Can Venous Thromboembolism Be Predicted after Ankle Fractures: A Machine Learning Analysis

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INTRODUCTION:

Venous thromboembolism (VTE) is a major complication of orthopaedic surgery that consists either deep vein thrombosis (DVT) or pulmonary embolism (PE) and one of the leading causes of mortality among trauma patients in orthopaedic settings. In order to prevent such a fatal complication, patients often receive prophylaxis as a means of preventing postoperative VTE, which has proven to be safe and effective to a certain extent, in fact, prophylactic measures also have side effects of bleeding complications, which emphasizes the need to administer them carefully in order to avoid adverse effects. In this study, we used both traditional statistics and machine-learning to determine the associated factors or in other words, potential risk factors, for VTE after ankle fracture and develop a patient-specific predictive model to assist clinicians with deciding upon the usefulness of prophylaxis administration after ankle fractures.

METHODS: In this preliminary machine-learning-based case-control study, 16,421 patients with ankle fractures were recruited retrospectively and screened for VTE from which 239 had confirmed VTE within 180 days of sustaining an ankle fracture (cases). We subsequently added 937 who did not (controls) in order to reach a 1:4 case to control ratio for our statistical analysis and ended up with 1,176 patients in total. Our population was further sub-divided into patients who had been receiving chemoprophylaxis and those who had not. Over 110 factors and variables including patient demographics, past-medical and surgical history, fracture characteristics, treatment, medications, and laboratory values were included in our machine-learning dataset. Three analytical algorithms were used in our machine-learning methods including backward-logistic-regression, decision-tree-classifier (depth=5), and neural networks (two dense layers [n=16 and 4], two drop-out layers, and a sigmoid classifier). Conventional statistics were also used to compare the case and control groups (chi-squared, t-test, $p<0.05$ considered significant), and the odds-ratio (OR) was calculated for significant parameters.

RESULTS: Based on overall performance scores including specificity, sensitivity, area under the ROC curve, accuracy, PPV, NPV, F-1 score, among the 3 machine-learning methods, Backward-Logistic-Regression model was superior in predicting VTE post ankle fracture and in determining whether administering prophylaxis can be beneficial for the patient or not (Tables 1 and 2). Other than the previously suggested risk factors, our analysis also showed positive correlation between the incidence of VTE and smoking (OR=2.09, $p<0.001$), age <55 y/o ($p=0.001$), open fracture (OR=2.49, $p<0.001$), male gender (OR=1.98, $p<0.001$), surgical treatment (OR=1.88, $p=0.001$), and multiple fractures (OR=1.9, $p=0.0012$). Factors that showed negative correlation with VTE include statins use (OR=0.36, $p<0.001$), hypertension (OR=0.53, $p<0.001$), vitamin D (OR=0.43, $p<0.001$), calcium supplementation (OR=0.43, $p=0.01$), hyperlipidemia (OR=0.55, $p=0.01$), cataract (OR=0.19, $p=0.01$), osteoporosis (OR=0.36, $p=0.02$), cardiovascular diseases (OR=0.54, $p=0.02$), hypokalemia (OR=0.26, $p=0.03$), and proton-pump-inhibitor use (OR=0.5, $p=0.03$).

DISCUSSION AND CONCLUSION:

Out of the three predictive models we have developed, the best performance was in the Backwards Logistic Regression model; it is more efficient in all populations and in the no-prophylaxis population. Our machine learning algorithms showed that factors such as tobacco use, younger age, open fracture, multi-trauma, operative treatment, as well as male sex heightened the risk of VTE. The machine learning algorithms we have created were able to act in a more complex manner and incorporated more factors in decision making compared to other conventional methods. By using these predictive models as clinical aids in choosing whether or not to administer prophylaxis to patient's ankle fracture or not, we hope to mitigate the risk of development of VTE after ankle fracture and decrease the over prescription of VTE prophylaxis.

One take-home message from this study is that using machine learning algorithms, larger, more granular and more comprehensive datasets can be evaluated. These algorithms can automatically assess notes and images and extract features that are hard to assess manually by humans. Moreover, if provided by enough data, the outcomes can be more accurate and reliable. However External validation using larger and more granular datasets as well as using the algorithms in trial modes (shadow modes) are needed to build trust in this algorithm to assist clinicians in predicting/preventing VTE after foot and ankle surgeries.

Table 1 Performance of three algorithms in prediction of VTE among patients with ankle fracture.

	Specificity	Sensitivity	AUROC	Accuracy	PPV	NPV	F-1 score
Backward Logistic Regression	0.61	0.46	0.497	58%	0.22	0.82	0.3
Decision Tree Classifier (depth = 5)	0.98	0*	0.519	79%	0*	0.8	0*
Neural Network	0.95	0.02	0.579	77.1%	0.1	0.8	0.04

* "0" zero sensitivity, PPV, and F-1 score means the model was not capable of predicting any cases correctly.

Table 2 Performance of three machine learning algorithms in predicting (suggesting) prophylaxis in patients who were not using any prophylactic method before ankle fracture.

	Specificity	Sensitivity	AUROC	Accuracy	PPV	NPV	F-1 score
Backward Logistic Regression	0.71	0.65	0.679	70%	0.35	0.89	0.46
Decision Tree Classifier (depth = 5)	0.99	0*	0.513	79%	0*	0.8	0*
Neural Network	0.43	0.82	0.619	50.6%	0.26	0.82	0.39

* "0" zero sensitivity, PPV, and F-1 score means the model was not capable of predicting any cases correctly.