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# Association of Perioperative Red Blood Cell Transfusion With Symptomatic Venous Thromboembolism Following Total Hip and Knee Arthroplasty

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ABSTRACT

*Background:* Prior registry data suggest that perioperative red blood cell (RBC) transfusion may increase the incidence of venous thromboembolism (VTE) in patients status post surgery. However, there are limited data that explore VTE risk after perioperative transfusion in the setting of primary total joint arthroplasty (TJA). Our aim is to investigate the association between perioperative RBC transfusion and the development of symptomatic VTE after adjusting for confounding variables.

*Methods:* We retrospectively reviewed all patients undergoing primary TJA at a single institution from 2001 to 2016. The primary outcome was development of symptomatic VTE (deep vein thrombosis or pulmonary embolism) up to 90 days following primary TJA. To identify the association between RBC transfusion and development of VTE, univariate and multivariate analyses were used, as well as a sensitivity analysis using propensity score matching based on patient comorbidities.

*Results:* Of the 29,003 patients who underwent TJA, 2500 (8.62%) received RBC transfusion perioperatively and 302 (1.04%) developed a postoperative VTE within 90 days of surgery. While univariate analysis did suggest a slightly increased incidence of VTE in association with RBC transfusion (odds ratio [OR], 1.53; 95% confidence interval [CI], 1.09-2.16), this difference was eliminated when multivariate analysis (OR, 0.42; 95% CI, 0.12-1.39) and propensity score matching (propensity-matched OR, 1.2; 95% CI, 0.7-1.8) were employed.

*Conclusion:* Perioperative RBC transfusion does not significantly increase the incidence of symptomatic VTE following primary TJA in the 90-day postoperative period after adjustment for host VTE risk scores and other confounding variables. Perioperative RBC transfusion may be safely administered if indicated following total hip and knee arthroplasty.



Perioperative red blood cell (RBC) transfusion is common in total joint arthroplasty (TJA). The reported incidence of allogenic blood transfusion varies from 3.5% to 18.5% in patients undergoing unilateral total knee arthroplasty (TKA) and from 5.4% to 26.2% in patients undergoing unilateral total hip arthroplasty (THA) [1], while the incidence was about 50% reported for patients undergoing bilateral procedures [2,3]. Transfusions are typically used in the preoperative period for patients with preexisting anemia, and in the intraoperative and postoperative periods for patients who have experienced significant blood loss [4]. Recent evidence suggests that perioperative RBC transfusions may increase the risk of developing venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) in patients following surgery [5,6]. However, these studies were conducted using registry data, precluding the ability to account for certain potential risk factors, and did not specifically assess the orthopedic surgery population.

This study was performed at Rothman Orthopaedic Institute.

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VTE is a potentially preventable life-threatening health risk that affects more than 350,000 patients in the United States each year who have been hospitalized secondary to critical illness or invasive surgery, with significantly increased risk extending up to 90 postoperative days [7–9]. In 2011, the annual cost burden of preventable and nonpreventable hospital-acquired VTEs was estimated to be between $13.5 and $27.2 billion [10]. VTE is also responsible for at least 100,000 deaths annually in the United States [7]. Common conditions associated with a significantly increased risk of VTE after TJA include metastatic cancer, stroke, hypercoagulable state, chronic obstructive pulmonary disease, and sepsis [11].

There is evidence that RBC transfusions may have a mechanistic role in the development of VTE [5,12,13]. One proposed mechanism suggests the storage of RBCs causes oxidative damage to the lipids on the RBC, which allow for proinflammatory and procoagulant RBC surfaces, increasing risk of developing VTE [12]. Another study suggests a metabolic mechanism involving RBC's ability to increase platelet reactivity [13]. Although this evidence is plausible, the

**Table 1**
Patient Characteristics Before Propensity Score Matching.

| Variables | Total (N = 29,003) | Nontransfusion (N = 26,503) | Transfusion (N = 2500) | *P* Value |
|---|---|---|---|---|
| Patient demographics | | | | |
| Age-group (y) | | | | <.001 |
| 18-44 | 1495 (5.2%) | 1364 (5.1%) | 131 (5.2%) | |
| 45-64 | 13,582 (46.8%) | 12,512 (47.2%) | 1070 (42.8%) | |
| ≥65 | 13,926 (48.0%) | 12,627 (47.6%) | 1299 (52.0%) | |
| BMI (kg/m$^2$) | | | | <.001 |
| <18.5 | 256 (0.9%) | 234 (0.9%) | 22 (0.9%) | |
| 18.5-29.9 | 14,325 (49.4%) | 12,942 (48.8%) | 1383 (55.3%) | |
| 30-39.9 | 10,293 (35.5%) | 9468 (35.7%) | 825 (33.0%) | |
| ≥40 | 1811 (6.2%) | 1652 (6.2%) | 159 (6.4%) | |
| Unknown | 2318 (8.0%) | 2207 (8.3%) | 111 (4.4%) | |
| Male | 12,622 (43.5%) | 11,719 (44.2%) | 903 (36.1%) | <.001 |
| Race | | | | <.001 |
| White | 22,321 (77.0%) | 20,389 (77.0%) | 1932 (77.4%) | |
| Black | 3360 (11.6%) | 3010 (11.4%) | 350 (14.0%) | |
| Other | 274 (0.9%) | 234 (0.9%) | 40 (1.6%) | |
| Unknown | 3029 (10.5%) | 2854 (10.8%) | 175 (7.0%) | |
| Hip | 15,447 (53.3%) | 14,243 (53.7%) | 1204 (48.2%) | <.001 |
| ASA ≥ 3 | 10,176 (35.1%) | 9003 (34.0%) | 1173 (46.9%) | <.001 |
| OP time group | | | | |
| <90 | 7141 (24.6%) | 6781 (25.6%) | 360 (14.4%) | |
| 90-120 | 10,201 (35.2%) | 9458 (35.7%) | 743 (29.7%) | |
| >120 | 9918 (34.2%) | 8595 (32.4%) | 1323 (52.9%) | |
| Unknown | 1743 (6.0%) | 1669 (6.3%) | 74 (3.0%) | |
| Anticoagulants | | | | |
| Warfarin | 24,596 (84.8%) | 22,291 (84.1%) | 2305 (92.2%) | <.001 |
| Prophylaxis options including aspirin | 6194 (21.4%) | 5764 (21.7%) | 430 (17.2%) | <.001 |
| Number of anticoagulants | | | | <.001 |
| 0 | 72 (0.2%) | 62 (0.2%) | 10 (0.4%) | |
| 1 | 27,053 (93.3%) | 24,811 (93.6%) | 2242 (89.7%) | |
| ≥2 | 1878 (6.5%) | 1630 (6.2%) | 248 (9.9%) | |
| VTE risk score | | | | |
| VTE risk score | 37.5 ± 30.3 | 36.4 ± 29.7 | 48.5 ± 34.8 | <.001 |
| Anemia | 3534 (12.2%) | 2857 (10.8%) | 677 (27.1%) | <.001 |
| Congestive heart failure | 110 (0.4%) | 92 (0.3%) | 18 (0.7%) | .004 |
| Coagulation deficiency | 243 (0.8%) | 198 (0.7%) | 45 (1.8%) | <.001 |
| Lymphoma | 82 (0.3%) | 72 (0.3%) | 10 (0.4%) | .236 |
| Fluid and electrolyte disorders | 596 (2.1%) | 493 (1.9%) | 103 (4.1%) | <.001 |
| Metastatic cancer | 52 (0.2%) | 40 (0.2%) | 12 (0.5%) | <.001 |
| Peripheral vascular disease | 369 (1.3%) | 333 (1.3%) | 36 (1.4%) | .434 |
| Nonmetastatic solid tumor | 204 (0.7%) | 176 (0.7%) | 28 (1.1%) | .009 |
| Weight loss | 26 (0.1%) | 19 (0.1%) | 7 (0.3%) | .005 |
| Chronic pulmonary heart disease | 82 (0.3%) | 70 (0.3%) | 12 (0.5%) | .052 |
| History of VTE | 765 (2.6%) | 677 (2.6%) | 88 (3.5%) | .004 |
| Myeloproliferative disorders | 42 (0.1%) | 35 (0.1%) | 7 (0.3%) | .088 |
| Hypercoagulability state | 59 (0.2%) | 50 (0.2%) | 9 (0.4%) | .097 |
| Myocardial infarction | 1288 (4.4%) | 1167 (4.4%) | 121 (4.8%) | .311 |
| Varicose veins | 119 (0.4%) | 110 (0.4%) | 9 (0.4%) | .681 |
| Fracture | 374 (1.3%) | 320 (1.2%) | 54 (2.2%) | <.001 |
| Inflammatory bowel | 74 (0.3%) | 68 (0.3%) | 6 (0.2%) | 1.000 |
| Sepsis | 9 (0.0%) | 6 (0.0%) | 3 (0.1%) | .036 |
| PJI | 11 (0.0%) | 7 (0.0%) | 4 (0.2%) | .011 |
| Atrial fibrillation | 1412 (4.9%) | 1262 (4.8%) | 150 (6.0%) | .006 |
| Stroke | 18 (0.1%) | 12 (0.0%) | 6 (0.2%) | .003 |
| Apnea | 1786 (6.2%) | 1629 (6.1%) | 157 (6.3%) | .791 |
| Age score | 6.4 ± 3.1 | 6.4 ± 3.0 | 6.7 ± 3.2 | <.001 |
| Bilateral | 3549 (12.2%) | 2921 (11.0%) | 628 (25.1%) | <.001 |
| Not primary THA | 13,556 (46.7%) | 12,260 (46.3%) | 1296 (51.8%) | <.001 |

BMI, body mass index; ASA, American Society of Anesthesiologists; VTE, venous thromboembolism; PJI, periprosthetic joint infection; THA, total hip arthroplasty; OP, operative time.

mechanistic involvement of RBCs may not be clinically relevant. To our knowledge, there are no studies that have evaluated the association between VTE and perioperative RBC transfusion in orthopedic patients using data from a large single-institution database, where detailed patient data and potentially confounding variables could be included in analysis.

The aim of this study is to identify an association between perioperative RBC transfusion and incidence of symptomatic VTE following primary THA and TKA up to 90 postoperative days. We hypothesize there is no difference in the incidence of VTE when comparing patients who did or did not receive perioperative RBC allogeneic transfusions.

## Materials and Methods

After institutional review board approval, we retrospectively reviewed all patients at a single tertiary care institution who underwent primary hip and knee arthroplasty between 2001 and 2016. Patients undergoing revision arthroplasty and those patients under 18 years of age were excluded from analysis.

The primary outcome was development of VTE after primary TJA, up to 90 postoperative days. All patients with a definitive diagnosis of symptomatic VTE, including PE or DVT, within 90 days of surgery were identified from review of administrative and radiological databases, as well as records of patient-provider phone communications and dictations from clinical encounters. Following our institutional protocol [14], patients were tested for PE and DVT at the discretion of the ordering provider based on clinical suspicion, which was based on a combination of clinical symptoms, physical examination, and laboratory values such as dyspnea or extremity pain, lower extremity swelling, and D-dimer values. Definitive diagnosis of VTE events was made using either computed tomography angiography of the chest (for PE) or ultrasound of the extremity of concern (for symptomatic deep vein thrombosis). In addition to a composite outcome of VTE, the occurrences of DVT and of PE up to 90 postoperative days were analyzed separately as secondary outcomes.

The primary independent variable of interest was the occurrence of any perioperative RBC allogeneic transfusions, from 72 hours before to 72 hours after surgery. Confounders reviewed were patient demographics including age, race, gender, body mass index, comorbidities, and operative factors including joint of surgery, operative time, and VTE prophylaxis (Table 1). Furthermore, a previously developed VTE risk stratification model [11] was used to determine a calculated risk score for each patient. The independent risk factors identified in developing the VTE risk stratification model were also included as individual independent variables in analysis.

### *Statistical Analysis*

Categorical variables were presented as frequencies and percentages, and continuous variables as means and standard deviations. The clinical characteristics between transfusion and nontransfusion groups were compared with the use of the independent *t*-test, or Mann-Whitney test if nonparametrically distributed, for the continuous variables and the chi-square test, or Fisher exact test if values less than 5 were observed or expected, for the categorical variables. Univariate logistic regression was used to identify the association between RBC transfusion and the development of VTE. In the multivariate analysis, model 2 adjusted model 1 for VTE risk scores, and model 3 adjusted model 1 for all the variables listed in Table 1 that changed the effect estimate of more than 10%. Age score and weight loss were not assessed in the model 3 as the 2 were duplicated with the variables of age group and body mass index group, respectively.

To verify our results further, a sensitivity analysis was performed using 1:1 propensity score matching (PSM) based on the patient information listed in Table 1. The nearest neighbor matching method was used and the maximum difference between propensity probabilities for matching was set at 0.05. A standardized mean difference (SMD) for each covariate was examined after applying the PSM adjustment. SMD $\leq$ 10% was considered suggestive of covariate balance. After matching, patient characteristics were again compared between the 2 groups. In the propensity score-matched subsample, univariate logistic regression analysis was performed to estimate matched odds ratios (OR) of VTE.

Furthermore, VTE score was categorized into tertiles. Then a stratified and interaction analysis was conducted according to VTE score tertiles before and after PSM. A *P* value of .05 was considered significant. All of the statistical analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation) and EmpowerStats (http://www.empowerstats.com, X&Y Solution, Inc, Boston, MA).

## Results

A total of 24,872 patients who underwent 29,003 TJA (15,447 THA and 13,556 TKA) were included in the final analysis. The patient characteristics before PSM were shown in Table 1. Of the 29,003 TJAs, 2500 procedures (8.62%) received RBC transfusion perioperatively. Patients receiving RBC transfusion had a significantly higher VTE risk scores ($48.5 \pm 34.8$ vs $36.4 \pm 29.7$, $P < .001$). A total of 302 (1.04%) patients developed a postoperative VTE within 90 days of surgery, with 38 (1.5%) patients in the transfusion group and 264 (1.0%) patients in the nontransfusion group. TKA patients had a higher rate of VTE (1.6% vs 0.6%, $P < .001$) and PE (1.5% vs 0.3%, $P < .001$) than THA patients, while there was no significant difference in DVT (0.2% vs 0.2%, $P = .77$) between TKAs and THAs.

Patients receiving perioperative RBC transfusion had significantly higher unadjusted odds of developing postoperative VTE (OR, 1.53; 95% confidence interval [CI], 1.09-2.16) and PE (OR, 1.78; 95% CI, 1.25-2.54) compared with patients never receiving an RBC transfusion (Table 2). There was no significant difference in DVT rate between 2 groups (OR, 0.58; 95% CI, 0.18-1.85). In the multivariate analyses, both in models 2 and 3, the differences were not

**Table 2**
Univariate and Multivariate Analyses of the Association Between Perioperative RBC Transfusion and the Development of Postoperative VTE, DVT, or PE.

| Models | VTE | | PE | | DVT | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| Model 1 | 1.53 (1.09, 2.16) | .014 | 1.78 (1.25, 2.54) | .002 | 0.58 (0.18, 1.85) | .355 |
| Model 2 | 1.04 (0.73, 1.49) | .824 | 1.21 (0.84, 1.75) | .308 | 0.37 (0.12, 1.22) | .103 |
| Model 3 | 0.93 (0.65, 1.34) | .703 | 1.06 (0.73, 1.55) | .752 | 0.42 (0.12, 1.39) | .154 |

Model 1: unadjusted.
Model 2: adjusting for VTE risk score.
Model 3: adjusting variables that changed the effect estimate of more than 10%.
RBC, red blood cell; VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism; OR, odds ratio; CI, confidence interval.

**Table 3**
Patient Characteristics After Propensity Score Matching.

| Variables | Nontransfusion (N = 2494) | Transfusion (N = 2494) | SMD | *P* Value |
|---|---|---|---|---|
| Patient demographics | | | | |
| Age-group (y) | | | | .607 |
| 18-44 | 128 (5.1%) | 131 (5.3%) | 0.0054 | |
| 45-64 | 1105 (44.3%) | 1070 (42.9%) | 0.0283 | |
| ≥65 | 1261 (50.6%) | 1293 (51.8%) | 0.0257 | |
| BMI (kg/m$^2$) | | | | .730 |
| <18.5 | 31 (1.2%) | 22 (0.9%) | 0.0352 | |
| 18.5-29.9 | 1373 (55.1%) | 1379 (55.3%) | 0.0048 | |
| 30-39.9 | 833 (33.4%) | 823 (33%) | 0.0085 | |
| ≥40 | 155 (6.2%) | 159 (6.4%) | 0.0066 | |
| Unknown | 102 (4.1%) | 111 (4.5%) | 0.0178 | |
| Male | 909 (36.4%) | 903 (36.2%) | 0.0050 | .883 |
| Race | | | | .139 |
| White | 1946 (78%) | 1929 (77.3%) | 0.0164 | |
| Black | 344 (13.8%) | 350 (14%) | 0.0070 | |
| Other | 22 (0.9%) | 40 (1.6%) | 0.0652 | |
| Unknown | 182 (7.3%) | 175 (7%) | 0.0109 | |
| Hip | 1188 (47.6%) | 1199 (48.1%) | 0.0088 | .777 |
| ASA ≥ 3 | 1131 (45.3%) | 1167 (46.8%) | 0.0290 | .321 |
| OP time group | | | | .117 |
| <90 | 352 (14.1%) | 359 (14.4%) | 0.0080 | |
| 90-120 | 769 (30.8%) | 742 (29.8%) | 0.0236 | |
| >120 | 1271 (51%) | 1319 (52.9%) | 0.0385 | |
| Unknown | 102 (4.1%) | 74 (3%) | 0.0609 | |
| Anticoagulants | | | | |
| Warfarin | 2307 (92.5%) | 2300 (92.2%) | 0.0106 | .749 |
| Prophylaxis options including aspirin | 427 (17.1%) | 426 (17.1%) | 0.0011 | 1.000 |
| Number of Anticoagulants | | | | .025 |
| 0 | 1 (0%) | 10 (0.4%) | 0.0770 | |
| 1 | 2249 (90.2%) | 2240 (89.8%) | 0.0120 | |
| ≥2 | 244 (9.8%) | 244 (9.8%) | 0.0000 | |
| NIS VTE score | | | | |
| Anemia | 663 (26.6%) | 673 (27%) | 0.0091 | .774 |
| Congestive heart failure | 17 (0.7%) | 18 (0.7%) | 0.0048 | 1.000 |
| Coagulation deficiency | 39 (1.6%) | 44 (1.8%) | 0.0157 | .658 |
| Lymphoma | 8 (0.3%) | 10 (0.4%) | 0.0134 | .813 |
| Fluid and electrolyte disorders | 103 (4.1%) | 97 (3.9%) | 0.0123 | .718 |
| Metastatic cancer | 16 (0.6%) | 12 (0.5%) | 0.0215 | .570 |
| Peripheral vascular disease | 28 (1.1%) | 36 (1.4%) | 0.0285 | .379 |
| Nonmetastatic solid tumor | 32 (1.3%) | 28 (1.1%) | 0.0147 | .697 |
| Chronic pulmonary heart disease | 13 (0.5%) | 12 (0.5%) | 0.0057 | 1.000 |
| History of VTE | 78 (3.1%) | 87 (3.5%) | 0.0202 | .527 |
| Myeloproliferative disorders | 7 (0.3%) | 7 (0.3%) | 0.0000 | 1.000 |
| Hypercoagulability | 9 (0.4%) | 9 (0.4%) | 0.0000 | 1.000 |
| Myocardial infarction state | 122 (4.9%) | 121 (4.9%) | 0.0019 | 1.000 |
| Varicose veins | 4 (0.2%) | 9 (0.4%) | 0.0393 | .267 |
| Fracture | 56 (2.2%) | 51 (2%) | 0.0138 | .696 |
| Inflammatory bowel | 2 (0.1%) | 6 (0.2%) | 0.0401 | .289 |
| Sepsis | 3 (0.1%) | 2 (0.1%) | 0.0127 | 1.000 |
| PJI | 5 (0.2%) | 4 (0.2%) | 0.0094 | 1.000 |
| Atrial fibrillation | 127 (5.1%) | 150 (6%) | 0.0403 | .175 |
| Stroke | 4 (0.2%) | 5 (0.2%) | 0.0094 | 1.000 |
| Apnea | 155 (6.2%) | 157 (6.3%) | 0.0033 | .953 |
| Bilateral | 637 (25.5%) | 626 (25.1%) | 0.0101 | .745 |
| Not primary THA | 1306 (52.4%) | 1295 (51.9%) | 0.0088 | .777 |

SMD, standardized mean difference; BMI, body mass index; ASA, American Society of Anesthesiologists; NIS, nationwide inpatient sample; VTE, venous thromboembolism; PJI, periprosthetic joint infection; THA, total hip arthroplasty; OP, operative time.

significant between the 2 groups for the incidences of DVT (in model 2: OR, 1.04; 95% CI, 0.73-1.49; in model 3: OR, 0.93; 95% CI, 0.65-1.34), PE (in model 2: OR, 1.21; 95% CI, 0.84-1.75; in model 3: OR, 1.06; 95% CI, 0.73-1.55), or VTE (in model 2: OR, 0.37; 95% CI, 0.12-1.22; in model 3: OR, 0.42; 95% CI, 0.12-1.39).

In the sensitivity analysis using 1:1 PSM, we generated a subsample of 2494 TJAs that received any perioperative RBC transfusion and 2494 matched controls that did not receive any RBC transfusions. Patient characteristics in this sensitivity analysis were shown in Table 3. The quality of PSM was considered balanced, with all SMD < 10%. In the univariate analysis, RBC transfusion was not associated with increased odds of developing VTE (propensity-matched OR, 1.2; 95% CI, 0.7-1.8), PE (propensity-matched OR, 1.2; 95% CI, 0.8-2.0), or DVT (propensity-matched OR, 0.5; 95% CI, 0.1-2.0) compared with patients who never received a transfusion (Table 4).

When stratified by VTE risk score tertiles, RBC transfusion was also not associated with an increased risk of VTE in any tertile before or after PSM. Additionally, the interaction analysis suggested that there was no interaction between VTE risk score and RBC transfusion in relation to VTE (Fig. 1).

**Table 4**
Univariate Analysis of the Association Between Perioperative RBC Transfusion and the Development of Postoperative VTE, DVT, or PE After Matching.

| Perioperative RBC Transfusion | VTE | | PE | | DVT | |
|---|---|---|---|---|---|---|
| | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value | OR (95% CI) | *P* Value |
| | | .550 | | .383 | | .326 |
| No | 1 (Reference) | | 1 (Reference) | | 1 (Reference) | |
| Yes | 1.2 (0.7, 1.8) | | 1.2 (0.8, 2.0) | | 0.5 (0.1, 2.0) | |

RBC, red blood cell; VTE, venous thromboembolism; DVT, deep vein thrombosis; PE, pulmonary embolism; OR, odds ratio; CI, confidence interval.

## Discussion

While current literature has investigated the mechanistic role of RBC's involvement in developing VTE status post perioperative blood transfusion [5], no study has explored this association in a clinical capacity. There is an apparent correlation between VTE risk and perioperative RBC transfusion. However, we do not believe transfusion itself to be an independent risk factor for developing VTE. Our study suggests the adverse outcomes after perioperative RBC transfusion may be secondary to the condition of the individual patient, for example, congestive heart failure or history of VTE.

This study used PSM and multivariate analysis to examine the independent association between VTE and perioperative RBC transfusion following primary TJA. The advantages of this study are that we were able to obtain data from a consistent patient population in our institutional large-volume arthroplasty database, which granted us access to hospital-level information and numerous potentially confounding variables, such as patient demographics, comorbidities, and procedural details. By using this detailed patient data, we were able to accurately identify and account for confounding variables in statistical analysis. Our data suggest that there are independent risk factors associated with the development of VTE after TJA, but that RBC transfusion is not included among these factors. However, patients receiving RBC transfusion were more likely to have 1 or more of these risk factors, likely explaining the observed association between VTE and transfusions in the unadjusted model.

Similar to our study, Hart et al [15] performed a multivariate logistic regression analysis using data from a large national registry to assess the association between perioperative RBC transfusion and 30-day incidence of complications, including VTE, in patients following THA and TKA. Their study did not find a strong association between perioperative RBC transfusion and VTE 30 days after THA or TKA when controlling for preoperative risk factors. Additionally, Frisch et al also found no statistical difference in the rates of DVT between transfused and nontransfused patients status post THA and TKA [16]. Both of these studies offer additional support that transfusion is not an independent risk factor for VTE in patients status post TJA.

In contrast to our study, Goel et al identified an increased incidence of VTE following surgery [5]. This study evaluated data obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Although the ACS-NSQIP database is a nationally validated surgical outcome database, the analysis performed in this study has significant limitations that should be noted. The ACS-NSQIP contains data from multiple hospitals throughout the nation, all of which have their own VTE prophylaxis guidelines and varying adherence policies; therefore, it is difficult to accurately evaluate the incidence of VTE after perioperative RBC transfusions. Also, the ACS-NSQIP database does not allow for the analysis of hospital-level information, such as accounting for patients with a history of chronic DVT and other potentially confounding variables, which may increase the risk of developing VTE.

Although we found no independent risk associated with perioperative RBC transfusion, current guidelines suggest placing an emphasis on the preoperative assessment of the patient and risk-benefit of transfusion, as well as the use of adjuvant medications to limit perioperative bleeding and secondary complications [4]. Perioperative RBC transfusions may be necessary in order to achieve adequate hemoglobin levels and maintain the blood's oxygen-carrying capacity, which may be negatively impacted by the substantial blood loss that can be associated with TJA procedures [17,18]. While hemoglobin levels are important, the decision to transfuse should be considered to be multifactorial [19,20].

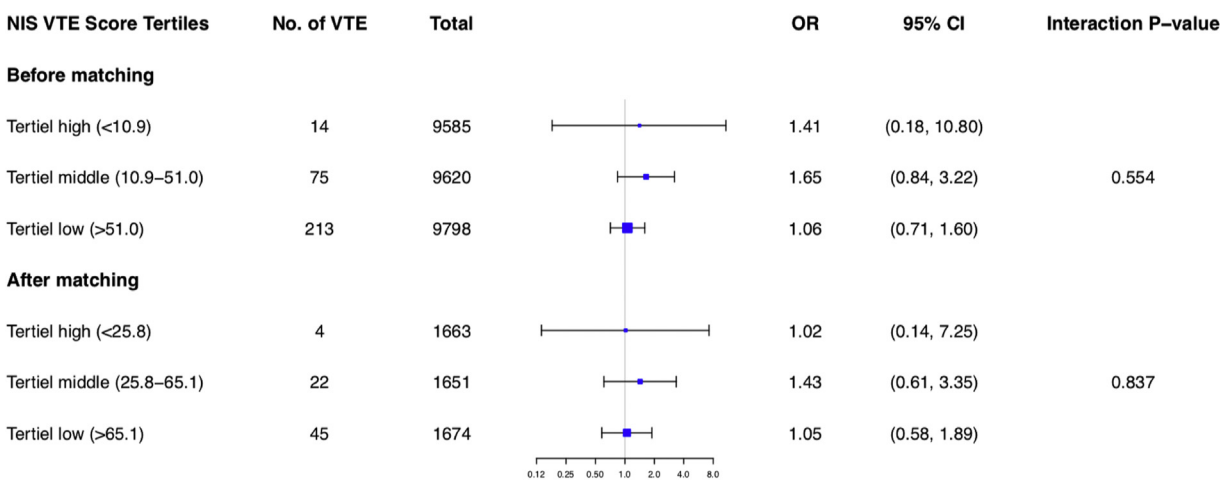


**Fig. 1.** Association between perioperative RBC transfusion and the development of postoperative VTE stratified by NIS VTE score tertiles. RBC, red blood cell; VTE, venous thromboembolism; NIS, nationwide inpatient sample; OR, odds ratio; CI, confidence interval.

There are several limitations to be considered with this study. As with most observational studies, our statistical outcomes are dependent on the accuracy of data extraction from the medical records reviewed during the data collection process. Additionally, patients with asymptomatic VTE or VTE that occurred greater than 90 postoperative days could not be measured in our study. Furthermore, patients readmitted to hospitals outside our institution for DVT/PE may not have been captured through query of our institutional database; however, we did review outpatient and telephone encounter notes to identify these patients. Another limitation is that the TJA protocol has changed over time, including pain management and thromboprophylaxis. Finally, while we attempted to account for all potentially confounding variables, there may exist additional risk factors which were not included in our analysis. One potential confounding variable is the use of tranexamic acid, which was not included in our study.

There are very few studies that have evaluated the perioperative VTE risk associated with transfusion in patients following TJA. More single-institution database studies, with large sample sizes, should be performed where additional confounders can be accounted for and the independent risk associated with receiving perioperative RBC transfusion further evaluated. This will help improve clinical decision-making and potentially reduce the risk of the unwanted secondary complications associated with perioperative RBC transfusion. It is also important to establish a universal transfusion criterion for orthopedic surgeons so they can easily identify transfusion triggers and improve perioperative outcomes [21]. Future, high-quality prospective studies determining risks associated with perioperative RBC transfusion may be beneficial to minimize the potential errors associated with retrospective observational database analysis.

## Conclusion

Our study suggests perioperative RBC transfusions do not increase the risk of symptomatic VTE status post TJA up to 90 postoperative days when adjusting for VTE risk scores and confounding variables. Perioperative RBC transfusion may be safely administered if indicated following THA and TKA. Appropriate prophylaxis should be administered to patients regardless of RBC transfusion using valid VTE risk measurements and recognizing their potentially high-risk comorbidities. Considering the inherent limitations of retrospective studies, additional evidence may be required to definitively determine the risks associated with perioperative RBC transfusions in patients undergoing TJA. However, this study presents strong evidence that there does not appear to be an increased risk of VTE associated with perioperative RBC transfusion in patients undergoing primary TJA.

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