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Risk Factors for Reaching the Post-Operative Transfusion Trigger in a Community Primary Total Knee Arthroplasty Population

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ABSTRACT

Background: Little data exist to evaluate an individual's pre-operative risk of blood transfusion following total knee arthroplasty (TKA). Our aim is to identify the risk factors associated with reaching the transfusion trigger of Hb <8 g/dL (TT8) following surgery and how perioperative tranexamic acid (TXA) affects that outcome.

Methods: Using a retrospective cohort study design, routine, unilateral TKAs performed between 2011 and 2013 in 19 hospitals were reviewed. Patients hospitalized ≤1 day or ≥4 days were excluded. Demographic data, clinical characteristics, and potential confounders were included in statistical models. Data were abstracted from electronic clinical and utilization databases. The main outcome was the risk of reaching the TT8. The primary exposure was use of single dose intravenous TXA. Logistic regression was used to model the adjusted association between TXA usage and post-operative risk of reaching TT8.

Results: A total of 10,518 TKAs met criteria; 2566 (24.3%) received TXA (+TXA). The proportion that reached the TT8 was 2.1% for + TXA and 5.3% for −TXA ($P < .0001$). Pre-operative Hb levels were associated with increasing odds of reaching the TT8. Increasing age was weakly associated with this outcome. The odds of reaching the TT8 were lower for patients who had received TXA, had increasing body mass index, and surgical duration in the third quartile.

Conclusion: Not receiving TXA within 24 hours of TKA and pre-operative Hb levels <13 g/dL were independently associated with the odds of reaching the post-operative TT8 following a primary TKA.

Total knee arthroplasty (TKA) surgery reduces pain and restores function but is associated with significant blood loss. A transfusion, when needed, can expose the patient to the risks associated with blood borne pathogens and transfusion reactions [1]. As a result, more stringent thresholds for transfusion of 7-8 g/dL of hemoglobin (Hb) have been recommended [2], and anti-thrombolytic agents such as tranexamic acid (TXA) have become increasingly popular in arthroplasty surgery as they reduce the rate of post-operative blood transfusion [3–8]. However, the decision to transfuse a patient following surgery can vary significantly from one clinical context to the next. This makes the reported transfusion rates following TKA a difficult outcome to use when trying to predict an individual patient's pre-operative risk of needing a blood transfusion, or the impact of an anti-thrombolytic on that risk.

We suggest that a more clinically relevant outcome, applicable across most clinical settings, would be to quantify the risk of reaching a specific post-operative Hb level above which a blood transfusion is rarely considered. This Hb level is commonly referred to as the post-operative transfusion trigger (TT) and is an objective endpoint. Understanding what pre-operative variables are associated with the risk of reaching the TT, and how an intervention such as the use of TXA can impact that risk, would provide a helpful and clinically useful parameter for individualized pre-operative risk

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assessment. For the purposes of this study, we used the conservative Hb level of 8 g/dL as the threshold value.

The aim is therefore to identify which pre-operative variables are associated with an individual's adjusted risk of reaching the post-operative TT of Hb 8 g/dL (TT8) and the impact of a single, perioperative dose of TXA on that risk.

Materials and Methods

Study Population

A retrospective cohort study was conducted in a large community-based setting. The primary exposure of interest was a single dose of intravenous TXA administered within 24 hours of the procedure. Secondary clinical and demographic patient characteristics including the use of prophylactic anticoagulants (aspirin, low molecular weight heparin [LMWH], factor Xa inhibitors, heparin, and warfarin) and surgical duration were also evaluated. This study collected data from electronic medical records. The source population for this study was all patients who had undergone a primary, unilateral TKA procedure from January 1, 2011 through December 31, 2013 in a single region of a large integrated healthcare system comprising 19 separate hospitals. Initial cases were identified from electronic databases for operating room (OR) events linked to principal International Classification of Diseases Version 9 (ICD-9) procedure code 81.54 (n = 15,306). The time period selected includes patients treated at multiple hospitals that do, however, share some practice patterns such as the region wide adoption of conservative transfusion thresholds and rapid functional recovery programs with short lengths of stay. Cases were included if the patient was enrolled in the health plan during the month prior through the month after the TKA event; had a post-operative length of stay (LOS) >1 and <4 days, a pre-operative hemoglobin (pHb) drawn within 8 weeks prior to surgery, and at least 1 post-operative Hb drawn during the hospitalization. A total of 12,288 TKA cases met these criteria; and among these, an additional 95 cases were excluded because it could not be determined if TXA was administered during the hospital stay. From the remaining 12,193 unique TKA events, if a member had a second TKA during the timeframe of the study, only the first TKA was included to avoid intra-subject correlation and immortal time bias [9]. This left 11,086 patients who underwent a primary, unilateral TKA between 2011 and 2013, inclusive. Among the subset of patients who received TXA, 568 were excluded because more than one dose was given within 24 hours of the TKA procedure (n = 194) or the medication was administered topically instead of intravenously (n = 374). The final cohort consisted of 10,518 TKA cases of which 2556 (24.3%) received TXA and 7962 did not (Fig. 1).

Data Sources

All data for the study were obtained from electronic clinical and administrative databases. TXA administration data, including dose and route, were obtained from the medication administration record linked to the hospital encounter. Only patients receiving intravenous doses administered within 24 hours of surgery were included in the TXA group. Data for deep vein thrombosis (DVT) prophylaxis therapy were also identified from the medication administration records. Agents relevant to DVT prophylaxis included factor Xa inhibitors, LMWH, aspirin (ASA), heparin, and Coumadin. If one or more of these medications was administered at any time during the hospitalization for the index TKA, then it was assumed that the patient received some form of DVT prophylaxis. For analytic purposes, mutually exclusive categories were created for LMWH, Coumadin, aspirin, and other agents (which included heparin, factor Xa inhibitors), where >1 agent was received during the hospital stay. Demographic data for birth date, gender, race/ethnicity, height, and weight were obtained from electronic data sources. Age was computed at the time of TKA event. Data for American Society of Anesthesiologists (ASA) score, surgical duration (in minutes calculated from incision start to incision closed times), and OR entry and departure times were extracted from the OR databases. Principal admitting diagnosis and hospital LOS were obtained from hospital discharge records. The Laboratory Utilization Reporting System was the source of all Hb and creatinine measurements. As with pHb, serum creatinine values measured up to 8 weeks prior to surgery were collected and the one closest to (but prior to entering the OR) was selected. All post-operative Hb measurements were extracted and categorized according to the day of the hospital stay relative to when the TKA procedure was performed (eg, day of surgery [post-operative day 0] included all measurements obtained after leaving the OR but on the same day as the TKA surgery, etc.). Glomerular filtration rate (GFR) was estimated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [10].

Statistical Analysis

Reaching the TT8 was defined as having an Hb measurement of <8.0 g/dL at any time during the post-operative period. The principal exposure, TXA administration, was defined as any single intravenous dose given within 24 hours of the TKA procedure. Bivariate analyses were conducted to compare demographic and clinical characteristics by both the principal exposure (TXA) and outcome (reaching the TT8). Chi-squared tests were used to compare categorical variables and t-tests and non-parametric tests (Wilcoxon-Mann-Whitney test) for continuous variables.

Logistic regression modeling was used to estimate odds ratios and 95% confidence intervals of reaching the TT8. In addition to TXA exposure (any vs none), other variables examined were age (modeled as categories <55, 55-64, 65-74, and ≥75 years, and scaled per 10-year increase), gender, body mass index (BMI entered as categories <25.0, 25.0-29.0, 30.0-34.9, ≥35.0 kg/m^2), estimated GFR (eGFR; as categories for stage of chronic kidney disease <60, 60-89, ≥90 mL/min per 1.73 m^2, and unknown), ASA rating (<3 and ≥3), pHb (entered as categories <11.0, 11.0-11.9, 12.0-12.9, ≥13.0 g/dL), race/ethnicity (White, African American, Asian/Pacific Islander, Hispanic, Other/unknown), surgical duration (as quartiles 20-74, 75-88, 89-103, 104-344 minutes), and type of DVT prophylaxis (LMWH, Coumadin, aspirin, and other). Models were developed and examined by adding each covariate of interest individually and evaluating the change in the OR for the main exposure (TXA administration). In addition, models were developed by adding covariates in a stepwise manner and evaluating the change in OR of the principal exposure and each factor included up to that point. A final model was selected that included covariates which were associated with the principal exposure and/or outcome or were clinically relevant. Besides TXA status, the final model included age, gender, race/ethnicity, BMI, pHb, surgical duration, ASA rating, eGFR (as CKD categories), and type of DVT prophylaxis.

Descriptive statistics comparing the 3162 unique patients who had a TKA between 2011 and 2013 but who were excluded from the final analytic cohort of 10,518 cases were obtained to identify any potential bias in our analysis.

All analyses were conducted using SAS 9.3 (SAS Institute, Inc, Cary, NC). The Institutional Review Board approved this study with waiver of consent.