Development of Machine Learning Algorithms for Predicting Preoperative and Postoperative Venous Thromboembolism in Patients Undergoing Surgery for Spinal Metastasis

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ABSTRACT

Objective: This study aims to develop and compare machine learning models (MLMs) for predicting venous thromboembolism (VTE) in patients undergoing surgery for spinal metastasis. The study evaluates the predictive capabilities of MLMs for preoperative and postoperative VTE within different time frames.

Materials and Methods: A total of 334 patients undergoing surgery for spinal metastasis were included, with a mean age of 57.6 years and 57.2% being male. The investigation assessed postoperative VTE prevalence within 30 and 90 days, with pulmonary embolism (PE) and deep vein thrombosis (DVT) rates at 20% and 80%, respectively. Key patient-related factors—age, body mass index, preoperative ambulatory status, albumin level, hemoglobin level, partial thromboplastin time, and operative time—were considered potential predictors of VTE.

Results: The postoperative VTE prevalence was 8.98% within 30 days and 13.47% within 90 days. Age, body mass index, preoperative ambulatory status, albumin level, hemoglobin level, partial thromboplastin time, and operative time emerged as significant VTE predictors. The gradient boosted tree algorithm was the best-performing MLM for predicting VTE within 90 days, with AUC values of 0.77 preoperatively and 0.71 postoperatively. For predicting VTE within 30 days, the support vector machine model was most effective, with AUCs of 0.72 preoperatively and 0.68 postoperatively.

Conclusion: Predictive analytics and MLMs effectively predict preoperative and postoperative VTE in patients undergoing surgery for spinal metastasis. Identified key factors and MLM performance metrics offer valuable insights for risk assessment and preventive measures in this patient population.

Keywords: Development; machine-learning algorithms; prediction; venous thromboembolism; surgery; spinal metastasis (Siriraj Med J 2024; 76: 381-388)

INTRODUCTION

Patients with cancer have a 4-6.5 times increased risk of developing venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE).[1-3] The incidence of VTE in spine surgery was reported to range from 0.15-29.38%[4], and the incidence of VTE among patients undergoing surgery for spinal metastasis was 9.48%-11%.[5,6] This data demonstrates that

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patients undergoing surgery for spinal metastasis are at far greater risk for developing VTE. The development of VTE in cancer patients is associated with both increased morbidity and mortality compared to non-cancer patients[3], and the cost of treatment is high.[7]

The two commonly used clinical assessments for VTE risk stratification among surgical patients are the Rogers score[8] and the Caprini risk assessment model.[9] The current models' lack of specificity and limited predictive accuracy for this subgroup necessitate a more focused and refined approach to risk assessment.[10,11]

Enter the realm of machine learning (ML), a subdivision of artificial intelligence that thrives on its capacity to decipher complex patterns within large datasets, a challenge often faced in medical research. ML's inherent capability to integrate and analyze multifaceted clinical data presents a promising avenue to enhance predictive models' accuracy significantly. Previous research has validated ML's potency in predicting adverse outcomes in spine surgery, setting a precedent for its application in VTE risk prediction.[12]

The urgency for advanced predictive analytics is clear: the current gap in precise VTE risk assessment for spinal metastasis surgery patients could be narrowed by employing machine learning models. By developing various MLM algorithms, this study aims to address this gap, offering potentially more accurate predictions for preoperative and postoperative VTE. Not only could this lead to better patient outcomes, but it also stands to optimize the use of healthcare resources and inform preventive strategies, thereby ameliorating the burden of VTE in oncological surgery. In doing so, we align our efforts with the evolving landscape of precision medicine, where patient care is increasingly informed by data-driven insights.

MATERIALS AND METHODS

Guidelines

We followed the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines, and the Guidelines for Developing and Reporting Machine Learning Models in Biomedical Research.[13,14]

Source of data

The data were obtained from the medical database of the Department of Orthopedic Surgery. We identified consecutive patients retrospectively who underwent spinal surgery between January 2009 and December 2020.

Participants

Participants were selected based on the following criteria: (1) a confirmed diagnosis of spinal metastases classified under the International Classification of Diseases, 10th Revision, Thai Modification (ICD 10-TM) with the specific codes C79.5 and C79.8, (2) being 18 years of age or older, and (3) a documented history of undergoing surgical intervention for spinal metastases located in the cervical, thoracic, lumbar, or sacral regions, which was categorized under the International Classification of Diseases, 9th Revision, Clinical Modification (ICD 9-CM) with the procedural codes 03.0, 03.4, 03.09, 81.0, and the range of 81.00 to 81.08.

We excluded patients with a history of VTE, who had major surgery or major trauma within one month before surgery, who were pregnant, or who had a genetic abnormality, such as anticoagulation proteins C and S, antithrombin III deficiency, or factor V Leiden mutation.

Outcome and predictive variables

The primary outcome of our study was the incidence of postoperative venous thromboembolism in patients with spinal metastasis at 30- and 90-days following surgery.

The following risk factor variables for VTE were identified from previous studies: gender[15,16], age[15-19], diabetes mellitus (DM)[20], hypertension (HT)[16], chronic kidney disease (CKD)[21,22], American Society of Anesthesiologists (ASA) classification[23], body mass index (BMI)[15,24,25], preoperative ambulation status[15,19], preoperative albumin level[23], preoperative hemoglobin level[5], preoperative partial thromboplastin time (PPT)[5], spinal surgery location[15], operative time[6,23], and postoperative blood transfusion.[26-28]

We divided the variables into two groups: the first one using only pre-operative data of patients, and the latter including intra-operative and post-operative data such as blood loss, operative time, etc. Patients with symptomatic venous VTE, as documented in the medical database, were used as the dependent variable in this investigation.

Preprocessing

Multiple imputations with chained equations imputed missing preoperative laboratory characteristics with less than 25% missing data. A class weighting strategy was also used to ensure that the trained model would take each class into account equally despite class imbalance. To reduce the influence of different variable units and quantity levels, we scale numerical variables to a standard

deviation of one and a mean of zero, and we employ dummy encoding for categorical variables. We also get rid of outliers whose lab values are three standard deviations from the average lab value at our hospital.

Algorithm training and validation

For the development and evaluation of our models, we opted for a suite of algorithms including random forest, neural network, logistic regression, gradient boosted tree, support vector machine, XGBoost, decision tree, and stochastic gradient descent. These were implemented using the Python 3.9 programming language and the Scikit-learn 1.0.1 library, which is distributed under a permissive open-source BSD license.

In the process of preparing the dataset for analysis, we performed both manual and automated tuning of hyperparameters via grid and random search methods to ensure the highest predictive accuracy during a fivefold internal cross-validation for each algorithm. The data were split into an 80:20 ratio for training and testing purposes, with the training set being utilized to fit the models, which were then validated through a fivefold cross-validation approach. To counteract any imbalance across the classes, a class weighting technique was employed during model training

The efficacy of the algorithms was assessed using the test set, scrutinizing metrics such as the area under the receiver operating characteristic (ROC) curve (AUC), the F1-score, overall accuracy, and calibration loss. The ROC curve is critical for illustrating the trade-off between the true positive and false positive rates that arise from various thresholds in the predictive model. An AUC score between 0.7 and 0.8 denotes fair model performance, while a score above 0.8 is indicative of good performance. The F1-score—a harmonic mean of precision and recall—reaches its optimal value at 1.0, representing impeccable precision and sensitivity. To evaluate a model's precision, we also analyzed the confusion matrix, which juxtaposes actual versus predicted outcomes. Given that different metrics may present certain trade-offs, such as the balance between precision and recall, the AUC was primarily used for selecting the most suitable model for practical application.

Statistical analyses

The baseline demographic and clinical characteristics of study patients were summarized using descriptive statistics. Continuous data, such as partial thromboplastin time and operative time, are presented as mean plus/minus standard deviation. All other evaluated factors are reported as number and percentage. Study data were recorded and calculated using Microsoft Excel software (Microsoft Corporation, Redmond, WA, USA).

RESULTS

A total of 334 patients were included in this study. The mean age of study patients was 57.6 years, and 191 (57.2%) of them were men. The postoperative prevalence of VTE within 30 and 90 days of surgery was 30 (8.98%) and 45 (13.47%), respectively (PE 20%, and DVT 80%). Patients who developed VTE were younger, had lower BMI, were not able to ambulate preoperatively, had a higher albumin level, and had a higher hemoglobin level. Other baseline demographic/clinical characteristics and patient outcomes are shown in Table 1. The most common primary tumor sites were lung (27.5%), breast (17.4%), and prostate gland (12.9%) (Table 2).

Regarding VTE prediction within 30 days before spinal surgery, the gradient boosted tree algorithm showed age, preoperative ambulatory status, BMI, albumin level, hemoglobin level, and PTT to be predictive factors (Fig 1). This algorithm had the best AUC (0.77) with accuracy (proportion of correct predictions within the test set) of 0.88, precision (proportion of positive predictions that were indeed positive) of 1, recall (proportion of actual positive values found by the classifier) of 0.11, and F1 score (harmonic mean between precision and recall) of 0.2 (Table 3).

Concerning VTE prediction within 90 days before spinal surgery, the support vector machine algorithm had the best AUC (0.72) with accuracy, precision, recall, and F1 scores of 0.58, 0.25, 0.82, and 0.38, respectively.

Regarding VTE prediction within 30 days after spinal surgery, the gradient boosted tree algorithm showed age, BMI, albumin level, hemoglobin level, PTT, and operative time to be predictive factors (Fig 2). This algorithm had the best AUC (0.71) with accuracy, precision, recall, and F1 scores of 0.88, 0.1, 0.11, and 0.2, respectively.

Concerning VTE within 90 days after spinal surgery, the support vector machine algorithm has the best AUC (0.68) with accuracy, precision, recall, and F1 scores of 0.86, 1.00, 0.09, and 0.17, respectively.

DISCUSSION

This study including cancer patients with spinal metastasis who underwent spinal surgery. The incidence of postoperative VTE events was 13.5%. Zacharia, et al.[5]

TABLE 1. Baseline Characteristics of Patients Undergoing Surgery for Spinal Metastatic Disease, n=334

Variable	Characteristic	Total	30-day VTE		90-day VTE	
		N=334	No, N=304	Yes, N=30	No, N=289	Yes, N=45
Sex	Male	191 (57.2%)	178 (58.6%)	13 (43.3%)	171 (59.2%)	20 (44.4%)
	Female	143 (42.8%)	126 (41.4%)	17 (56.7%)	118 (40.8%)	25 (55.6%)
Age (Years)	<65	241 (72.2%)	218 (71.7%)	23 (76.7%)	206 (71.3%)	35 (77.8%)
	65-79	86 (25.7%)	79 (26%)	7(23.3)	76(26.3%)	10 (22.2%)
	>79	7 (2.1%)	7 (2.3%)	0	7(2.4%)	0
Body mass index (kg/m^2)	<25	258 (77.2%)	233 (76.6%)	25 (83.3%)	223 (77.2%)	35 (77.8%)
	25-30	62 (18.6%)	59 (19.4%)	3 (10%)	55 (19%)	7 (15.6%)
	>30	14 (4.2%)	12 (4%)	2 (6.7%)	11 (3.8%)	3 (6.6%)
American Society of Anesthesiologists Classification	1-2	195 (58.4%)	181 (59.5%)	14 (46.7%)	171 (59.2%)	24 (53.3%)
	3-5	139 (41.6%)	123 (40.5%)	16 (53.3%)	118 (40.8%)	21 (46.7%)
Comorbidities	Diabetes	51 (15.3%)	46 (15.1%)	5 (16.7%)	44 (15.2%)	7 (15.6%)
	Hypertension	119 (35.6%)	106 (34.9%)	13 (43.3%)	99 (83.2%)	20 (16.8%)
	Chronic kidney disease	15 (4.5%)	14 (4.6%)	1 (3.3%)	14 (4.8%)	1 (2.2%)
Preoperative ambulatory activity status	No	187 (56%)	165 (54.3%)	22 (73.3%)	154 (53.3%)	33 (73.3%)
	Yes	147 (44%)	139 (45.7%)	8 (26.7%)	135 (46.7%)	12 (26.7%)
Albumin (g/dL)	<3.5	80 (24%)	74 (24.3%)	6 (20%)	71 (24.6%)	9 (20%)
	≥3.5	249 (76%)	230 (75.7%)	24 (80%)	218 (75.4%)	36 (80%)
Hemoglobin (g/dL)	<10	40 (12%)	35 (11.5%)	5 (16.7%)	34 (11.8%)	6 (13.3%)
	≥10	294 (88%)	269 (88.5%)	25 (83.3%)	255 (88.2%)	39 (86.7%)
Partial thromboplastin Time (Sec.)		26±3.6	26.12±3.63	25.03±3.88	26.14±3.65	25.21±3.72
Index spinal location	Cervical	33 (9.9%)	26 (8.6%)	7 (23.3%)	25 (8.7%)	8 (17.8%)
	Thoracic	186 (55.7%)	175 (57.6%)	11 (36.7%)	167 (57.8%)	19 (42.2%)
	Lumbar	112 (33.5%)	100 (32.8%)	13 (40%)	94 (32.5%)	18 (40%)
	Sacral	3 (0.9%)	3 (1.0%)	0 (0%)	3 (1.0%)	0 (0%)
Operative Time (min.)		192.04±65.93	192.49±65.66	187.50±69.60	193.32±65.58	183.89±68.29
Postoperative blood transfusion		243 (72.8%)	221 (72.7%)	22 (73.3%)	209 (72.3%)	34 (75.6%)

TABLE 2. Origin of the primary tumor (n=334)

Characteristic	N (%)
Lung	92 (27.5)
Breast	58 (17.4)
Prostate	43 (12.9)
Liver	21 (6.3)
Kidney	17 (5.1)
Colorectal	14 (4.2)
Thyroid	14 (4.2)
Hematology	12 (3.6)
CholangioCA	11 (3.3)
Nasopharyngeal cancer	9 (2.7)
Cervix	6 (1.8)
Unknown	8 (2.4)
Others*	29 (8.7)

*pancreatic cancer 4 (1.2%), soft tissue sarcoma 4 (1.2%), Endometrial cancer 3 (0.9%), tongue cancer 3 (0.9%), bladder cancer 2 (0.6%), esophagus cancer 2 (0.3%), neuroendocrine tumors 1 (0.3%) and hard palate cancer 1 (0.3%).

conducted preoperative DVT screening in patients who were to undergo surgical treatment for spinal metastasis, and they found a 9.48% preoperative incidence of DVT. Groot, et al.[6] reported that 11% of patients developed symptomatic VTE within 90 days of surgical treatment for spinal metastasis. Based on the results of the present study, the most accurate model for predicting VTE within 30 days before or after surgery is the gradient boosted tree algorithm (AUC for preoperative prediction: 0.77, and AUC for postoperative prediction: 0.71). We also found the most accurate model for predicting VTE within 90 days before or after surgery to be the support vector machine algorithm (AUC for preoperative prediction: 0.72, and AUC for postoperative prediction: 0.68). The most important variables in these algorithms are age, BMI, preoperative ambulatory status, albumin level, hemoglobin level, PTT, and operative time. These factors are consistent with previously published studies that reported risk factors for VTE after spine surgery.[5,15,18,19,23,24,26]

Other studies have investigated models that predict complications after spine surgery. Bekelis, et al.[29] conducted a retrospective cohort study that included 13,660 patients. The 30-day incidence of DVT was only 0.6%. Increasing age, alcohol consumption, preoperative neurologic deficit, and corpectomy were found to be significantly associated with a higher likelihood of postoperative DVT. Their model to predict postoperative risk of DVT had an AUC of 0.74. Han, et al.[12] developed machine learning models for predicting adverse events following spine surgery. The incidence of DVT in their study was a low 1.8%; however, the AUC for an overall AE was 0.7 among the six individual prediction models that they had developed.

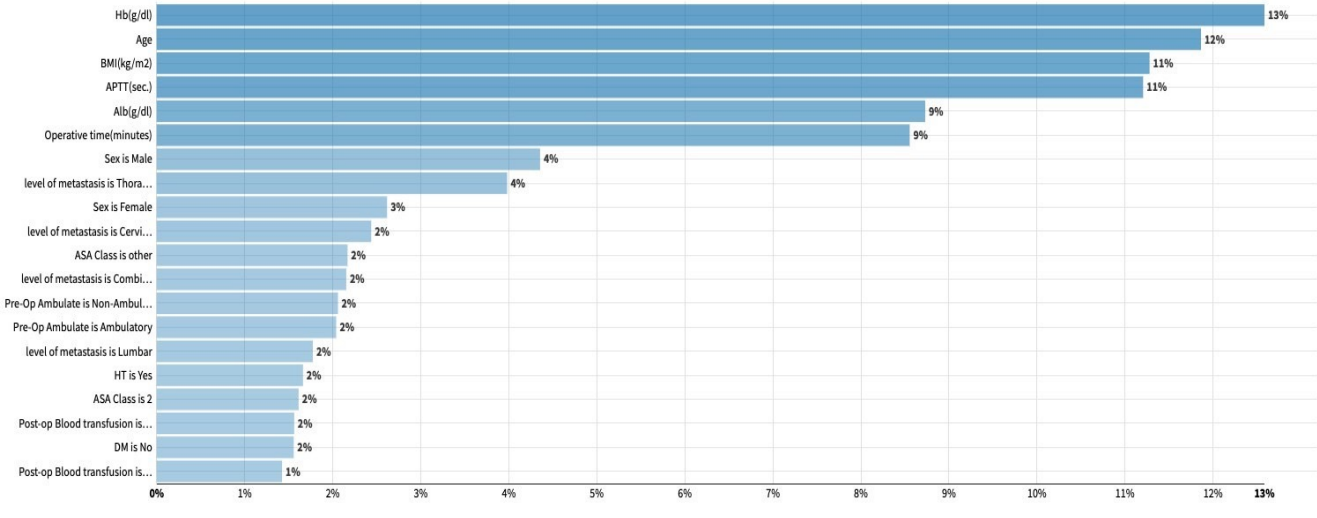


Fig 1. Variable importance for the preoperative prediction model.

TABLE 3. Machine Learning Model Performance for 30 and 90 days VTE Prediction in Patients Undergoing Surgery for Spinal Metastatic

Metric	Machines learning algorithm							
	Random forest	Logistic Regression	SVM	SGD	Gradient Boosted Trees	Decision Trees	Artificial Neural Network	XG Boost
Pre op 30 days Prediction								
AUC	0.62	0.64	0.59	0.65	0.77	0.59	0.63	0.69
Accuracy	0.88	0.87	0.88	0.87	0.88	0.87	0.87	0.87
Precision	1	0.5	1	1	1	1	0.5	1
Recall	0.11	0.11	0.11	0	0.11	0	0.11	0
F1 score	0.2	0.18	0.2	0	0.2	0	0.18	0
Pre op 90 days Prediction								
AUC	0.69	0.63	0.72	0.66	0.61	0.56	0.63	0.56
Accuracy	0.59	0.59	0.58	0.7	0.57	0.16	0.52	0.57
Precision	0.24	0.23	0.25	0.27	0.21	0.16	0.21	0.19
Recall	0.73	0.64	0.82	0.55	0.64	1	0.73	0.55
F1 score	0.36	0.33	0.38	0.36	0.32	0.27	0.33	0.29
Post op 30 days Prediction								
AUC	0.62	0.65	0.66	0.63	0.71	0.55	0.61	0.6
Accuracy	0.88	87	0.87	0.87	0.88	0.87	0.87	0.87
Precision	1	1	0.5	1	1	0.5	1	0.5
Recall	0.11	0	0.11	0	0.11	0.11	0	0.22
F1 score	0.2	0	0.18	0	0.2	0.18	0	0.31
Post-op 90 days Prediction								
AUC	0.67	0.59	0.68	0.66	0.63	0.55	0.63	0.65
Accuracy	0.86	0.84	0.86	0.86	0.84	0.86	0.86	0.84
Precision	1	1	1	1	1	1	1	1
Recall	0	0	0.09	0.09	0	0.09	0.09	0.09
F1 score	0.17	0	0.17	0.17	0	0.17	0.17	0

Abbreviations: AUROC = area under the receiver operating characteristic, SVM = Support Vector Machine, SGD = Stochastic Gradient Descent

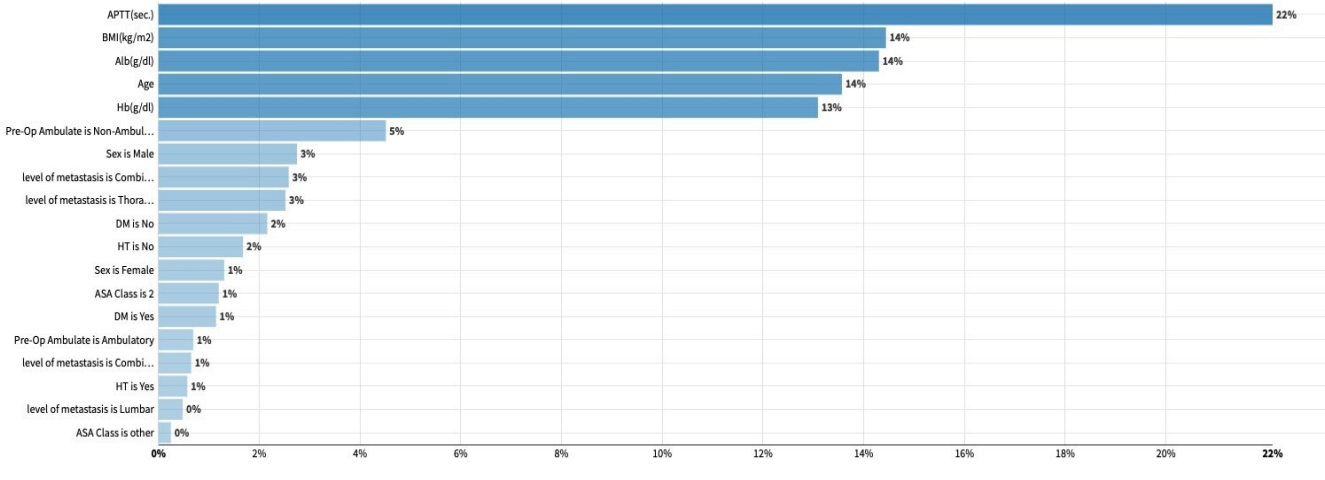


Fig 2. Variable importance for the postoperative prediction model.

Rogers score[8] and Caprini score[9] are two commonly used VTE risk assessment models in surgical patients. However, neither of these tools is in any way specific to spinal metastasis surgery, neither includes operative time or blood chemistry investigations, which may influence postoperative VTE development.

Previously developed prediction models included fewer risk factors due to analytic limitations. However, with the use of machine learning modeling, we were able to include 14 important risk factors in the development of our prediction algorithms. To our knowledge, this is the first study in machine learning prediction algorithm development to include both preoperative and postoperative factors in the development of algorithms that predict preoperative and postoperative VTE in patients scheduled to undergo surgery for spinal metastasis.

Limitations

This study's findings are subject to several limitations, including the inability to differentiate between symptomatic and asymptomatic VTE, which may affect the clinical application of our predictive models. The external validity of our results is constrained by the use of data from a single institution, which may not be representative of broader patient populations. Furthermore, the potential for algorithmic overfitting and the inherent complexity of the machine learning models used could limit the interpretability and generalizability of our findings. Future research should focus on external validation with diverse cohorts, incorporate a broader array of predictive variables, and explore a range of performance metrics beyond AUC to ensure the clinical relevance of the predictive models.

CONCLUSION

Our study affirms the utility of machine learning models in predicting VTE for spinal metastasis surgery patients, with the gradient boosted trees algorithm showing strong predictive performance for the 30-day timeframe and the support vector machine algorithm standing out for the 90-day predictions. These models have demonstrated good to fair predictive capabilities, as indicated by AUC values aligning with established thresholds. Key factors like age, BMI, and preoperative status, consistent with prior studies, have been instrumental in model accuracy, supporting their integration into clinical risk assessments to potentially enhance patient care.

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Conflits of interest

All authors declare no personal or professional conflicts of interest relating to any aspect of this study.

Ethics approval

The protocol for this study was approved by the Siriraj Institutional Review Board (SIRB) (COA no. Si 1065/2020), and written informed consent was not obtained due to the retrospective nature of this study.

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