low-grade glioma case series

2023

Rauch et al. retrospectively included 349 low-grade glioma patients to develop a prediction model using clinical, anatomical, and preoperative MRI data. Before performing radiomics analysis, a U2-model for glioma segmentation was utilized to prevent bias, yielding a mean whole tumor Dice score of 0.837. Overall survival and time to malignancy were estimated using Cox proportional hazards model. In a postoperative model, they derived a C-index of 0.82 (CI 0.79-0.86) for the training cohort over 10 years and 0.74 (CI 0.64-0.84) for the test cohort. Preoperative models showed a C-index of 0.77 (CI 0.73-0.82) for training and 0.67 (CI 0.57-0.80) test sets. The findings suggest that they can reliably predict the survival of a heterogeneous population of glioma patients in both preoperative and postoperative scenarios. Further, they demonstrate the utility of radiomics in predicting biological tumor activity, such as the time to malignancy and the LGG growth rate [1)].

2020

Skjulsvik et al. wanted to explore whether defining molecular markers in low-grade gliomas (LGG; WHO grade II) is related to distance to the neurogenic niches.

Patients treated at two Norwegian university hospitals with population-based referrals were included. Eligible patients had histopathological verified supratentorial low-grade glioma. IDH mutational status and 1p19q co-deletion status was retrospectively assessed. 159 patients were included, and semi-automatic tumor segmentation was done from pre-treatment T2-weighted (T2W) or Fluid-Attenuated Inversion Recovery (FLAIR) images. 3D maps showing the anatomical distribution of the tumors were then created for each of the three molecular subtypes (IDH mutated/1p19q co-deleted, IDH mutated and IDH wild-type). Both distance from tumor center and tumor border to the neurogenic niches were recorded.

In this population-based cohort of previously untreated low-grade gliomas, they found that low-grade gliomas are more often found closer to the SVZ than the SGZ, but IDH wild-type tumors are more often found near SGZ.

The study suggests that the stem cell origin of IDH wild-type and IDH mutated low-grade gliomas may be different [2)].

Postoperative functional neuroimaging provides a unique opportunity to investigate the neural mechanisms that facilitate language network reorganization. Previous studies in patients with low-grade gliomas (LGGs) in language areas suggest that postoperative recovery is likely due to functional neuroplasticity in peritumoral and contra-tumoral healthy regions, but have attributed varying degrees of importance to specific regions. In this study, Lizarazu et al. used Magnetoencephalography (MEG) to investigate functional connectivity changes in peritumoral and contra-tumoral regions after brain tumor resection. MEG recordings of cortical activity during resting-state were obtained from 12 patients with LGGs in left-hemisphere language brain areas. MEG data

were recorded before (Pre-session), and 3 (Post_1 session) and 6 (Post_2 session) months after awake craniotomy. For each MEG session, we measured the functional connectivity of the peritumoral and contra-tumoral regions to the rest of the brain across the 1-100 Hz frequency band. We found that functional connectivity in the Post_1 and Post_2 sessions was higher than in the Pre-session only in peritumoral regions and within the alpha frequency band. Functional connectivity in peritumoral regions did not differ between the Post_1 and Post_2 sessions. Alpha connectivity enhancement in peritumoral regions was observed in all patients regardless of the LGG location. Together, these results suggest that postoperative language functional reorganization occurs in peritumoral regions regardless of the location of the tumor and mostly develops within 3 months after surgery [3].

2019

Patients diagnosed with LGG from 1973 to 2013 were identified using the Surveillance, Epidemiology, and End Results database (SEER). A total of 3732 patients were randomly divided into a training set (2612) and a validation set (1120), and univariate and multivariate Cox regression analyses of clinical variables were performed to screen for significant prognostic factors. Then, a nomograph that included significant prognostic variables was formulated to predict LGG. Harrell's concordance index (C-index), calibration plots were formulated to evaluate the reliability and accuracy of the nomograph by bootstrapping based on internal (training set) and external (validation set) validity.

A nomogram was developed to predict 5- and 9-year OS rates based on seven variables in the training set: age, tumor site, sex, marital status, histology, tumor size, and surgery ($p < 0.05$). The C-index for internal validation, which the nomogram used to predict OS based on the training set, was 0.777 (0.763-0.791), and the C-index for external validation (validation set) was 0.776 (0.754-0.797). Based on calibration plots, the actual observation and prediction values obtained by the nomogram had good consistency between the two sets.

Zhao et al. developed a ready-to-use nomogram model based on clinical characteristics to predict survival outcomes and the nomogram may provide consultation and risk assessments for subsequent treatment in patients with LGG [4].

Forty-two patients who had previously undergone surgical or multimodal treatment for a histologically verified low-grade glioma (LGG) were referred for FET PET assessment because of clinical signs and/or MRI findings suggestive of tumor progression. Maximal and mean tumor-to-brain ratios (TBRmax and TBRmean, respectively) on FET PET as well as kinetic FET PET parameters (time to peak [TTP] and time-activity curve [TAC]) were determined. Final diagnoses were confirmed histologically. The diagnostic accuracy of FET parameters, separately and combined, for the detection of malignant progression was evaluated using receiver operating characteristic (ROC) curve analysis. Possible predictors that might influence the diagnostic accuracy of FET PET were assessed using multiple linear regression analysis. Spearman's Rank Correlation Coefficient r method was applied to determine the correlation between TBRmax and TAC, and molecular biomarkers from tumor tissues.

A total of 47 FET PET scans were obtained and showed no significant association between FET parameters and contrast enhancement on MRI. ROC curve analyses overall were unable to demonstrate any significant differentiation between nontransformed LGGs and LGGs that had transformed to high-grade gliomas when evaluating FET parameters separately or combined. After excluding the oligodendroglial subgroup, a significant difference was observed between nontransformed and transformed LGGs when combining FET parameters (i.e., TBRmax > 1.6, TAC

describing a plateau or decreasing pattern, and TTP < 25 minutes), with the best result yielded by a combined analysis of TBRmax > 1.6 and TAC with a plateau or decreasing pattern (sensitivity 75% and specificity 83%, p = 0.003). The difference was even greater when patients who had previously undergone oncological treatment were also excluded (sensitivity 93% and specificity 100%, p = 0.001). Multiple linear regression analysis revealed that the presence of an oligodendroglial component (p = 0.029), previous oncological treatment (p = 0.039), and the combined FET parameters (p = 0.027) were significant confounding factors in the detection of malignant progression. TBRmax was positively correlated with increasing cell density (p = 0.040) and inversely correlated with IDH1 mutation (p = 0.006).

A single FET PET scan obtained at the time of radiological and/or clinical progression seems to be of limited value in distinguishing transformed from nontransformed LGGs, especially if knowledge of the primary tumor histopathology is not known. Therefore, FET PET imaging alone is not adequate to replace histological confirmation, but it may provide valuable information on the location and delineation of active tumor tissue, as well as an assessment of tumor biology in a subgroup of LGGs [5].

Preoperative MRI scans of 47 patients diagnosed with low-grade glioma with IDH1 mutation and a genetic analysis for 1p/19q deletion status were included in this study. A total of 152 features, including size, location and texture, were extracted from fluid-attenuated inversion recovery images, [Formula: see text]-weighted images (WI) and post-contrast [Formula: see text]. Classification was performed using 17 machine learning classifiers. Results were evaluated by a fivefold cross-validation analysis.

Radiomic analysis differentiated tumors with 1p/19q intact ([Formula: see text]; astrocytomas) from those with 1p/19q codeleted ([Formula: see text]; oligodendrogliomas). Best classification was obtained using the Ensemble Bagged Trees classifier, with sensitivity [Formula: see text] 92%, specificity [Formula: see text] 83% and accuracy [Formula: see text] 87%, and with area under the curve [Formula: see text] 0.87. Tumors with 1p/19q intact were larger than those with 1p/19q codeleted ([Formula: see text] vs. [Formula: see text] cc, respectively; [Formula: see text]) and predominantly located to the left insula ([Formula: see text]).

The proposed method yielded good discrimination between LGG with and without 1p/19q codeletion. Results from this study demonstrate the great potential of this method to aid decision-making in the clinical management of patients with LGG [6].

A retrospective consecutive assessment of patients treated for LGGs (World Health Organization grade II) with iMRI-guided resection at 6 neurosurgical centers was performed. Eloquent location, extent of resection, first-line adjuvant treatment, neurophysiological monitoring, awake brain surgery, intraoperative ultrasound, and field-strength of iMRI were analyzed, as well as progression-free survival (PFS), new permanent neurological deficits, and complications. Multivariate binary logistic and Cox regression models were calculated to evaluate determinants of PFS, gross total resection (GTR), and adjuvant treatment.

A total of 288 patients met the inclusion criteria. On multivariate analysis, GTR significantly increased PFS (hazard ratio, 0.44; P < .01), whereas “failed” GTR did not differ significantly from intended subtotal-resection. Combined radiochemotherapy as adjuvant therapy was a negative prognostic factor (hazard ratio: 2.84, P < .01). Field strength of iMRI was not associated with PFS. In the binary logistic regression model, use of high-field iMRI (odds ratio: 0.51, P < .01) was positively and eloquent

location (odds ratio: 1.99, P < .01) was negatively associated with GTR. GTR was not associated with increased rates of new permanent neurological deficits.

GTR was an independent positive prognostic factor for PFS in LGG surgery. Patients with accidentally left tumor remnants showed a similar prognosis compared with patients harboring only partially resectable tumors. Use of high-field iMRI was significantly associated with GTR. However, the field strength of iMRI did not affect PFS [7].

A collection of 210 archived adult low-grade glioma (LGG) previously stratified by IDH mutation, MGMT methylation (MGMTmet), 1p19q combined loss of heterozygous (1p19qloh) and TP53 immunopositivity (TP53pos) status was analyzed. We used multistate models to assess MT-free survival, considering one initial, one transient (MT), and one absorbing state (death). Missing explanatory variables were multiply imputed. Overall, although associated with a lower risk of death (HRDEATH = 0.35, P = 0.0023), IDHmut had a non-significantly higher risk of MT (HRMT = 1.84; P = 0.1683) compared to IDH wild type (IDHwt). The double combination of IDHmut and MGMTmet and the triple combination of IDHmut, MGMTmet and 1p/19qloh, despite significantly lower hazards for death (HRDEATH versus IDHwt: 0.35, P = 0.0194 and 0.15, P = 0.0008, respectively), had non-significantly different hazards for MT. Conversely, the triple combination of IDHmut/MGMTmet/TP53pos, with a non-significantly different hazard for death, had a significantly higher hazard for MT than IDHwt (HRMT versus IDHwt: 2.83; P = 0.0452). Although IDHmut status is associated with longer overall patient survival, all IDHmut/MGMTmet subsets consistently showed higher risks of MT than of death, compared to IDHwt LGG. This supports the findings that molecular events relevant to IDH mutations impact early glioma development prior to malignant transformation [8].

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