A Clinic-Radiomics Model for Identifying Improved Functional Performance Status Post-Surgery in High-Grade Glioma Patients

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Introduction

Glioma grade 4 (GG4) tumors, including astrocytoma IDH-mutant grade 4 and the astrocytoma IDH wt are the most common and aggressive primary brain tumors. The introduction of radiomics data in innovative multi-parametric prognostic models developed by machine learning (ML) may allow prognosis refinement of these GG4 patients[1]. Karnofsky performance status (KPS) is a well-established pre-surgical prognostic factor for survival of GG4 patients[2,3].

AIM

Here, we developed a clinical model to identify patients with better functional performance status, as defined by KPS, after surgery by analyzing radiomic features from preoperative 3D-MRIs[4].

Methods

The study included 157 patients who underwent a surgical resection of a newly diagnosed GG4 (according to the WHO 2007 and 2016 classification of brain tumors) at the Neurosurgery Department of Udine Hospital between 2014 and 2019. All patients were treated with combinations of concomitant adjuvant radiotherapy and chemotherapy, followed by adjuvant chemotherapy, as recommended by Stupp. Quantitative imaging features were extracted from the 3D MRI-T1Gd sequence were used to develop the ML model[5,6]. To improve applicability, multivariable logistic regression analysis was performed to build a model incorporating clinical characteristics and Rad-scores. The study followed the CLEAR checklist initiative[7].

Results

Among the 157 GG4 patients, 51 cases were female (32%) and 106 male (68%). The average age of the patients is 61 (53-70) years. The vast majority of the patients complete the radiotherapy and chemotherapy (96%). Among them, 17 (11%) had a mutated IDH status and 95 (61%) had a MGMT methylated status. IDH mutated status was associated with age (p=0.001) and with preoperative volume (measured on MRI-T2, p=0.043).
MGMT methylation status was associated with the EOR (p=0.042). The localization was associated with ependyma involvement (p<0.001), the shift (p=0.004) and the preoperative volume (Volume MRI-T2,

p=0.011). Furthermore, cases that after surgery had a KPS greater than 90 showed an association with involvement of the ependyma (p=0.003) and the average hospital length of stay (p <0.001).
To develop the prognostic model, we calculated the difference in KPS status before and after surgery. We found 55 cases (35%) with a kps-flag.
GG4 cases classified as cases with a kps-flag =1 for having an improvement of performance status were characterized by a heterogeneity of localization, side and different rates of EOR. For these reasons there is the need of using other information such as radiomics data to improve the way to classify that condition
A total of 1132 features from MRI-T1Gd images were extracted using Pyradiomics, including shape (14 features), first-order intensity statistics (18 features), Gray Level Co-occurrence Matrix (22 features), Gray Level Size Zone Matrix (16 features), Gray Level Run Length Matrix (16 features), Gray Level Dependence Matrix (14 features), logarithm (344 features), and wavelet (688 features).
The data were divided into train and test as 80:20. No significant difference was found in the clinical variables between training and test. Due to the large number of extracted features from the MRI segmentation, we combined many feature selection methods to obtain an optimal number of features. After the elimination of highly correlated features and the Boruta method, a set of 174 features was retained and used in the further steps.
To test the association between a kps-flag and the preoperative radiomics data from the MRI-T1Gd, two ML algorithms were used: Random forest (RF) and Extreme Gradient Boosting (XGBoost). For both the approaches, we used Bayesian optimization to adjust hyper-parameters to obtain the best area under the Receiver Operating Characteristic Curve (ROC-AUC) and Matthews correlation coefficient (MCC).
The XGBoost achieved a mean cross-validation MCC of 0.418 (95% bootstrapped confidence interval: 0.407-0.430), significantly higher than the RF model with a mean cross-validation MCC of 0.104 (-0.07-0.26) (Kruskal-Wallis p = 0.034). On the test set, an out-of-sample MCC of 0.235 was obtained.
In order to obtain that simplifies decision making, we collected the main radiomic features from the ML model and combined them with the clinical variables. Then we performed a univariate logistic regression analysis. The variables that resulted significant by univariate logistic regression were included in the multivariate analysis and, after stepwise selection, the final model was categorically adjusted for age, gender status and extent of resection (Hosmer and Lemeshow goodness of fit p=0.852 AUC 0.82395% CI: 66.1%-96.41% 100 stratified bootstrap replicates). The clinical radiomics nomogram yielded a C-index of 0.825 and of 0.760 in the train and the validation cohorts, respectively. The nomogram showed the same diagnostic efficacy as the radiomics model.

Conclusion

MRI radiomic analysis represents a powerful tool to predict postoperative functional outcome, as evaluated by KPS.

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