be a risk factor for the receipt of a blood transfusion and adverse surgical outcomes.[11, 17, 18] Patients with anemia are 3.71 times more likely to receive a transfusion than those without and persons with a lower preoperative hemoglobin require a transfusion 37.8% of the time. [19, 20] Consideration of these risk factors is key since low pre- and post-operative hemoglobin values have also been identified as risk factors for increased length of hospital stay.[18]

Although few other comorbid conditions have been studied as risk factors for the receipt of a blood transfusion in patients with RA, there are some studies investigating the risk of diabetes mellitus.[5, 21] In the general population, diabetes mellitus is one risk factor identified as having a poor surgical outcome in patients who have received total elbow arthroplasty.[21] In contrast, for patients with RA who underwent total joint arthroplasty, diabetes mellitus Type 1 ($p = .15$) and Type 2 ($p = .19$) was not a risk factor for receiving a blood transfusion.[5] Consistent with this finding, the same study also found that persons with higher BMIs were less likely to require a blood transfusion ($p < .001$).[5]

Other risk factors for requiring a blood transfusion following the receipt of total joint arthroplasty in the general population include ethnicity, sex, and age.[11, 17, 19, 22, 23] Hispanics and Asian persons have been identified to have an increased risk for receiving a blood transfusion and lower pre-operative hemoglobin when compared to Caucasians, respectively.[17, 19]

There are conflicting results relative to the role of sex as a risk factor for requiring a blood transfusion, regardless of RA status. Ryan et al. found that women were more likely than men to have blood transfusions and Cushner et al., Grosflam et al. and Prasad et al. found that males had a higher risk than females.[17, 19, 22, 24] Cushner et al. found that although males had a higher pre-operative hemoglobin value, they had a higher rate of intraoperative blood loss than females, contributing to the higher risk of post-operative transfusion.[22] However, in a previous study of patients with RA, there was not a significant difference in the percent of males versus females that required a blood transfusion.[5]

Advanced age also increases the probability of a patient requiring a blood transfusion. In the general population, Millett et al. found that 26% of those over 75 years of age required blood transfusions, and Ryan et al. found that of persons 85 years of age or older were 4.02% more likely than those persons with ages between 18 to 44 years to require a blood transfusion. [19, 20] Duncan found that the odds of requiring a blood transfusion increased 2.2% with every additional 10 years of age.[23] Similarly, of those with RA, persons of older age were at increased risk of requiring a blood transfusion following total joint arthroplasty ($p = .004$). [5]

Finally, although some general blood management strategies have been put forward, the decision to transfuse a patient in the perioperative total joint arthroplasty period is not standardized and varies from provider to provider. [11, 17, 22, 25, 26] This observation suggests that geographic area of residence might play a role in the receipt of a blood transfusion following total joint arthroplasty.

Materials and Methods

Purpose

Because of the dearth of research reporting risk factors for requiring a blood transfusion among patients with RA, we aim to identify clinical and demographic variables associated with the receipt of a blood transfusion following total joint arthroplasty. We will also describe regional practices pertaining to the administration of blood transfusions following total joint arthroplasty in patient with RA.

Study Design and Sample

This retrospective analysis was based on a dataset comprising a commercially-insured population of 15 million patients annually, with 1,284,681 prescribers and 3,631 health care provider designations from all geographic regions in the United States. Patients' health claim information including: administrative demographic data (e.g., sex, age) and physician and facility claims data (e.g., procedure codes, diagnosis codes) were extracted from January 1, 2007 to December 31, 2009. Medical Institutional Review Board approval was obtained for the use of this dataset.

Our sample of 3,270 patients was obtained by extracting all patients with two diagnoses of RA (ICD-9: 714.0, 714.2, 714.4) who had undergone a total joint arthroplasty during the 2-year interval. The retained CPT codes included: total knee arthroplasty (27447); total hip arthroplasty (27130); and total shoulder arthroplasty (23472). Of these patients, 291 were missing at least one demographic (including location of residence) or clinical factor; thus the sample size for the logistic model was 2,979. Only one operative event was included for each patient. If a patient had more than one total joint arthroplasty during the period under consideration, only the first surgery was retained in this analysis.

Measures

Demographic and clinical variables—Demographic information extracted from the database included age, sex (male, female), education (some college, no college education), income (quintiles based on the Congress of the United States, Congressional Budget Office, Distribution of Household Income and Federal Taxes 2008–2009) [27], race (white, Other race), location of joint arthroplasty (total hip arthroplasty, total knee arthroplasty, or total shoulder arthroplasty), anemia diagnosis (yes/no) and residence (Based on the U.S. Census Regions [28]). Based on prior research and clinical plausibility, ICD-9 codes were used to extract clinical information for comorbid conditions that could potentially affect blood loss following total joint arthroplasty including: obesity/morbid obesity, diabetes mellitus [DM], systemic lupus erythematosus [SLE], human immunodeficiency virus infection and acquired immune deficiency syndrome [HIV/AIDS], cancer, and gout.[17, 29]

Transfusion status—This outcome variable was determined by assessing whether or not the patient had received a blood transfusion within one week following total joint arthroplasty (CPT code: 36430; transfusion, blood or blood components).

Data Analysis

Descriptive statistics, including means and standard deviations or frequency distributions, were used to summarize study data. Multivariate logistic regression was used to assess the demographic and clinical factors associated with transfusion status. The Hosmer-Lemeshow goodness-of-fit test evaluated overall model fit, and variance inflation factors were used to check for multicollinearity. For these data analyses, SAS version 9.4 was used with an alpha level of .05.

Results

The predominantly female (73.6%) and White (78.9%) sample had a mean age of 58.5 years ($SD = 10.8$ years; see Table 1). The geographic region with the smallest number of patients was the Northeast (8.6%), followed by the West region (14.9%). Larger subsets of patients were from the Midwest (26.7%) and South (49.8%). The majority had at least some college education (57.0%). Half of the patients were in the two lowest quintiles of income ($< \$60,000$: 50.5%); the smallest percentage of subscribers was in the highest quintile ($> \$150,000$: 2.8%). [27] As shown in Table 1, more than half of patients had a total knee arthroplasty (65.5%), while only 4.3% had total shoulder arthroplasty. In the full sample, approximately one quarter of patients were obese (25.6%) and diabetic (27.4%). Relatively few patients had SLE (12%), HIV/AIDS (0.4%), cancer (2.1%), and gout (6.3%). The majority of this sample was anemic (61.6%), and about one-fifth received a transfusion following surgery (19.9%).

Identification of Associated Demographic and Clinical Risk Factors

Of the demographic risk factors evaluated for association with post-operative blood transfusion among patients with RA who had received total joint arthroplasty, the factors that were significant in the logistic model included sex and geographic region of residence (see Table 2). Of the demographic factors, race, age, education, and income were not associated with transfusion status in this patient sample. Females were more likely to receive a blood transfusion when compared to males (Odds Ratio [OR] = 1.48, 95% Confidence Interval [CI]: 1.16–1.89; $p = .001$). When compared to those in the South, patients residing in the Midwest were less likely to receive a blood transfusion following total joint arthroplasty (OR=0.56, 95% CI: 0.44–0.71; $p < .001$). Compared to the reference group of patients in the South, the rate of transfusion was not significantly different in the Northeast ($p = .054$) or the West ($p = .14$).

Of the risk factors evaluated for association with post-operative transfusion among patients with RA who had undergone a total joint arthroplasty, the clinical factors that were significant in the logistic model included the location of joint arthroplasty and anemia status (see Table 2). The other clinical factors (obesity, diabetes, SLE, HIV/AIDS, cancer, and gout) were not associated with transfusion status in this patient sample. Relative to total

knee arthroplasty patients, those in the sample who received total hip arthroplasty were more likely to experience a transfusion (OR=1.39, 95% CI: 1.14–1.79; $p=.001$). With total knee arthroplasty as the reference, those who had total shoulder arthroplasty were less likely to require a transfusion (OR=0.14, 95% CI: 0.05–0.38; $p<.001$). Patients in this sample with an anemia diagnosis were more likely to have a post-operative transfusion, compared to those without this health condition (OR=3.30, 95% CI: 2.62–4.14; $p<.001$).

Discussion

This study identified female sex, geographic region of residence, location of total joint arthroplasty and history of anemia as risk factors for the receipt of a blood transfusion following total joint arthroplasty in patients with RA. Because there are few published articles with limited consensus on risk factors for this population, this article provides important insight which could aid in directing future research to establish best practices for transfusion management in the perioperative total joint arthroplasty period for patients with RA.

We found that females with RA have an increased risk of requiring a blood transfusion following total joint arthroplasty. One study reported an increased risk for women in the general population [19] and one study reporting no effect from sex in RA patients [5], the majority of studies investigating this variable found men to be at increased risk.[17, 22, 24] Authors of prior studies suggest that increased peri-operative blood loss in men [17] and lower pre-operative hemoglobin in females [22] could contribute to the need for a blood transfusion. Although our sample accurately represents the predominant female prevalence of RA [30], the conflicting findings could be attributed to the varying composition of samples (e.g., general population, RA, predominantly White and female). With this being said, it is clear that further research should be conducted to clarify these conflicting findings in the context of peri-operative blood loss and hemoglobin levels.

We found that patients residing in the Midwest were significantly less likely to receive a blood transfusion following total joint arthroplasty compared to those in the South. The differences were not significant when comparing the South to the Northeast or West. Prior research suggests that the decision to transfuse a patient following total joint arthroplasty varied from provider to provider, potentially resulting in geographically different treatment practice trends.[11, 17, 22] Thus, our findings are supported by prior research. This finding elucidates a larger clinical issue- provider decision-making processes in regards to blood transfusions following total joint arthroplasty. Because of the clinical and fiscal implications of these decisions, further studies should fully describe this process in efforts to establish practice guidelines.

Race, age, race, education, and income were not associated with receiving a blood transfusion in this sample. One prior study found that race is a risk factor; thus conflicts with findings in our study.[19] These results could be due to the classification of race/ethnicity used or the high prevalence of White patients in our sample. Similarly, we did not find age to be a significant risk factor for requiring a blood transfusion in this sample of RA patients; yet there is prior research suggesting an increased risk exists for those of advanced age in the

general population.[19, 20, 23] The difference in these findings could be attributed to the younger age of RA patients when undergoing total joint arthroplasty when compared to the general population.[4] Further prospective research should be conducted, controlling for anemia to clarify these conflicting findings among RA patients.

We evaluated comorbid conditions including obesity, diabetes, SLE, HIV/AIDS, cancer, gout and anemia along with location of total joint arthroplasty. Only location of the total joint arthroplasty and anemia status were associated with having a blood transfusion. From our review of the literature, obesity, diabetes, anemia, and the location of the joint arthroplasty were the only clinical risk factors investigated in prior research. In one prior study of patients with RA, diabetes mellitus Type 1 and Type 2 status was not predictive of requiring a blood transfusion and patients with a higher BMI were less likely to require a blood transfusion.[5] These findings are in support of the results of this study which did not find that having the diagnosis of diabetes or obesity affected the risk of requiring a blood transfusion. It is plausible that persons who are severely underweight and with poor nutrition are outliers affecting these findings. Prospective studies with in-depth data on nutritional status relative to BMI and diabetes status should be conducted.

Anemia was a clinical risk factor identified to increase risks in patients with RA who underwent total joint arthroplasty. This finding is concordant with previous studies.[5] The magnitude of the effect that we identified along with the overwhelming evidence supporting this finding suggests that this risk factor should be carefully considered by providers in the pre-operative period. Once this risk factor is acknowledged in the preoperative period, initiating preventative actions could improve post-surgical outcomes. Although standardized guidelines could not be identified, Lui and colleagues recently published an article providing an algorithm for blood management in the perioperative period in patient undergoing total knee arthroplasty in the general population.[25] The algorithm suggests that persons with a post-operative hemoglobin less than 7 or 8 with symptoms of anemia are candidates for allogenic transfusion and that patients should undergo pre-operative assessment and management of anemia.[25]

The final risk factor we identified was the location of the joint replaced during total joint arthroplasty. Patients who underwent a total hip arthroplasty were significantly more likely to receive a transfusion compared to those who underwent a total knee arthroplasty. It is possible this findings reflects that knee replacements can be performed under tourniquet control in contrast to hip replacements which can not. We also found that those who underwent a total shoulder arthroplasty were significantly less likely to require a blood transfusion, again compared with the knee arthroplasty group. These data conflict with at least one published study which found no significant difference in transfusion requirements between hip and knee arthroplasty.[6] However, the transfusion difference may be specific to RA patients as this study did not differentiate between patient populations. Interestingly, Carling, et. al, also demonstrated a significant difference between observed blood loss for hip as compared to knee arthroplasty. Perhaps observing the blood loss intraoperatively prompts a more liberal approach to transfusion.[6] Our results underscore the need to evaluate risk relative to location of arthroplasty prior to surgery.

This study used retrospective data from commercial insurance database, as such, our analysis was limited by data available for medications and treatments that were charged by health care providers and paid for using insurance coverage. The dataset was maintained from 2007 to 2009, therefore it may not represent the most recent changes to clinical practice. For example, minimally invasive joint replacements likely have decreased transfusion risks. With this being said, 70% to 80% of total knee replacements are performed using the traditional approach. Because this dataset represents persons with commercial insurance, study findings may not be generalizable to other populations such as those without private insurance. Although the racial/ethnic composition of the sample is not representative of the U.S. population, it is consistent with previous studies of racial variations in total joint arthroplasty [36]. There is also the potential for inaccuracies in ICD-9 and CPT codes available for extraction from the dataset. With this being said, we have validated the diagnosis of RA with two diagnoses codes. The modest number of persons with HIV/AIDS, cancer, and SLE is an additional limitation of this study despite our robust sample size.

Conclusion

This study identifies important demographic and clinical risk factors for the receipt of a blood transfusion in patients with RA who underwent total joint arthroplasty. Because adverse health outcomes, such increased mortality, have been found in persons receiving blood transfusions, an understanding of the risks could change the preoperative evaluation and, in turn, post-operative surgical outcomes.[9] This article contributes to the body of knowledge to establish best practices and standardized guidelines for the management of RA patients in the perioperative total joint arthroplasty period.

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Table 1Descriptive summary of study variables ($N = 3270$)

Age, $M \pm SD$	58.5 $\pm$ 10.8
Race, no. (%)	
White	2,581 (78.9%)
Other	689 (21.1%)
Gender, no. (%)	
Male	862 (26.4%)
Female	2,408 (73.6%)
Region, no. (%)	
Midwest	872 (26.7%)
Northeast	282 (8.6%)
South	1,629 (49.8%)
West	487 (14.9%)
Education, no. (%)	
Some college	1,818 (57.0%)
No college	1,369 (43.0%)
Income, no. (%)	
<\$39,000	751 (24.7%)
\$40,000–\$59,000	785 (25.8%)
\$60,000–100,000	998 (32.8%)
\$100,000–\$149,000	426 (14.0%)
>\$150,000	85 (2.8%)
Joint Arthroplasty, no. (%)	
Total knee arthroplasty	2141 (65.5%)
Total hip arthroplasty	989 (30.2%)
Total shoulder arthroplasty	140 (4.3%)
Obesity, no. (%)	
Yes	837 (25.6%)
No	2,433 (74.4%)
Diabetes, no. (%)	
Yes	896 (27.4%)
No	2,374 (72.6%)
Lupus, no. (%)	
Yes	392 (12.0%)
No	2,878 (88.0%)
HIV, no. (%)	

Yes	12 (0.4%)
No	3,258 (99.6%)
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Cancer, no. (%)	
Yes	70 (2.1%)
No	3,200 (97.9%)
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Gout, no. (%)	
Yes	207 (6.3%)
No	3,063 (93.7%)
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Anemia, no. (%)	
Yes	2,013 (61.6%)
No	1,257 (38.4%)
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Transfusion, no. (%)	
Yes	650 (19.9%)
No	2,620 (80.1%)
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Table 2Multiple logistic regression modeling the likelihood of transfusion following TJA ($n = 2,979^*$)

	Estimated Odds Ratio (OR)	95% Confidence Interval for OR	p
Gender			
Female vs. Male	1.48	1.16 – 1.87	.001
Region			
Midwest vs. South	0.56	0.44 – 0.71	<.001
Northeast vs. South	1.36	1.00 – 1.87	.054
West vs. South	0.80	0.60 – 1.07	.14
Race			
White vs. Other	0.96	0.77 – 1.21	.74
Age	1.01	1.00 – 1.02	.13
Education			
Some college vs. No college	0.85	0.67 – 1.08	.19
Income			
\$40–59,000 vs. <\$39,000	0.81	0.61 – 1.07	.14
\$60–100,000 vs. <\$39,000	1.19	0.89 – 1.60	.24
\$100–149,000 vs. <\$39,000	1.28	0.89 – 1.83	.19
>\$150,000 vs. <\$39,000	1.47	0.82 – 2.62	.19
Joint Arthroplasty			
Total hip arthroplasty vs. Total knee arthroplasty	1.39	1.14 – 1.70	.001
Total shoulder arthroplasty vs. Total knee arthroplasty	0.14	0.05 – 0.38	<.001
Anemia			
Yes vs. no	3.30	2.62 – 4.14	<.001
Obesity			
Yes vs. no	0.92	0.74 – 1.15	.47
Diabetes			
Yes vs. no	1.02	0.82 – 1.26	.88
SLE			
Yes vs. no	1.04	0.79 – 1.38	.77
HIV/AIDS			
Yes vs. no	1.04	0.21 – 5.19	.97
Cancer			
Yes vs. no	0.92	0.49 – 1.71	.78
Gout			

	Estimated Odds Ratio (OR)	95% Confidence Interval for OR	p
Yes vs. no	0.80	0.53 – 1.20	.28

* missing data on one or more variables for 291 of the total sample of 3,270 patients

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