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A MACHINE LEARNING APPROACH TO FIRST PASS REPERFUSION IN MECHANICAL THROMBECTOMY: PREDICTION AND FEATURE ANALYSIS

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ABSTRACT:

Introduction: Novel machine learning (ML) methods are being investigated across medicine for their predictive capabilities while boasting increased adaptability and generalizability. In our study, we compare logistic regression with machine learning for feature importance analysis and prediction in first-pass reperfusion.

Methods: We retrospectively identified cases of ischemic stroke treated with mechanical thrombectomy (MT) at our institution from 2012-2018. Significant variables used in predictive modeling were demographic characteristics, medical history, admission NIHSS, and stroke characteristics. Outcome was binarized TICI on first pass (0-2a vs 2b-3). Shapley feature importance plots were used to identify variables that strongly affected outcomes.

Results: Accuracy for the Random Forest and SVM models were 67.1% compared to 65.8% for the logistic regression model. Brier score was lower for the Random Forest model (0.329 vs 0.342) indicating better predictive capability. Other supervised learning models performed worse than the logistic regression model, with accuracy of 56.2% for Naïve Bayes and 61.6% for XGBoost. Shapley plots for the Random Forest model showed use of aspiration, hyperlipidemia, hypertension, use of stent retriever, and time between symptom onset and catheterization as the top five predictors of first pass reperfusion.

Conclusion: Use of machine learning models, such as Random Forest, for the study of MT outcomes, is more accurate than logistic regression for our dataset, and identifies new factors that contribute to achieving first pass reperfusion. The benefits of machine learning, such as improved predictive capabilities, integration of new data, and generalizability, establish ML as the preferred model for studying outcomes in stroke.

INTRODUCTION:

Mechanical thrombectomy has been established as the standard of care for acute ischemic stroke secondary to large vessel occlusion[1]. While outcome measures in mechanical thrombectomy have been extensively studied, recent analysis has suggested that successful reperfusion on the first device pass is an independent factor for favorable clinical outcome[2,3,4]. Modifiable factors predicting successful first pass reperfusion are being currently studied as methods to improve overall outcomes for patients undergoing thrombectomy, but these have not been substantially characterized.

Machine learning (ML) is a branch of artificial intelligence (AI) and is a class of algorithms and computational techniques designed to be able to learn and improve from data without explicit programming[5]. These algorithms can broadly be divided into supervised learning, which includes algorithms such as Support Vector Machines (SVM), Random Forest (RF), and Naïve Bayes (NB) to produce predictions from labeled and categorized data, and unsupervised learning, which uses algorithms such as K-means clustering, Apriori algorithms, and Principal Component Analysis (PCA) for investigating data clusters and hidden relationships (Figure 1).

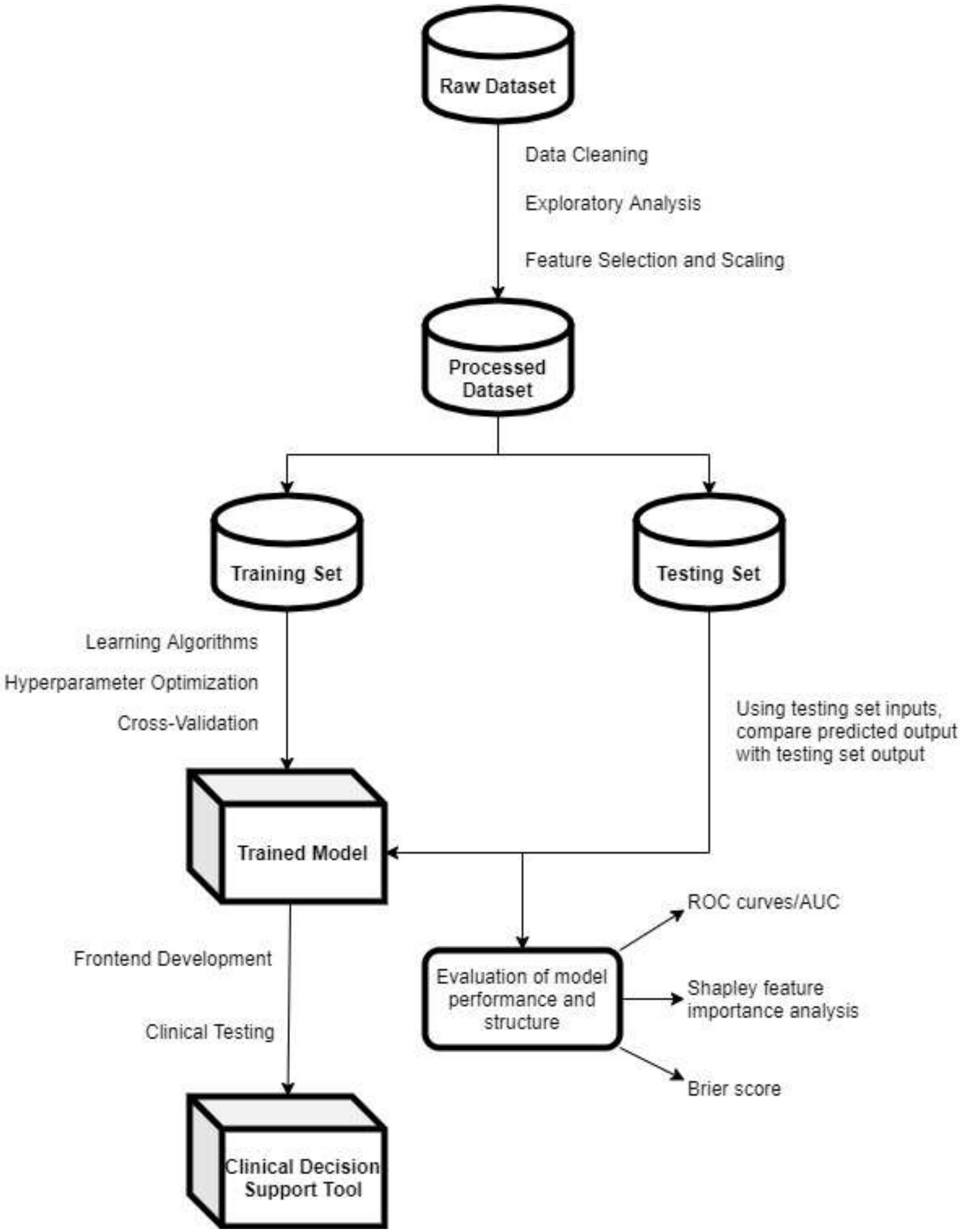

Figure 1: Supervised Learning Workflow

Machine learning algorithms are being increasingly studied in medicine due to advantages over traditional statistical analysis methods such as logistic regression, including improved predictive capability, improved identification of trends in opaque data, and ability to incrementally improve results with new data with minimal human intervention[6]. Recently, machine learning has been applied to stroke research and is being studied in stroke risk factor identification, diagnosis and imaging analysis, and treatment decision making and prognostication[6–11].

In this study, we investigate the utility of supervised machine learning algorithms for prediction and feature analysis of first pass reperfusion in patients undergoing mechanical thrombectomy. We hypothesize that supervised learning algorithms will have improved predictive capability compared to logistic regression and will identify novel factors predicting first pass reperfusion.

METHODS:

Patient Selection

A retrospective chart review was conducted of all patients presenting with acute ischemic stroke who underwent mechanical thrombectomy at our institution between January 2010 and March 2019. Patients with stroke affecting multiple vessels were excluded from the analysis. IRB approval was obtained, and all information was de-identified.

Procedural Details

Briefly, patients were treated by one of three attending vascular neurosurgeons. Where possible, aspiration was the method of choice (ADAPT technique), however, in cases without a favorable proximal thrombus and accessible anatomy (tortuous vessels, difficult arch, etc.), stent retriever was also used[12]. In addition, stent retriever was also used alongside aspiration for thrombi in the M2 vessel and distal due to lack of luminal support and inadequate size of vessels for aspiration catheter. Cases were distributed between the Solumbra technique and the CAPTIVE technique based on attending preference[13–15].

Patient Variables

Patient records were reviewed for age, gender, body mass index (BMI), and past medical history of cerebrovascular accident (CVA), coronary artery disease (CAD), hypertension (HTN), diabetes mellitus type 2 (DM2), hyperlipidemia (HLD), and atrial fibrillation (AFib). Smoking status and use of statins and blood thinners (including single antiplatelet, dual antiplatelet, and anticoagulation) were also recorded.

Pre-procedural variables collected included NIHSS score on presentation, use of tissue plasminogen activator (tPA), time from symptom onset to catheterization, time from onset to catherization, time from symptom onset to reperfusion, and procedural time were also recorded. Strokes were divided into anterior (MCA, ACA, ICA) or posterior (basilar, PCA, vertebral) occlusions and proximal (ICA, M1, A1, basilar, PCA, vertebral) or distal (M2, M3/4, A2) occlusions.

Procedural variables used included technique used for first pass mechanical thrombectomy (stent retriever, aspiration, or combination), use of intra-arterial tPA, successful reperfusion status (defined as mTICI score of 2b indicated filling of >50% of occluded territory or 3 indicating normal filling of all distal vessels), and number of passes used for each intervention.

Post-operative variables included peri-procedural complications (including intracranial hemorrhage, vessel dissection, or vessel perforation) and post-procedural symptomatic intracranial hemorrhage. NIHSS score at discharge was used to determine dichotomized NIHSS improvement (defined as improvement of > 3 points at discharge)[16–18]. In addition, hospital length of stay, inpatient mortality, and follow-up mRS (dichotomized into favorable (0-2) and unfavorable (3+) scores) at two weeks or three months depending on available data were also collected.

Feature Selection and Scaling

Data collected was subjected to data cleaning and scaling to improve model predictive capability. Feature selection employed correlation plots to remove variables that were redundant or closely correlated with other variables. One-hot encoding was used to remodel technique used in first pass as Boolean columns for stent retriever or aspiration. Only pre- or peri-procedural variables were used to predict first pass reperfusion to enhance clinical applicability.

After redundant features were removed, final variables included in the model included: age > 65, age > 80, BMI (categorical low, medium, high based on standard deviation), sex, history of CVA, CAD, HTN, DM2, HLD, or AFib, smoking status, blood thinner use, statin use, NIHSS on presentation, anterior or posterior stroke, proximal or distal stroke, use of tPA before procedure, time between symptom onset to catheterization, use of stent retriever, and use of aspiration. Outcome variable of interest was reperfusion status on first pass.

Feature scaling was used to produce a better fitted model and used the following formula:

$$X' = \frac{X - X_{min}}{X_{max} - X_{min}}$$

A 66%/33% split was used for training and testing datasets.

Model Development and Analysis

Supervised learning algorithms were applied to this dataset, drawn from the scikit-learn package for Python[19]. These included logistic regression, random forest, support vector machine (SVM), Naïve Bayes, and gradient boosting (using XGBoost).

Models were compared using multiple evaluation statistics such as ROC/AUC curves (0 to 1 with scores closer to 1 indicating higher accuracy), accuracy scores, Matthews correlation coefficient (-1 to 1, with higher score indicating better prediction) and Brier score (0 to 1 with scores closer to 0 indicating higher accuracy). Sensitivity and specificity were also calculated from confusion matrix. Feature importance analysis was done the Shapley Additive Explanations (SHAP) method, which utilizes Shapley value plotting[20]. Larger Shapley values indicate greater contribution of a feature to the overall prediction.

RESULTS:

264 patients fit the inclusion criteria for this study. After data cleaning, removal of outliers and patients with missing critical data, 220 patients were included in the dataset used to create these models. Patient baseline characteristics are included in Table 1.

Models were created and tested against the testing set. Results of model testing are included in Table 2 indicating performance measures and Figure 2 showing ROC curve from which AUC was calculated.

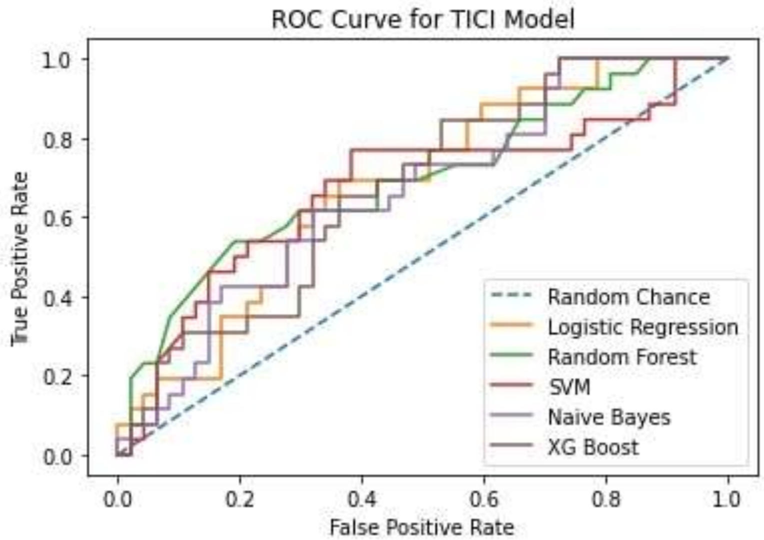

Figure 2: ROC Curves for Predictive Models

Shapley feature importance analysis was done by plotting calculated Shapley values based on impact on model output (Figure 3).

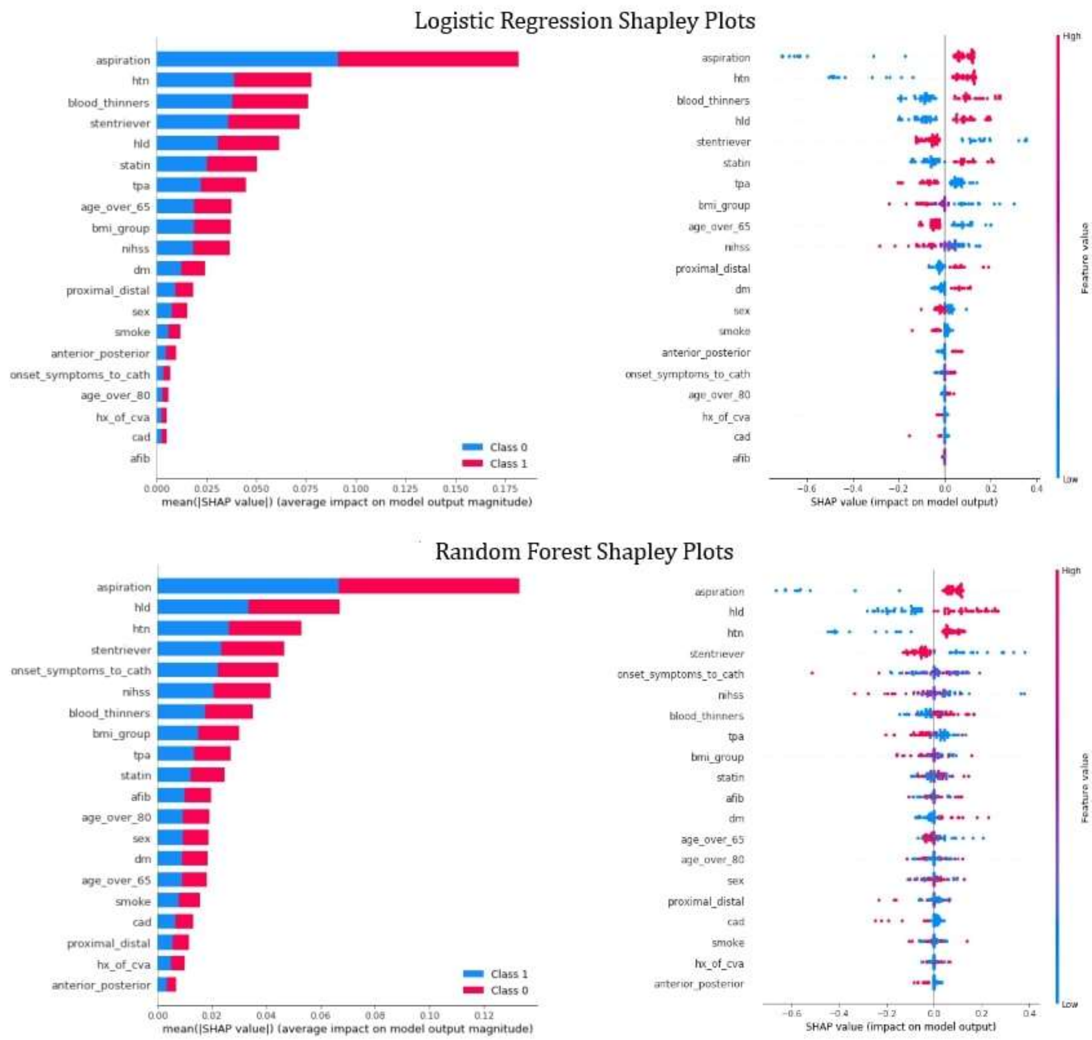

Figure 3: Shapley Plots

Variables are ordered from highest to lowest influence on the model (left), and direction of association is represented by color (right, high indicated a positive value and low indicating a negative value). A predominance of Shapley values in a certain region indicates direction of association (ex. aspiration has a predominance of red (high) values on the positive side (right of 0 SHAP value), indicated a correlation between use of aspiration and achievement of TICI in first pass).

DISCUSSION:

In this study, we demonstrate the efficacy of machine learning algorithms in predicting first pass reperfusion in mechanical thrombectomy. Both the Random Forest algorithm and the SVM algorithm demonstrated improved predictive accuracy and Brier score compared to the traditional logistic regression model derived from the same data. Random Forest also demonstrated improved AUC and Matthews correlation coefficient compared to the logistic regression model. The reasoning behind using multiple classification measurements has been detailed in methodological analysis of classification algorithms and the aim is to capture multiple aspects of an algorithm such as precision, sensitivity, and accuracy and aggregate them to better understand the utility of these models as a whole[21,22]. Demonstrating equal or improved efficacy across multiple classification performance measures, such as in this case with Random Forest, suggests improved predictive capability.

In addition, Shapely analysis of Random Forest, the best performing model in this study, reveals additional features related to achieving first pass reperfusion as compared to logistic regression. Both models identify aspiration as the leading factor related to prediction of first pass reperfusion, which, while not delineating a causative relationship, suggests that use of aspiration is indeed related to achieving first pass reperfusion. Aspiration has been investigated in mechanical thrombectomy as a adjunct or alternative to stent retriever in studies such as the ASTER, COMPASS, and ADAPT FAST trials, and our data suggests that exploration of the use of aspiration and subsequent impact on achieving first pass reperfusion is warranted[12,23,24]. In addition, the Random Forest model more heavily relied on factors such as time between symptom onset and catheterization, use of stent retriever, and NIHSS score on presentation, which were weighted less heavily in the logistic regression model. These factors have been extensively investigated in other literature regarding mechanical thrombectomy outcomes, lending credence to the possibility that these variables do influence rates of first pass reperfusion[25–29].

Machine learning models in the literature have been investigated due to having several advantages over traditional statistical models. One advantage is that machine learning models are specialized toward prediction, and often offer better predictive capability when used for the same datasets than traditional logistic regression. Another advantage is the ability to learn based on new data without the need for statisticians or data scientists to recreate the model from scratch, as would be required of a traditional statistical model. In adding new data, machine learning algorithms can adapt to parameters that are not explicitly defined by a human but rather identified by the algorithm itself, increasing the capabilities for automation. These advantages have been extensively characterized and offer tremendous potential within neurosurgery when applied[30–33]. However, one commonly cited limitation of machine learning is the "black box" methodology; not only are outsourced machine learning models in healthcare opaque to the physicians who ultimately make use of the model, but also machine learning algorithms by design are more difficult to interrogate for parameters such as importance of specific variables, relationships between variables, and quantifiable impact of features than statistical models[34,35]. Shapley feature importance analysis, based on Shapley values calculated using game theory mathematics, is one of the foremost methods for this study and has been widely validated, but still is not as straightforward or easy to quantify as measures such as an odds ratio producible from logistic regression model[20,36]. In addition, dataset quality greatly influences machine learning models, and thus creation of valid prediction models depends on having high quality and representative samples to avoid hidden bias.

Limitations of our study include a small patient population, bias produced from the retrospective study design, and absolute predictive capability for the machine learning models. Machine learning models used in the computer science industry often contain many millions of cases, an aspect which is largely unfeasible within the neurosurgical literature. This can produce a lower absolute predictive capability; however, despite this we aim to show improved capability when compared to logistic regression rather than absolute predictive capability given this limited cohort available. In addition, retrospective bias due to attending preference could have influenced our results. However, factors such as attending-dependent technique and adaptation of thrombectomy method to patient-specific anatomy and surgical characteristics are largely shared among large vascular centers, limiting the ability to standardize our data. Further studies, utilized multicenter or large national/international patient cohorts, would demonstrate greater absolute predictive capability, and could result in clinically applicable decision support tools while retaining the advantages over regression models that we demonstrate in our studies.

CONCLUSION:

First pass reperfusion has been investigated as an independent factor for improved clinical outcomes in mechanical thrombectomy, but characterization of variables associated with improved first pass reperfusion has been systematically performed. We present a machine learning analysis for prediction of first pass reperfusion, utilizing supervised learning algorithms, and compare them to traditional logistic regression models. We also present the results of Shapley feature importance analysis for determination of significant variables that influence first pass reperfusion. Machine learning shows promise in increasing predictive capability, but issues such as dataset quality and "black box" methodology must be investigated further before it becomes widely applied in neurosurgery.

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Table 1

Variable	Descriptive Statistics
Sex	45% Male
Comorbidities	History of Cerebrovascular Accident: 15.5% (34/220) Coronary Artery Disease: 17.3% (38/220) Hypertension: 82.7% (182/220) Diabetes Mellitus Type 2: 24.1% (53/220) Hyperlipidemia: 50.5% (111/220) Atrial Fibrillation: 42.7% (94/220)
Smoking	25.0% (55/220)
Medication Use	Blood Thinners: 47.7% (105/220) Statins: 39.5% (87/220)
NIHSS on Presentation	Mean: 15.14 (SD: 6.78)
Location of Stroke	Anterior Circulation: 90.5% (199/220) Posterior Circulation: 9.5% (21/220)
Pre-operative use of tPA	39.5% (87/220)
Surgical Technique:	Stent Retriever: 72.3% (159/220) Aspiration: 83.2% (183/220)
Achieved TICI 2B/3 on first pass	42.3% (93/220)
Total Number of Passes	Mean: 2.68 (SD: 1.09)
Procedure Time	Mean: 48.58 minutes (SD: 29.08)
Post-Procedural sICH	4.5% (10/220)
Length of Stay	Mean: 7.72 Days (SD: 6.35)

Table 2:

Model	Accuracy	AUC	Matthews Correlation Coefficient	Brier Score	Sensitivity	Specificity
Logistic Regression	65.8%	0.657	0.302	0.342	65.4%	65.9%
Random Forest	67.1%	0.659	0.309	0.329	61.5%	70.2%
SVM	67.1%	0.642	0.283	0.329	53.8%	74.5%
Naïve Bayes	56.2%	0.599	0.195	0.438	73.1%	46.8%
XGBoost	61.6%	0.599	0.193	0.384	53.8%	66.0%