Dynamic Susceptibility Contrast Perfusion MR imaging of Low-grade Gliomas:Cerebral Blood Volume Predicts Patient Outcome Better than Histopathology

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INTRODUCTION: The current gold standard for determining glioma grade is histopathologic assessment. However, the limitations of histopathology are well known: 1) Since only a few small samples of tissue are assessed, particularly from stereotactic biopsy, the most malignant portion of a tumor may not be sampled (sampling error); 2) It may be difficult to obtain a range of samples if the tumor is inaccessible to the surgeon; 3) The large range of classification/grading systems used between different institutions; 4) Inter-pathologist and intra-pathologist variability; 5) The dynamic nature of CNS tumors, with at least 10% de-differentiating into more malignant grades, it is the belief of some neurosurgeons that given time, all LGGs will de-differentiate (1, 2). The purpose of this study is to determine whether cerebral blood volume (CBV) can predict patient outcome, specifically tumor progression and malignant transformation, in low-grade gliomas (LGGs) and thus overcome some of the limitations of histological assessment.

MATERIALS AND METHODS: Thirty-five patients with histologically diagnosed LGGs (21 low-grade astrocytomas and 14 low-grade oligodendroglioma and low-grade mixed oligo-astrocytomas), were studied with dynamic susceptibility contrast-enhanced perfusion MRI (DSC MRI). Wilcoxon tests were used to compare patients in different response categories (complete response, stable, progressive, death) with respect to baseline CBV. Kaplan-Meier time-to-progression curves were generated. Weibull survival models were used to predict the association of CBV with survival and time to progression. Tumor volumes and CBV measurements were obtained at the initial examination and again at follow up.

RESULTS: Lesions with CBV < 1.75 had a median time to progression of 4620 ± 433 days and lesions with CBV > 1.75 had a median time to progression of 245 ± 62 days (Figure 1). Patients manifesting an adverse event (either death or progression) had significantly higher (p = 0.003) CBV than patients without adverse events (either complete response or stable disease). Using Weibull survival models, neither age (p = 0.339) nor gender (p = 0.90) was associated with overall survival, whereas CBV exhibited a significant negative association with survival (p = 0.001) such that low CBV values were associated with longer survival times. The same basic conclusion held for time to progression: neither age (p = 0.312) nor gender (p = 0.285) was associated with time to progression, whereas CBV exhibited a significant negative association with disease-free survival (p = 0.001), such that low CBV values were associated with longer disease-free survival times. Baseline CBV was not correlated with tumor volume changes seen in post contrast T1 (p = 0.896) or T1 (p = 0.338) on follow up imaging.

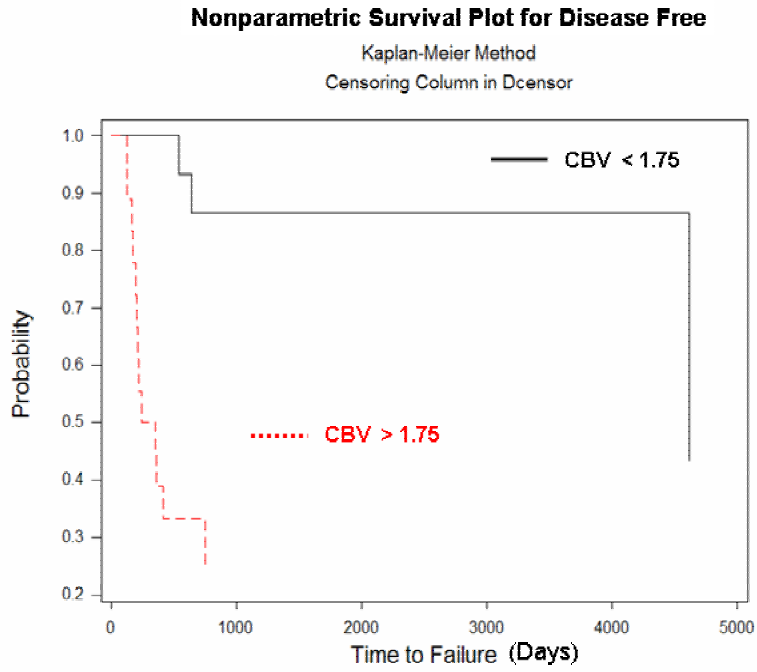

Figure 1. Kaplan-Meier survival curves for demonstrating the probability of time to progression at the most recent clinical follow up. LGGs with CBV < 1.75 had a median time to progression of 4620 ± 433 days (black solid curve which is far right shifted). LGGs with CBV > 1.75 had a median time to progression of 245 ± 62 days (red dashed curve which is far left shifted, p < 0.005). The data suggests that baseline CBV may be a stronger predictor of patient outcome than the initial

CONCLUSION: The current gold standard of histopathologic glioma grading has limitations. Partly because of this, the triage, treatment and survival statistics of low-grade gliomas remain unclear. However, patients with misclassified gliomas will not receive optimum treatment. Our study strongly suggests that cerebral blood volume measurements correlate more accurately with time to progression than initial histolopathologic grading.

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