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Predicting 30-Day Venous Thromboembolism Following Total Joint Arthroplasty: Adjusting for Trends in Annual Length of Stay

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A R T I C L E I N F O

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A B S T R A C T

Background: Venous thromboembolism (VTE) following total hip arthroplasty and total knee arthroplasty (TKA) is linked to immobility, and preoperative prediction remains difficult. We aimed to evaluate whether annual mean length of stay (LOS) is associated with the incidence of VTE and develop a generalizable machine learning model to preoperatively predict the incidence of symptomatic VTE following total hip and TKA using National Surgical Quality Improvement Program.
Methods: Annual incidence of 30-day postoperative VTE, deep vein thrombosis, and pulmonary embolism was calculated over 6 years and tested for trend. Correlation between annual VTE rates and mean LOS was calculated. Predictive models (logistic regression, random forest, and XGBoost) were trained and tested based on year of surgery with different oversampling algorithms used to address data imbalance.
Results: A total of 498,314 patients were included, with 0.88% developing a VTE within 30 days. VTE rates decreased from 1.11% in 2014 to 0.76% in 2019 ($P < .001$). There was a strong correlation between the yearly incidence of VTE, pulmonary embolism, and deep vein thrombosis and mean LOS ($r = 0.96$, 0.87, and 0.98, respectively). Univariate analysis demonstrated that TKA, inpatient setting, American Society of Anesthesiologists classification, and various patient comorbidities were significantly associated with VTE. The logistic regression model trained on all data with a balanced loss scoring function performed the best (area under the curve = 0.600).
Conclusions: This study revealed declining VTE rates strongly correlated to decreasing postoperative LOS and identified patient and surgery-specific factors associated with VTE risk. Development of more accurate machine learning models for VTE prediction may improve risk stratification, prevention, and monitoring for arthroplasty patients.

Introduction

Venous thromboembolism (VTE), encompassing deep vein thrombosis (DVT) and pulmonary embolism (PE), is a dreaded complication following total hip and knee arthroplasty (THA and TKA, respectively). Despite attempts to reduce these complications with routine anticoagulation, compression devices, and early mobilization, they still occur in approximately 0.6%-1.5% of cases. [1,2] As around 1.6 million total joint arthroplasty (TJA) procedures are performed annually in the United States and Canada, this complication affects a large number of patients. [3,4] These complications necessitate prolonged anticoagulant use and can result in post-thrombotic syndrome, chronic pulmonary hypertension, persistent perfusion defects, or death. [5] Furthermore, they are also associated with worse patient-reported outcomes. [6,7] The ability to accurately predict these events preoperatively may lead to

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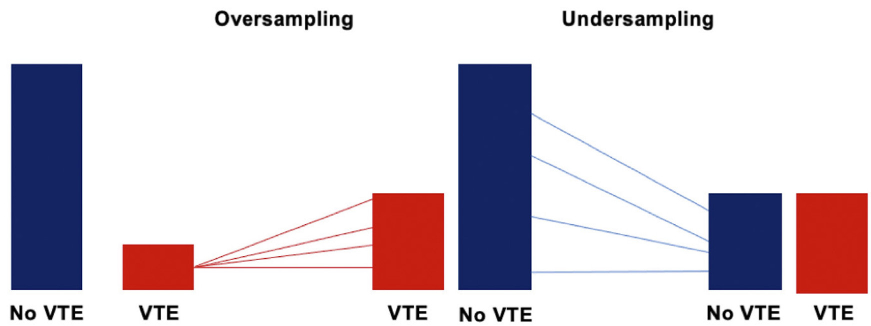

Figure 1. Representation of oversampling (10×) with adaptive synthetic (ADASYN) or support vector machine-synthetic minority oversampling technique (SVM-SMOTE) algorithms, followed by undersampling.

improved risk stratification, patient counseling, postoperative monitoring, and prevention practices to reduce the incidence. [8]

Prolonged immobility has been identified as a significant risk factor for developing VTE. [9] Immobility leads to venous stasis and predisposition for the initiation of the coagulation cascade. [10] Moreover, regular mobility and exercise have been shown to reduce hemostatic and inflammatory factors. [11] Early postoperative mobilization and physiotherapy protocols have been developed to facilitate earlier discharge. [2] Earlier mobilization, along with improvements in perioperative pain management and blood conservation strategies, has led to decreased postoperative length of stay (LOS). [12] LOS following TJA has been decreasing with a rapid shift toward outpatient or same-day discharge procedures. [13,14] Shorter LOS has been associated with a decreased risk of postoperative VTE. [15] However, the trend of VTE rates following widespread implementation of rapid discharge protocols at the population level has not been evaluated.

Various patient characteristics, including age, sex, and certain medical comorbidities, including specific renal, cardiac, or respiratory conditions, have been shown to be associated with increased VTE risk. [16] Furthermore, surgery-specific factors including longer duration of surgery and need for blood transfusion, have also been shown to be associated with an increased risk of VTE. [16-18] Despite this, few studies have used these factors to predict the incidence of VTE after primary TJA surgeries using machine learning (ML) techniques. [19,20] These studies include a combination of primary and revision procedures and some features that may not be known preoperatively. Overall, there is a lack of studies that have applied these techniques to predict VTE after primary TJA.

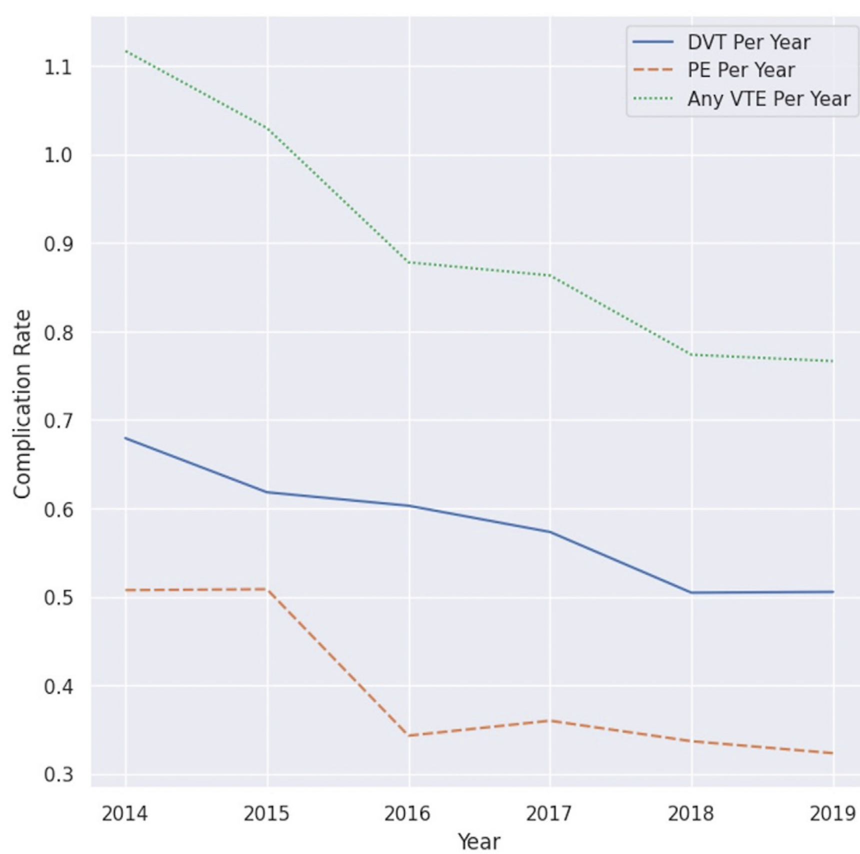

Figure 2. Rates of venous thromboembolism in patients undergoing total hip or knee arthroplasty from 2014 to 2019.

Table 1
Annual number and incidence of overall VTE, DVT, and PE events and mean annual length of stay.

Year of TKA/THA	VTE events (n)	VTE rate	DVT events (n)	DVT rate	PE events (n)	PE rate	Mean length of stay (days)
2014	592	1.12%	360	0.68%	269	0.51%	2.86
2015	733	1.03%	440	0.62%	362	0.51%	2.67
2016	750	0.88%	515	0.61%	293	0.34%	2.41
2017	789	0.86%	524	0.57%	329	0.36%	2.25
2018	742	0.77%	484	0.50%	323	0.34%	1.90
2019	799	0.77%	527	0.50%	337	0.32%	1.74

We hypothesized that reduced LOS over time is correlated with reduced rates of VTE due to a reduction in patient immobility and that this can be predicted. The aims of this study were to 1) identify if there is an association between annual incidence of 30-day VTE events and annual postoperative LOS following primary TJA; and 2) develop an ML model to preoperatively predict 30-day VTE for patients undergoing primary TJA accounting for annual trends in VTE rates.

Material and methods

Data source

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database was used. This is a large, prospective, and anonymized database that collects data from over 600 hospitals in the United States and Canada. [21] The database contains information on patient factors such as comorbidities, preoperative laboratory values, and surgical outcomes. All primary THA and TKA surgeries over 6 years, from the period of 2014 to 2019, were identified using appropriate Current Procedural Terminology codes (27130 and 27447, respectively).

Outcomes and statistical analysis

Outcomes included 30-day postoperative symptomatic DVT, PE, and any VTE event. Within NSQIP, these are defined as a blood clot or thrombus within the superficial or deep venous system of the leg (DVT) or pulmonary artery (PE) confirmed by duplex, venogram, computed tomography scan, or ventilation-perfusion scan that were treated with anticoagulation. The NSQIP database has good accuracy for tracking VTE events compared to institutional and administrative databases. [22,23] Annual incidence of each outcome was calculated. A Cochran-Armitage test for trend was utilized to detect a change in rates of VTE over time. The association between the annual rate of VTE, DVT, and PE and the mean annual LOS following TJA was determined using the Pearson correlation coefficient.

Patient factors including age, sex, race, body mass index, medical comorbidities, and preoperative laboratory values were collected. Additionally, surgical factors such as anesthesia type and admission type were included (Supplementary Table 1). Of note, postoperative chemoprophylaxis is unrecorded in NSQIP and was therefore an unknown key variable. Univariate analysis between each outcome and presence of VTE was performed using Student's *t*-test or odds ratio (OR) for continuous and categorical variables, respectively.

Machine learning model development

Models were trained to predict a VTE event (DVT and/or PE). All features listed in Supplementary Table 1 were included in the models. Notably, LOS was excluded as the purpose of the models was to predict the risk of VTE based on known preoperative factors. Patients with unrecorded outcomes (n = 2,862, 0.6%) were excluded. Features with 0%-25% missing data were multiply imputed using all other features. Data were then normalized using a robust scaler algorithm. [24]

To adjust models for the trend in VTE rate, data was split by year, with training and validation of models using procedures from 2014 to 2018 and testing conducted on TJAs from 2019. This ensures that the models generalize to future, unseen data and accounts for the trend of VTE incidence over time. This ensures a model that more accurately represents real-world performance. Model training and hyperparameter tuning were performed using 5-fold cross-validation. A multivariate logistic regression model was trained as well as a random forest and XGBoost model. [25] Model performance was evaluated using area under the curve (AUC) score, accuracy, precision, recall, and F1-score. The percentage of patients the model predicted to develop a VTE was also analyzed.

As VTE occurred in less than 1% of cases, data imbalance was addressed using a combination of oversampling and undersampling techniques. [26] Oversampling involves increasing the number of samples in the underrepresented class (patients with VTE), while undersampling involves reducing the number of samples in the overrepresented class (no VTE). These techniques were

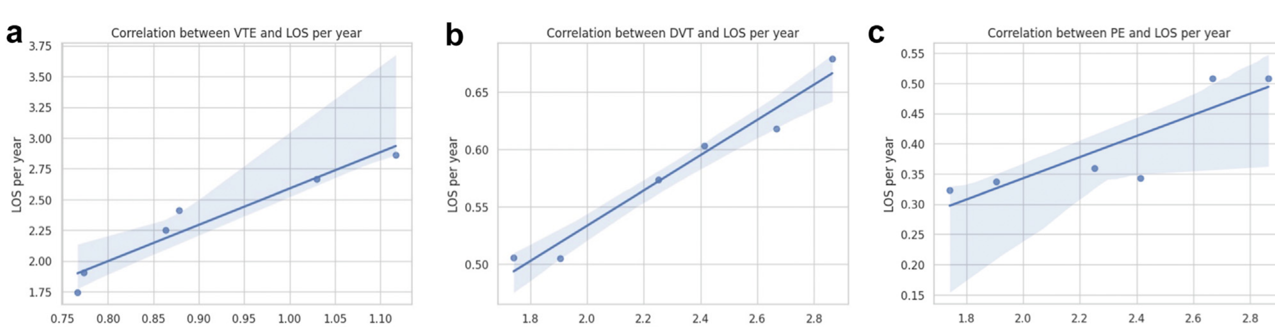

Figure 3. Correlation between annual mean postoperative length of stay following total joint arthroplasty and annual rates of (a) venous thromboembolism, (b) deep vein thrombosis, and (c) pulmonary embolism.

utilized to balance the training dataset and improve the performance of the models. Oversampling was performed using an adaptive synthetic (ADASYN) oversampling algorithm and a support vector machine synthetic minority oversampling technique (SVM-SMOTE) algorithm. [27,28] Ten times oversampling of the minority class was performed, followed by complete undersampling (Fig. 1). All analysis was performed using Python 3.9 (Python Software Foundation, www.python.org).

Results

A total of 498,314 patients were included, 308,175 (61.8%) TKAs and 190,139 (38.2%) THAs. Of the patients, 58.8% were female, and the most common admission type was inpatient (93.1%). Most of the patients had no history of diabetes (84.0%), chronic obstructive pulmonary disorder (COPD) (96.5%), or dyspnea (94.9%). Overall, 4405 (0.88%) developed a postoperative VTE by 30 days, 2850 (0.57%) DVTs, and 1913 (0.38%) PEs.

Trends of venous thromboembolism and length of stay

The rates of 30-day postoperative VTE following TJA decreased from 1.11% in 2014 to 0.76% in 2019 ($P < .001$) (Fig. 2). This is a result of a decrease in both DVT and PE rates (Table 1). Over this 6-year period, there was a year-over-year decrease in the mean LOS from 2.86 to 1.74 days (Table 1). There was a strong correlation between

Table 2
Univariate analysis for all categorical features.

Variable	Category	N (%)	Odds ratio (95% confidence interval)	*P*-value
Sex	Female	293,091 (58.8)	-	-
	Male	205,219 (41.2)	0.96 (0.90-1.01)	.156
	Nonbinary	4 (0)	-	-
Race	White	361,587 (72.6)	0.96 (0.63-1.48)	.870
	Unknown/not reported	84,380 (16.9)	1.33 (0.73-1.75)	.575
	Black or African American	39,228 (7.9)	1.36 (0.88-2.11)	.168
	Asian	9085 (1.8)	0.79 (0.48-1.29)	.346
	American Indian or Alaska Native	2427 (0.5)	-	-
	Native Hawaiian or Pacific Islander	1608 (0.3)	1.15 (0.6-2.21)	.672
Principle Operation	Total knee arthroplasty (CPT 27447)	308,175 (61.8)	2.08 (1.93-2.23)	**<.001**
	Total hip arthroplasty (CPT 27130)	190,139 (38.2)	-	
Patient setting	Inpatient	463,926 (93.1)	-	
	Outpatient	34,388 (6.9)	0.78 (0.68-0.89)	**<.001**
Anesthesia type	General	217,672 (43.7)	1.33 (0.86-2.07)	.204
	Spinal	193,801 (38.9)	1.23 (0.79-1.92)	.350
	MAC/IV Sedation	75,140 (15.1)	1.14 (0.73-1.79)	.553
	Regional	8209 (1.6)	1.20 (0.73-1.97)	.479
	Epidural	2846 (0.6)	-	-
	Unknown/other	646 (0.1)	2.96 (0.39-22.51)	.294
Diabetes	No	418,826 (84)	0.88 (0.76-1.02)	.091
	Noninsulin	60,730 (12.2)	1.01 (0.86-1.19)	.885
	Insulin	18,757 (3.8)	-	-
Smoking	No	450,014 (90.3)	0.74 (0.66-0.82)	**<.001**
	Yes	48,300 (9.7)	-	-
Dyspnea	No	473,089 (94.9)	0.45 (0.27-0.73)	**.001**
	Moderate exertional	24,386 (4.9)	0.68 (0.41-1.12)	.129
	At rest	839 (0.2)	-	-
Functional status	Independent	490,514 (98.4)	-	-
	Partially dependent	5454 (1.1)	1.32 (1.03-1.69)	**.031**
	Unknown	2180 (0.4)	1.41 (0.97-2.07)	.075
	Totally dependent	167 (0)	1.37 (0.34-5.51)	.661
Dialysis	No	497,467 (99.8)	-	-
	Yes	847 (0.2)	1.48 (0.81-2.68)	.20
Disseminated Cancer	No	497434 (99.8)	-	-
	Yes	880 (0.2)	1.82 (1.07-3.08)	**.027**
History of COPD	No	480,643 (96.5)	-	-
	Yes	17,671 (3.5)	1.38 (1.20-1.56)	**<.001**
History of CHF	No	496,702 (99.7)	-	-
	Yes	1612 (0.3)	1.71 (1.12-1.60)	**<.001**
Hypertension requiring medication	Yes	303,402 (60.9)	1.17 (1.10-1.25)	**<.001**
	No	194,912 (39.1)	-	-
Renal failure	No	498,182 (100)	-	-
	Yes	132 (0)	2.60 (0.83-8.18)	.101
Steroid use for chronic condition	No	480,458 (96.4)	-	-
	Yes	17,856 (3.6)	1.21 (1.04-1.40)	**.011**
Bleeding disorder	No	488,977 (98.1)	-	-
	Yes	9337 (1.9)	1.74 (1.47-2.06)	**<.001**
Preoperative transfusion of $\geq$ 1 unit of whole/packed RBCs in 72 hours prior to surgery	No	498,126 (100)	-	-
	Yes	188 (0)	3.07 (1.26-7.45)	**.013**
ASA score	1	12,487 (2.5)	-	-
	2	248,691 (49.9)	1.16 (0.93-1.44)	.191
	3	228,876 (45.9)	1.49 (1.20-1.86)	**<.001**
	4	8241 (1.7)	1.69 (1.25-2.27)	**.001**
	5	20 (0)	-	-

CPT, Current Procedural Terminology; CHF, congestive heart failure; RBC, red blood cell; ASA, American Society of Anesthesiologists.
Bold values represent statistical significance between groups.

Table 3
Univariate analysis for all continuous features.

Variable	No VTE	VTE	*P*-value
	Mean (SD)	Mean (SD)	
Height (in)	65.1 (10.9)	65.3 (10.2)	.463
Weight (lbs)	197.0 (48.3)	201.3 (48.0)	**<.001**
Sodium	139.7 (2.7)	138.0 (2.5)	.152
Blood urea nitrogen	17.9 (6.8)	18.4 (8.2)	**<.001**
Creatinine	0.9 (0.4)	0.9 (0.5)	.225
Albumin	4.1 (0.4)	4.1 (0.4)	.155
Bilirubin	0.6 (0.4)	0.6 (0.4)	.132
Glutamic-oxaloacetic transaminase	23.5 (12.9)	22.8 (11.0)	.233
Alkaline phosphatase	80.9 (29.0)	80.1 (29.0)	.161
White blood cell count	7.0 (2.2)	7.0 (2.1)	.612
Hematocrit	41.2 (4.0)	41.1 (4.2)	.195
Platelet count	247.0 (67.5)	245.0 (71.0)	.932
Prothrombin time	29.4 (4.9)	29.0 (4.4)	.814
INR	1.0 (0.3)	1.0 (0.4)	.061

INR, international normalized ratio.
Bold values represent statistical significance between groups.

the yearly rate of VTE and LOS (Pearson correlation coefficient: 0.96, $P = .002$) (Fig. 3a). Similarly, there was a strong correlation between yearly DVT and PE rates and LOS (Pearson correlation coefficient: 0.98, $P < .001$, Pearson correlation coefficient: 0.87, $P = .024$, respectively) (Fig. 3b and c).

Univariate analysis

Univariate analysis showed that American Society of Anesthesiologists classification scores ≥3 were significantly associated with VTE (OR: 1.49-1.69; $P < .001$) as well as patients undergoing TKA (OR: 2.08, $P < .001$) and preoperative transfusion (OR: 3.07; $P = .013$) (Table 2). A significant association between VTE and various medical conditions was also identified, including COPD (OR: 1.38, $P < .001$), congestive heart failure (OR: 1.71, $P < .001$), hypertension (OR: 1.17, $P < .001$), bleeding disorders (OR: 1.74, $P < .001$), and metastatic cancer (OR: 1.82, $P = .027$). Patient sex was not significantly associated with VTE (Table 2). Analysis of continuous variables revealed significantly greater patient weight and blood urea nitrogen values in patients who developed a VTE (Table 3).

VTE prediction models

The training and validation set consisted of 394,724 patients, while the testing set consisted of 103,590 patients. The results of all ML models are presented in Table 4. Results during training and validation were better than the out-of-sample test set (surgeries performed in 2019) (Supplementary Table 2).

The best overall model in terms of receiver operating curve AUC score was the logistic regression model (Fig. 4). Using oversampling, the SVM-SMOTE models had a better receiver operating curve AUC score but lower overall accuracy compared to the models developed using ADASYN. The model with the best recall, or sensitivity, was the XGBoost model using SVM-SMOTE oversampling at 64.3%. This model also predicted the greatest number of patients to develop a VTE (58.3%) (Table 4). The most important predictive features from the logistic regression model were preoperative transfusion status, history of metastatic cancer, race, history of a bleeding disorder, age, and body mass index.

Discussion

The aims of this study were to identify if the incidence of VTE events, including DVTs and PEs, has decreased with decreasing LOS following TJA and if these events can be preoperatively predicted. The key findings are that the rates of 30-day VTE following TJA have decreased from 2014 to 2019, and this was highly correlated with a decrease in the mean annual postoperative LOS. We believe this is the first time this correlation between decreasing LOS and VTE rates has been identified. This study also attempted to develop and internally validate a generalizable ML model to predict the incidence of symptomatic VTE following primary TJA (accounting for procedure type of THA or TKA) on unseen future data. This is an important step toward improving risk stratification, counseling, prevention practices, and monitoring. In this study, we used one of the largest surgical datasets, the ACS-NSQIP database, to train and internally validate our models. Using a database like this is integral to creating generalizable models that account for trend changes in practice patterns. While most ML models split their data samples into training and testing sets randomly, we split ours temporally by year of surgery to account for changes in VTE incidence and practice patterns. Despite this, a generalizable model to accurately predict these events remains difficult.

The shorter LOS is a result of a combination and quicker discharge for inpatient TJA and the rise in same-day discharge TJA, with 36.4% of Medicare TKAs performed as same-day in 2019. [29] The shorter length of in-hospital stay following TJA has demonstrated significant cost savings and improved patient satisfaction. [30-32] Our study demonstrated that a shorter LOS may also confer a safer postoperative recovery due to the decreasing rate of postoperative VTE events, likely related to the widespread adoption of rapid recovery pathways and early mobilization. Early physiotherapy and discharge reduces immobilization, likely explaining the decrease in VTE rates. [33] Early discharge home likely reduce immobilization as patients are “forced” to mobilize, for example, to the bathroom or to eat, compared to being in hospital. We believe VTE rates will continue to fall with decreasing LOS; however, this phenomenon can only continue until the number of patients undergoing same-day discharge TJA stabilizes, at which point we believe VTE rates will also stabilize.

Table 4
Logistic regression model results on test set using cross-entropy scoring loss.

Model	Accuracy	F1 score	Precision	Recall	ROC AUC	Log loss	Predicted VTE percent
Logistic regression	0.780	0.022	0.011	0.321	0.600	7.59	21.7%
SVM-SMOTE oversampling + near miss undersampling							
Random forest	0.440	0.017	0.009	0.638	0.539	19.336	56.2%
XGBoost	0.420	0.017	0.008	0.643	0.531	20.049	58.3%
ADASYN oversampling + near miss undersampling							
Random forest	0.530	0.016	0.008	0.499	0.515	16.222	47.0%
XGBoost	0.528	0.017	0.009	0.537	0.532	16.311	47.3%

Random forest and XGBoost model results on test set training with SVM-SMOTE and ADASYN oversampling and near miss undersampling.
SVM-SMOTE, support vector machine synthetic minority oversampling technique; ADASYN, adaptive synthetic algorithm; ROC AUC, receiver operating curve area under the curve.

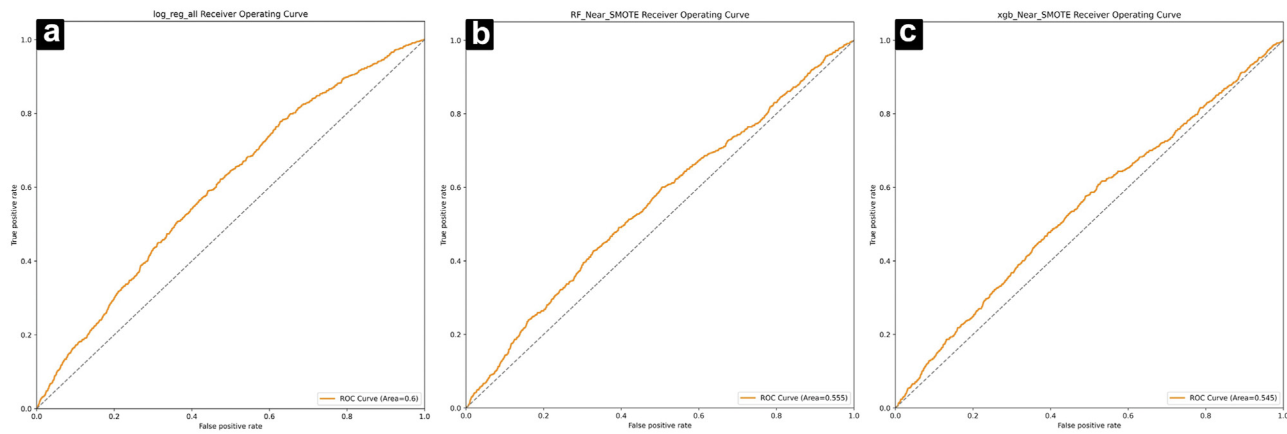

Figure 4. Receiver operating curves of (a) logistic regression model with cross-entropy scoring loss. (b) Random forest model with SVM-SMOTE oversampling; (c) XGBoost with SVM-SMOTE oversampling. SVM-SMOTE, support vector machine synthetic minority oversampling technique; ADASYN, adaptive synthetic algorithm.

Our logistic regression model trained on all data was our best performing model in terms of AUC. The logistic regression model only performed slightly better than the random forest and XGBoost models. However, it is important to note that AUC is not always the best metric for imbalanced datasets, as it can be influenced by the distribution of the classes in the dataset. In terms of recall score, the performance of the random forest and XGBoost outperformed the logistic regression model. These findings suggest that the random forest and XGBoost models were able to identify more true positive VTE cases than the logistic regression model. However, this was done by predicting VTE for a significantly larger number of cases (56.2%-58.3% vs 21.7% of patients predicted to develop VTEs).

Logistic regression with regularization is the most commonly used ML model, which has limitations, particularly when predicting in the setting of complex, highly interdependent factors and significantly unbalanced data sets. [17,18] More complex models can capture interdependent relationships between different factors, which could enable improved predictions. Despite the strengths of the random forest and XGBoost models in their ability to capture more complex nonlinear relationships between features and outcomes compared to regression, their ability to preoperatively predict the incidence of 30-day VTE was suboptimal. As mentioned, the random forest and XGBoost models preoperatively predicted 56.2% and 58.3% of patients to develop a VTE, while capturing 63.8% and 64.3% of VTE events. This may have some clinical usefulness as it can reliably identify the top half of patients at higher risk of developing VTE and captures 3 in 5 VTE events. This may help clinicians identify patients at risk of developing a VTE prior to their surgery to help personalize their prevention and surgical plan.

Currently, it is recommended that high-risk patients (personal or family history of VTE, active cancer, hypercoagulable state, multiple medical comorbidities [cardiac, pulmonary, obesity, or diabetes]) receive anticoagulant prophylaxis for 4 weeks. [34-36] The patient and surgery-specific factors associated with an increased risk of VTE that this study identified were comorbidities such as COPD, congestive heart failure, and hypertension, and surgery-specific factors such as type of operation and preoperative blood transfusion (defined in NSQIP as any blood transfusion within 72 hours of surgery). While the latter was a rare event, it likely represents medically complex with pre-existing anemia or hematological conditions. [37] Our findings are consistent with previous studies on this topic and highlight the importance of considering these factors in VTE risk assessment. [38-42] A machine-learning algorithm that generates a patent-specific preoperative risk profile may help personalize management regimens including use of combined chemical and physical VTE prophylaxis, higher doses, or longer duration of anticoagulation. [43]

Despite the following limitations, these findings are important as this is one of the largest administrative surgical databases capturing patient complications, so the findings are widely generalizable. As well, this study employed the use of oversampling and undersampling techniques and was tested on data from unseen “future” years, which more accurately represents performance of the model should it be deployed. This dataset only captures complications up to 30 days; therefore, approximately one third of VTEs presenting after 30 days were missed. [44-49] Despite the strong correlation between VTE events and LOS, there may be other factors contributing to the decreased incidence of postoperative VTE. Our findings are still important and previously undocumented in the period of contemporary perioperative TJA management following the latest CHEST guidelines. [29] Although in NSQIP, there is no data regarding VTE prophylaxis, there have been standard guidelines since 2012 suggesting a minimum of 14 days of anticoagulant prophylaxis postoperatively. [50] While this may confound the results, we believe within this timeframe most patients included in the database will have received some form of VTE chemoprophylaxis for a minimum of 14 days postoperatively. Finally, the limited number of features present in the dataset may have affected the performance of our models. The NSQIP dataset was collected retrospectively and may have been subject to missing data or incorrect entries, leading to lower accuracy and recall in our models.

Conclusions

Our study identified an association between mean annual LOS and annual rates of VTE following TJA, with a strong correlation between these changes. This finding underscores the importance of continued implementation of rapid recovery pathways and early mobilization. However, these events still remain difficult to predict, highlighting the limitations of ML models when dealing with complex and highly interdependent factors and significantly unbalanced outcome rates. [51,52] Despite this, the most important factors identified from these models may be used to define high-risk patients. Further curation of accurate large-scale data to develop more accurate and robust ML models for VTE prediction may guide individualized prophylaxis strategies and improve postoperative monitoring and management.

Conflicts of interest

A. Abbas receives research support from Arthrex Inc. J. Lex is an unpaid consultant for PrecisionOS Technologies, receives research support from Arthrex Inc., and is a board/committee member of the AAHKS YAG Committee. R. Koucheki is an unpaid consultant for PrecisionOS Technologies. J. Wolfstadt is a speaker bureau of Depuy-Synthes; is a paid consultant for Depuy-Synthes and Microport Orthopaedics; and is a board/committee member of AAHKS, COA, and CAS. All other authors declare no potential conflicts of interest.

For full disclosure statements refer to https://doi.org/10.1016/j.artd.2024.101491.

CRediT authorship contribution statement

Johnathan R. Lex: Writing – original draft, Visualization, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Robert Koucheki:** Writing – review & editing, Visualization, Software, Investigation, Formal analysis, Conceptualization. **Aazad Abbas:** Validation, Software, Resources, Methodology, Data curation. **Jesse I. Wolfstadt:** Writing – review & editing, Validation, Supervision, Investigation. **Alexander S. McLawhorn:** Writing – review & editing, Validation, Supervision, Project administration, Methodology. **Bheeshma Ravi:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Data curation.

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Supplemental Table 1
Included features utilized to generate the preoperative predictive ML models.

Feature type	Feature
Categorical	Sex, race, operation, patient setting, anesthesia type, diabetes, smoking, dyspnea, functional status, dialysis, disseminated cancer, history of COPD, history of CHF, hypertension requiring medication, renal failure, steroid use for chronic condition, bleeding disorder, preop transfusion of 1 or more unit of whole/packed RBCs in 72 hrs prior to surgery, American Society of Anesthesiologists score
Continuous	Weight, preoperative lab values: serum sodium, blood urea nitrogen, creatinine, albumin, bilirubin, glutamic-oxaloacetic transaminase, alkaline phosphatase, white blood cell count, hematocrit, platelet count, prothrombin time, international normalized ratio

COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; RBC, red blood cell.

Supplemental Table 2
Mean training and validation model results from the 5-fold cross-validation training and testing with oversampling of minority class followed by undersampling using near miss undersampler

Model	Training						Validation					
	Accuracy	F1 Score	Precision	Recall	ROC AUC	Log loss	Accuracy	F1 Score	Precision	Recall	ROC AUC	Log loss
SVM-SMOTE oversampling + near miss undersampling												
Random forest	0.955	0.954	0.965	0.944	0.990	−0.189	0.918	0.908	0.941	0.895	0.983	−0.247
XGBoost	0.950	0.949	0.968	0.930	0.986	−0.149	0.907	0.883	0.960	0.863	0.978	−0.249
ADASYN oversampling + near miss undersampling												
Random forest	0.955	0.954	0.970	0.938	0.993	−0.151	0.884	0.871	0.945	0.815	0.954	−0.280
XGBoost	0.966	0.965	0.979	0.952	0.991	−0.112	0.925	0.913	0.969	0.882	0.976	−0.228