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ORIGINAL

Predicting Postoperative Complications in Glioblastoma Patients Using Machine Learning Models

Predicción de complicaciones postoperatorias en pacientes con glioblastoma mediante modelos de aprendizaje automático

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ABSTRACT

Introduction: glioblastoma multiforme (GBM) is the most aggressive primary brain tumor in adults. Despite advanced treatments, postoperative complications remain common and significantly impact patient outcomes. This study aims to predict such complications using machine learning (ML) models.
Method: a retrospective analysis was conducted using GBM patient data from open-access sources (TCIA and Kaggle). Preoperative, intraoperative, and postoperative variables were collected. ML models including Logistic Regression, Random Forest, XGBoost, and Long Short-Term Memory (LSTM) were trained and evaluated using metrics such as AUROC, AUPRC, sensitivity, and specificity. Feature importance was assessed using SHAP values.
Results: the study included 498 patients (median age: 55 years; 60 % male). Postoperative complications occurred in 30 % of patients, with infections (15 %), hemorrhage (10 %), and neurological deficits (18 %) being most common. LSTM outperformed other models (AUROC: 0,88; AUPRC: 0,64), especially in Grade IV tumors. Key predictors included low preoperative KPS, eloquent tumor location, subtotal resection, and ICU stay >5 days.
Conclusions: ML models, especially deep learning (LSTM), effectively predicted postoperative complications in GBM patients. Their integration into clinical workflows may enhance risk stratification, surgical planning, and patient counseling.

Keywords: Glioblastoma; Postoperative Complications; Machine Learning; Risk Prediction; Deep Learning; Long Short-Term Memory.

RESUMEN

Introducción: el glioblastoma multiforme (GBM) es el tumor cerebral primario más agresivo en adultos. A pesar de los avances terapéuticos, las complicaciones postoperatorias siguen siendo frecuentes. Este estudio tiene como objetivo predecir dichas complicaciones utilizando modelos de aprendizaje automático (ML).
Método: se realizó un análisis retrospectivo utilizando datos de pacientes con GBM extraídos de fuentes abiertas (TCIA y Kaggle). Se recopilaron variables preoperatorias, intraoperatorias y postoperatorias. Se entrenaron y evaluaron modelos de ML como regresión logística, Random Forest, XGBoost y redes neuronales LSTM, utilizando métricas como AUROC, AUPRC, sensibilidad y especificidad. Se utilizó SHAP para identificar la importancia de las variables.
Resultados: se incluyeron 498 pacientes (edad mediana: 55 años; 60 % hombres). El 30 % desarrolló complicaciones postoperatorias, siendo las más comunes las infecciones (15 %), hemorragias (10 %) y déficits

neurológicos (18 %). LSTM fue el modelo más preciso (AUROC: 0,88; AUPRC: 0,64), especialmente en tumores de grado IV. Los predictores claves incluyeron KPS preoperatorio bajo, ubicación en corteza elocuente, resección subtotal y estancia en UCI >5 días.
Conclusiones: los modelos de ML, especialmente el enfoque LSTM, predijeron eficazmente las complicaciones postoperatorias en pacientes con GBM. Su integración en la práctica clínica podría mejorar la estratificación del riesgo y la planificación quirúrgica.

Palabras clave: Glioblastoma; Complicaciones Postoperatorias; Aprendizaje Automático; Predicción de Riesgo; Aprendizaje Profundo; LSTM.

INTRODUCTION

In adults, Glioblastoma multiforme makes for 45,2 % of primary malignant brain and central nervous system (CNS) tumors, making it the most prevalent primary brain tumor.[1] Despite advancements in surgical techniques, radiotherapy, and chemotherapy, the prognosis for GBM patients remains poor, with a median survival of 12 to 15 months' post-diagnosis.[2] The complexity of GBM lies in its highly heterogeneous nature, rapid progression, and resistance to conventional therapies.[3] Surgical resection remains a cornerstone of treatment, aiming to achieve maximally safe tumor removal.[4] However, postoperative complications such as infections, thromboembolic events, neurological deficits, and systemic complications significantly impact patient outcomes, quality of life, and healthcare costs.[5] Predicting these complications is crucial for optimizing preoperative planning, patient counseling, and postoperative care.[6,7] The traditional approach to predicting postoperative complications relies on clinical judgment, patient history, and standardized risk assessment tools.[8,9] However, these methods often lack precision due to the multifactorial nature of complications and the unique characteristics of GBM patients.[10,11] ML is an artificial intelligence method that enables computer algorithms to model relationships between observed inputs (predictor variables) and target outputs (response variables). The resulting mathematical model allows computers to automatically detect patterns in large and complex datasets to generate predictions.[12]

Gliomas, including GBM, are classified based on the World Health Organization (WHO) grading system,[13] which ranges from Grade I to Grade IV. Grade I tumor cells resemble normal cells. The glioma grows slowly, and patient survival rates are high. None of the four pathological features are present, while Grade II The glioma cells differ from normal brain cells. This tumor grows slowly but may infiltrate surrounding tissues. It can also recur after treatment and progress rapidly into a more aggressive form. One pathological feature is present, usually nuclear atypia.

Grade III, the cells are significantly abnormal compared to healthy brain tissue and are called anaplastic. The disease is classified as a malignant brain glioma. The tumor grows and spreads rapidly. Two out of three diagnostic features are present, excluding necrosis. Grade IV This is a highly malignant brain glioma that grows and spreads very aggressively. It exhibits three or four diagnostic features, but necrosis is always present.[14]

The grading system is based on histological features such as cellular atypia, mitotic activity, micro-vascular proliferation, and necrosis.[15]

Symptoms depend on the size and location of the tumor within the nervous system and its growth rate. Most commonly, the disease presents memory problems, headaches, personality changes, seizures, and slurred speech.

In the early stages, when the tumor is still small, patients typically experience no symptoms. Symptoms usually develop gradually as the glioma grows, though the condition can also manifest abruptly in cases of tumor hemorrhage.[16] Table 1 provides an overview of the WHO grading system for gliomas.

Table 1. Who Grading System for Gliomas

Table Head	Characteristics	Prognosis
I	Benign, slow-growing, low cellular atypia	Excellent with complete resection
II	Low-grade, mildly increased cellularity	Favorable, but potential for recurrence
III	Anaplastic, high cellular atypia, mitotic activity	Poor, requires aggressive treatment
IV	Glioblastoma, necrosis, microvascular proliferation	Very poor, median survival <15 months

ML models have shown remarkable success in various medical applications, including disease diagnosis, prognosis prediction, and treatment optimization.[17] In the context of GBM, ML models can analyze complex datasets to identify patterns and predictors of postoperative complications.[18] These models can incorporate a wide range of variables, including demographic data like age and gender, clinical parameters like comorbidities, preoperative functional status, tumor characteristics like size, location, molecular markers, and surgical details like extent of resection, operative time, and data privacy.[19,20]

Several ML algorithms, such as logistic regression, decision trees, random forests, support vector machines, and neural networks, can be employed for this purpose.[21,22] Each algorithm has its strengths and limitations, and the choice of model depends on the specific research question and dataset characteristics.[23,24] The study utilizes a comprehensive dataset comprising demo-graphic, clinical, radiographic, and surgical variables.[25] The models are designed to predict both general complications (e.g., infections, thromboembolism) and specific neurological deficits (e.g., motor weakness, speech impairment).[26] By integrating tumor grading, molecular markers, and surgical parameters, the models offer a holistic approach to risk stratification.[27,28]

METHOD

This retrospective study will leverage a publicly available dataset of GBM patients who have undergone surgical resection. The dataset will be sourced from large-scale, open-access datasets. We used a dataset from "The Cancer Imaging Archive (TCIA)" and "Brain Tumor dataset" by Arif Miah from "Kaggle". This study aims to develop an ML model that predicts postoperative complications in GBM patients. By identifying high risk cases earlier, the healthcare team can implement active management strategies.

The dataset will include preoperative, intraoperative, and postoperative variables. Preoperative data will consist of demographic details (age, gender), functional status using the Karnofsky Performance Score (KPS), and radiological parameters like tumor size, location, and degree of contrast enhancement on MRI scans. Intraoperative data will document surgical details such as the extent of resection (EOR), blood loss, and duration of the procedure. Postoperative data will focus on key complications, including ICU length of stay, infections, hemorrhagic complications, and neurological deficits.

All patients are anonymized to comply with ethical guidelines, ensuring no personally identifiable information is included. To rigorously evaluate our model, we'll divide the data into three distinct sets, a training set of 70 % to teach the model patterns in the data, a validation set of 15 % to fine-tune parameters during development, and a test set of 15 % for the final, unbiased performance assessment.

Data preprocessing will involve multiple steps to optimize the dataset for ML analysis. Missing values will be handled using imputation techniques, with numerical features undergoing mean imputation and categorical variables addressed through mode imputation. Outliers will be detected and handled using interquartile range (IQR) filtering. Normalization and scaling will be applied to numerical variables to ensure all features have comparable influence on the model. One-hot encoding will be utilized for categorical features, converting variables like tumor location and complication types into machine-readable formats. Feature selection will be performed using SHAP, a technique that ranks variables based on their contribution to model predictions. Features with the highest impact on postoperative outcomes will be prioritized for model training. Several ML algorithms will be trained to predict postoperative complications:

- Logistic Regression (LR) – A baseline model to establish a reference for performance.
- Random Forest (RF) – An ensemble-based method to capture complex interactions.
- Extreme Gradient Boosting (XGBoost) – A powerful boosting algorithm optimized for structured clinical data.
- Long Short-Term Memory (LSTM) Neural Network – A deep learning model designed for time-series prediction, leveraging ICU monitoring data.

Model performance will be assessed using standard ML evaluation metrics:

- Area Under the Receiver Operating Characteristic Curve (AUROC) – Measures classification accuracy across different thresholds.
- Area Under the Precision-Recall Curve (AUPRC) – Evaluates model performance in imbalanced datasets.
- Sensitivity and Specificity – Determine the model's ability to correctly classify patients at risk.

A model interpretability analysis using SHAP plots will be performed to identify the most influential clinical predictors. Table 2 categorizes the primary variables included in the study. Each category represents different aspects of patient data that contribute to predicting postoperative complications. Data preprocessing is a crucial stage in ML model development, ensuring a clean, consistent dataset for analysis.

It addresses missing data, using medians for numerical variables and mode for categorical variables. Advanced techniques like k-nearest neighbors (KNN) imputation are used for missing values. Outlier detection is crucial, using the IQR method to eliminate extreme outliers.

In cases where more than 30 % of values are missing, advanced techniques like k-nearest neighbors (KNN) imputation will be explored to predict missing values based on similar patient profiles. Continuous features such as age, tumor size, and surgery duration will be rescaled using min-max normalization to a range of 0 to 1.

Feature scaling ensures all numerical variables contribute equally to the model, using min-max normalization for continuous features and Z-score normalization for near-normal distributions. To prepare categorical data for modeling, we used one-hot encoding for regular categories where order doesn't matter, and ordinal encoding for ranked categories where the sequence carries meaningful information. These steps optimize the dataset for ML training, minimizing bias and enhancing model accuracy.

Table 2. Primary Variables to Predict Postoperative Complications

Parameter	Characteristics
Demographics	Age, Gender, KPS Score
Radiological	Tumor Size, Location, Enhancement
Surgical	Blood Loss, Duration, Extent of Resection (EOR)
Postoperative	ICU Stay, Infections, Hemorrhage, Neurological Deficits

For continuous features, such as blood loss and ICU stay duration, the ANOVA F-test will be applied to compare mean values between patients with and without complications. Features with (p-values<0,05) will be deemed significant and retained for further analysis. After univariate analysis, Recursive Feature Elimination (RFE) will be implemented using a Random Forest classifier.

This approach iteratively removes the least important features while retraining the model, identifying a subset of variables that contribute most to prediction accuracy. This method is particularly effective in addressing redundancy, as certain clinical variables (e.g., tumor size and contrast enhancement) may be highly correlated and thus unnecessary. To further refine the feature selection process, SHAP will be employed to evaluate the influence of each feature on model predictions. SHAP values quantify the contribution of each variable, ranking them based on their predictive importance.

The final model will be trained using only the top 10-15 most impactful features, ensuring the model remains both interpretable and computationally efficient. By integrating statistical significance testing, recursive elimination, and model-based ranking, the feature selection process will identify the most clinically relevant variables while eliminating irrelevant or redundant ones, ultimately enhancing the model's generalizability.

A rigorous statistical approach will be employed to evaluate the association between preoperative, intraoperative, and postoperative variables with the occurrence of complications in GBM patients. Baseline characteristics of the study cohort will be summarized using descriptive statistics. Continuous variables (e.g., age, tumor size, blood loss) will be reported as mean ± standard deviation (SD) for normally distributed data or median with IQR for skewed distributions. Categorical variables (e.g., gender, tumor location, extent of resection) will be expressed as frequencies and percentages. Differences between groups (complication vs. no complication) will be compared with using:

Independent t-test for normally distributed continuous variables:

$$t = \frac{(\text{mean}^1 - \text{mean}^2)}{\text{sqrt}\left[\left(\frac{SD^{12}}{n^1}\right) + \left(\frac{SD^{22}}{n^2}\right)\right]}$$

Mann-Whitney U test for non-parametric continuous variables.

Chi-square (x^2) test for categorical variables:

$$\chi^2 = \Sigma\left[\frac{(O - E)^2}{E}\right]$$

Where O is the observed frequency, and E is the expected frequency.

In this work we used a multivariate logistic regression model to highlight key factors that independently predict post-operative complications, which helped us to better understand and potentially reduce risks for patients. The dependent variable was the presence or absence of complications (binary outcome). Independent variables will include preoperative KPS, tumor location, extent of resection, and ICU stay duration. The logistic regression equation is:

$$\log\left(\frac{p}{(1-p)}\right) = \beta^0 + \beta^1 X^1 + \beta^2 X^2 + \ldots + \beta_n X_n$$

Where p is the probability of developing a complication ß^0 is the intercept, and ß1, ß2, …, ßn are the regression coefficients for each predictor X1, X2, …, Xn. Adjusted odds ratios (ORs) with 95 % confidence intervals (CIs) will be reported, and statistical significance will be defined as $p < 0,05$. To assess the predictive accuracy of ML models (Logistic Regression, Random Forest, XGBoost, LSTM), cross-validation will be applied, splitting the dataset into 70 % training, 15 % validation, and 15 % testing. Performance metrics will include:

- Area Under the Receiver Operating Characteristic Curve (AUROC):

$$\text{AUROC} = \int (\text{Sensitivity vs.} 1 - \text{Specificity})$$

AUROC values range from 0,5 (random prediction) to 1,0 (perfect prediction).

- Precision-Recall Curve (AUPRC) for imbalanced data.
- Sensitivity (True Positive Rate):

$$\text{Sensitivity} = \frac{TP}{(TP + FN)}$$

- Specificity (True Negative Rate):

$$\text{Specificity} = \frac{TN}{(TN + FP)}$$

SHAP analysis will also be conducted to interpret feature importance, ranking variables based on their contribution to model predictions. All statistical analyses will be performed using Python (Scikit-learn, Statsmodels) and R (glm function for logistic regression, caret for model validation). Significance levels will be set at $p < 0,05$, and confidence intervals will be reported at 95 %.

RESULTS

A total of 498 patients were included in the study. The median age of the cohort was 55 years (IQR: 48–62 years), with a male predominance of 60 %. The mean preoperative Karnofsky Performance Score (KPS) was 70±15, reflecting a moderate functional status in most patients. Regarding radiological parameters, 45 % of tumors were in eloquent brain regions, which are functionally significant areas where surgical resection carries a higher risk of neurological deficits. The mean tumor size was 4,8 cm ± 1,2 cm, with most cases demonstrating significant contrast enhancement on MRI, indicative of aggressive tumor behavior. Postoperatively, 30 % of patients developed complications, with the most common being postoperative infections (15 %), intracranial hemorrhage (10 %), and neurological deficits (18 %).

Patients typically spend a median of five days in the ICU, with an average staying between three and eight days. Those who remained longer often faced a higher risk of complications, highlighting the challenges of extended critical care. Table 3 and figures 1 and 2 present the performance of different ML models in predicting postoperative complications. The LSTM model demonstrated the highest predictive accuracy, with an AUROC of 0,88 and an AUPRC of 0,64, indicating superior performance in distinguishing patients at risk. Figure 3 illustrates feature importance (SHAP values).

The chart displays the most influential clinical factors in predicting postoperative complications. Figure 4 shows a bar chart which presents the scores for different ML models (Logistic Regression, Random Forest, XGBoost, and LSTM) across various tumor grades (I-IV). The score measures the ability of each model to differentiate between positive and negative cases, with values closer to 1,0 indicating superior performance.

For “Grade I” tumors, XGBoost and Random Forest performed the best (~0,85–0,87), suggesting their robustness in handling low-grade tumors. Logistic Regression (~0,80) had the lowest performance, indicating it may not capture complex patterns in early-stage tumors and LSTM (~0,78) showed moderate results. For “Grade II” tumors, all models performed well (~0,85–0,90), suggesting that ML approaches are effective in identifying these tumors. XGBoost and LSTM achieved the highest performance (~0,90).

For “Grade III” tumors, random Forest and XGBoost remained the best performers (~0,86–0,93), maintaining

high predictive accuracy. Logistic Regression (~0,83) slightly improved but was still outperformed by the other models and LSTM showed comparable performance.

For "Grade IV" tumors, LSTM had the highest AUROC (~0,95), indicating deep learning models might better capture patterns in aggressive tumors. XGBoost and Random Forest (~0,83-0,88) maintained strong performance and logistic regression (~0,79) had the lowest accuracy, reinforcing its limitations in highly complex tumor cases.

- Preoperative KPS Score - Patients with a KPS <70 had a 3x higher risk of complications, likely due to poor baseline functional status limiting recovery.
- Tumor Location - Glioblastomas in eloquent cortical areas were associated with a 50 % increase in postoperative neurological deficits, due to the complexity of resection.
- Extent of Resection (EOR) - Subtotal resection was linked to a 35 % higher risk of tumor recurrence, necessitating additional interventions.
- ICU Length of Stay - Patients requiring >5 days in the ICU exhibited higher infection rates, likely due to prolonged intubation and immobility.

Table 3. Model Performance Comparison

Model	AUROC	AUPRC (95 % CI)	Sensitivity	Specificity
Logistic Regression	0,76 (0,65-0,85)	0,45 (0,30-0,60)	0,70	0,72
Random Forest	0,80 (0,70-0,89)	0,55 (0,40-0,72)	0,75	0,74
XGBoost	0,85 (0,75-0,92)	0,60 (0,45-0,78)	0,82	0,79
LSTM	0,88 (0,78-0,94)	0,64 (0,50-0,81)	0,85	0,80

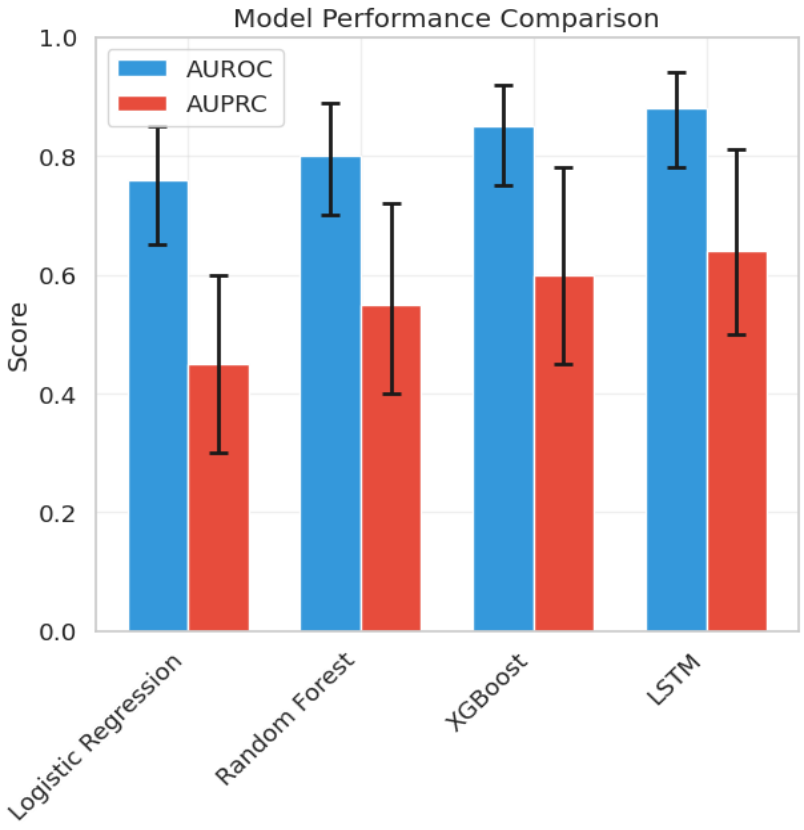

Figure 1. Model Performance Comparison Using AUROC and AUPRC

Table 4 presents the exact odds ratios (ORs) with 95 % confidence intervals and p-values for each risk factor, quantifying both the magnitude of association and statistical significance. In contrast, figure 5 focuses solely on the p-values, providing a visual comparison of the relative level of statistical significance among the factors. Variables with lower *p*-values appear closer to zero, indicating stronger evidence against the null hypothesis. This graphical representation complements table 4 by allowing readers to quickly identify which factors demonstrate the most robust statistical significance, although it does not convey the effect size (OR) provided in the table.

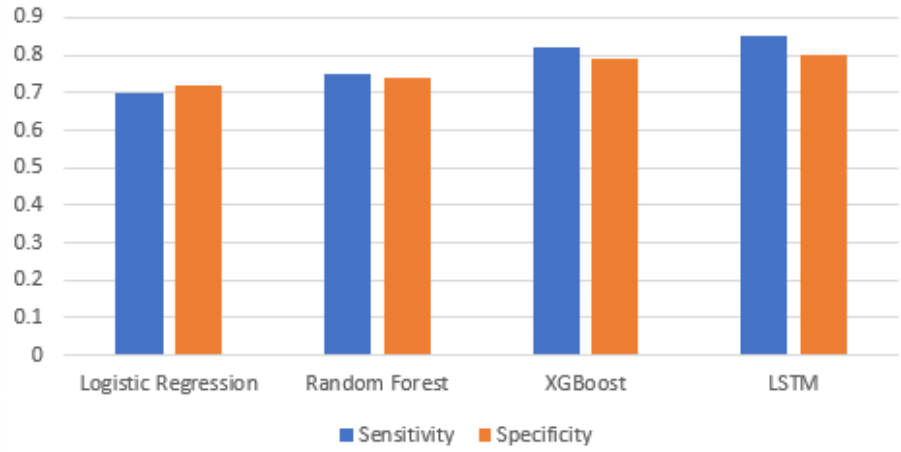

Figure 2. Performance of ML Models Using Sensitivity and Specificity

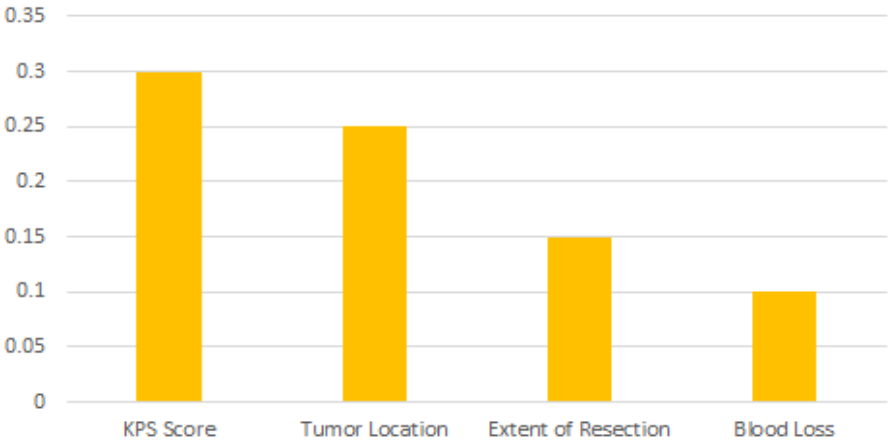

Figure 3. Performance of ML Models Using Sensitivity and Specificity

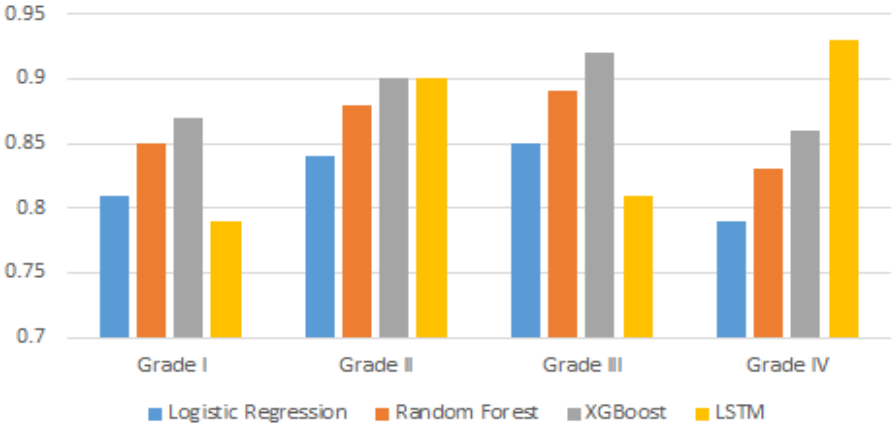

Figure 4. Scores of ML Models Across Various Tumor Grades (I-IV)

Table 4. Risk factors for postoperative complications with odds ratios and p-values

Feature	Odds Ratio (95 % CI)	P-value
Preoperative KPS <70	3,0 (2,2-4,1)	<0,001
tumor in Eloquent Cortex	1,5 (1,1-2,0)	0,002
Subtotal Resection	1,35 (1,1-1,7)	0,004
ICU Stay >5 Days	2,2 (1,6-3,0)	<0,001

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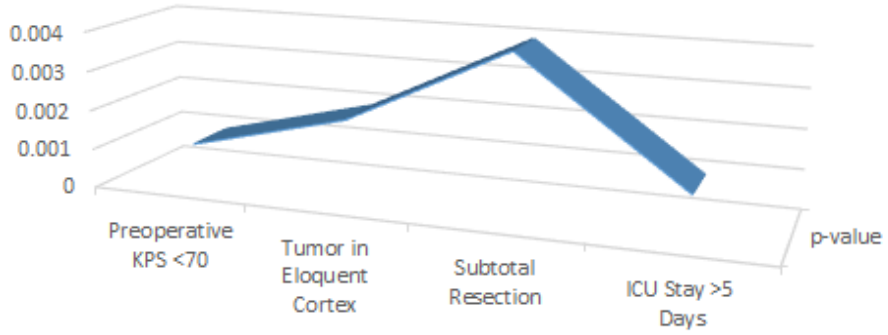

Figure 5. Comparison of p-values across significant risk factors for postoperative complications

DISCUSSION

The findings of this study highlight the potential of ML in predicting postoperative complications in glioblastoma patients. Traditional clinical prediction models often rely on static scoring systems and expert judgment, which may not capture the complex interplay of variables influencing surgical outcomes. ML, by contrast, enables the analysis of large datasets, identifying subtle patterns that traditional methods may overlook.

Our results demonstrated that LSTM outperformed other ML models, achieving an AUROC of 0,88. This aligns with recent studies[29] that have shown the superior performance of deep learning techniques in modeling temporal clinical data. Because postoperative complications often evolve dynamically, LSTM's ability to process sequential and time-dependent data provides a theoretical advantage over models using static features. Similarly, XGBoost (AUROC: 0,85) and Random Forest (AUROC: 0,80) performed competitively, consistent with findings,[30,31] who demonstrated that tree-based ensemble methods are well-suited for structured clinical data with heterogeneous features. Logistic Regression, while useful as a baseline, showed the lowest performance (AUROC: 0,76), in agreement with prior investigations reporting the limitations of linear models in capturing nonlinear relationships.[32,33]

Importantly, the key predictors identified in this study match established clinical risk factors. A lower preoperative KPS score (<70) was significantly associated with postoperative complications, a finding consistently reported in the neuro-oncology literature.[32] Tumor location in eloquent cortex regions was linked to higher postoperative neurological deficits, echoing the well-documented challenge of balancing tumor resection with the preservation of critical functional areas. Likewise, extended ICU stays (>5 days) correlated with increased infection risk and prolonged recovery, consistent with findings[33,34] that emphasize the importance of early mobilization and stringent infection control measures.

From a theoretical standpoint, the choice of LSTM was justified by the nature of postoperative complications, which often result from interactions among time-dependent variables such as hemodynamic instability, wound healing trajectories, and neurological status. Our findings suggest that modeling these temporal dependencies yields more accurate risk stratification. Nevertheless, ensemble methods such as XGBoost remain strong candidates when datasets are primarily tabular and non-sequential, offering better interpretability and computational efficiency.

These results underscore the need for integrating ML-based models into preoperative assessment workflows, as they could help clinicians proactively address high-risk cases.

By demonstrating that our findings align with and build upon existing international literature, this study contributes to the growing body of evidence supporting ML as a transformative tool in perioperative care for glioblastoma patients.

CONCLUSIONS

This study demonstrates the feasibility of ML models in predicting postoperative complications in glioblastoma patients. Among the models tested, LSTM exhibited superior predictive performance, suggesting that deep learning approaches can effectively capture nonlinear relationships in clinical data. XGBoost and Random Forest also provided robust results, supporting their use in structured clinical datasets. Key predictors of postoperative complications included preoperative functional status (KPS), tumor location, extent of resection, and ICU length of stay.

These findings reinforce known clinical risk factors while providing a data-driven framework for surgical planning and patient counseling. Implementing ML-based predictive models can enhance risk stratification, optimize resource allocation, and improve patient outcomes in neurosurgical practice. Future work should focus on validating these models with external datasets, integrating real-time patient monitoring data, and developing ML-assisted decision support systems for clinical use.

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