Early Relative Cerebral Blood Volume Changes Predict Progression After Convection-Enhanced Delivery of Topotecan for Recurrent Malignant Glioma

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Introduction

After treatment of glioma by a variety of modalities, an increase in contrast-enhancing volume can represent progression of disease or pseudoprogression, a radiographic phenomenon that is followed by reduction in tumor size. Radiographic differentiation between these two entities could be invaluable as it would allow more rapid advancement of therapy for progression, or no change in therapy for pseudoprogression. We performed the following analyses in an attempt to use relative cerebral blood volume (rCBV) as an early indicator of progression in a select group of patients.

Methods

Sixteen patients were enrolled in a Phase I trial of convection-enhanced delivery of topotecan for recurrent malignant glioma. Each patient was evaluated with serial follow up MR imaging at baseline and at 4 to 8 week intervals. Changes of rCBV at one month were evaluated as a potential predictor of 6-month progression, classified as progressive disease (PD) or nonprogressive disease (NPD). The relationship between percent change in rCBV at one month and the probability of progressive disease at 6 months was estimated using logistic regression analysis.

Conclusions

In this selected population of patients with recurrent malignant glioma treated with convection-enhanced delivery of topotecan, early changes in rCBV at four weeks after therapy may help predict progression status at 6 months.

Results

There was a significant difference in the percent change in rCBV at one month in patients with PD as compared to those with NPD at six months (+12% vs. -29%, p=0.02). Logistic regression analysis demonstrated that each 10% increase in rCBV at one month portends 1.7 times the odds of developing progressive disease at six months (95% CI: 1.0, 2.9 p=0.05).

ROC analysis demonstrated that the optimal maximum cutoff for percent change in rCBV at one month from baseline for predicting nonprogressive disease at 6 months was -1.9% (sensitivity, 80%; specificity 83%; positive predictive value, 89%; negative predictive value, 83%, efficiency, 81.2%). The threshold percent change in rCBV associated with the highest efficiency in predicting nonprogressive disease at 6 months was -25.5% (sensitivity, 100%; specificity 67%; positive predictive value, 83%; negative predictive value, 100%, efficiency, 87.5%) (See ROC figure).

Learning Objectives

By the conclusion of this session participants should be able to 1)Describe the importance of early monitoring of rCBV in high grade glioma patients to differentiate pseudoprogression from true progression, 2)Discuss, in small groups, the utility and implementation of using rCBV in post-treatment MRIs for patients with high grade gliomas.

ROC curve for rCBV at 1 month post-treatment as predictor of progressive disease at 6 months post-treatment