Evaluation of dynamic contrast-enhanced MRI derived microvascular permeability in recurrent glioblastoma treated with bevacizumab.

Bevacizumab, an antibody to vascular endothelial growth factor, is commonly used in the setting of recurrent glioblastoma (rGB). The aim of the present study was to evaluate whether dynamic-contrast-enhanced MRI (DCE-MRI) derived microvascular permeability is related to bevacizumab treatment outcome in rGB. Twenty-two patients with rGB underwent DCE-MRI at a median of 2.6 weeks prior initializing bevacizumab therapy. Follow-up MRI-scans (DCE-MRI available for 19/22 patients) were obtained after a median of 9.9 weeks. The volume transfer constant ($K_{(\text{trans})}$)–an estimate related to microvascular permeability–at baseline and voxel-wise-reduction (VWR) in $K_{(\text{trans})}$ at first follow-up were measured from the entire contrast-enhancing tumor (CET) and correlated with progression-free and overall survival (PFS, OS) using univariate and multivariate cox-regression (significance-level p< 0.05). Baseline $K_{(\text{trans})}$ ranged from 0.050 to 0.205 min(-1) (median, 0.109 min(-1)). The VWR in $K_{(\text{trans})}$ ranged from 19.9 to 97.2 % (median, 89.4 %). Patients with lower baseline $K_{(\text{trans})}$ and higher VWR in $K_{(\text{trans})}$ showed significantly longer PFS and OS. Given the strong correlation of VWR in $K_{(\text{trans})}$ and CET-volume changes
(Spearman's $\rho = -0.73, p< 0.01$) both variables were included in a multivariate model. Thereby, neither VWR in $K(\text{trans})$ nor CET-volume changes retained independent significance for PFS or OS. Pre-treatment $K(\text{trans})$ stratifies PFS and OS in patients with bevacizumab-treated rGB. Although early pharmacodynamics changes in $K(\text{trans})$ were not assessed, the VWR in $K(\text{trans})$ at first follow-up had no additional benefit over assessment of CET-volume changes. Further prospective trials are needed to confirm these findings and to elucidate the potential role of pre-treatment $K(\text{trans})$ as a predictive and/or prognostic biomarker.