Blood Pool Contrast Agent High Resolution MR Angiography in Glioblastoma: Tumor Vasculature as a Biomarker for Survival

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Purpose:

Vascularity, defined histologically or with molecular techniques, correlates with poor survival in patients with glioblastoma. Regionally heterogeneous vascularization limits histologic markers, which are measured only in some tissue sections. More accurate assessment of valid vascular biomarkers such as digital subtraction angiography or dynamic susceptibility contrast (DSC) perfusion MRI represents a challenge; thus far, MR angiography has been unable to characterize glioblastoma vascularity. Gadofosveset is an albumin-binding contrast agent approved for imaging blood vessels. It remains largely intravascular because it forms reversible noncovalent bonds with albumin, resulting in a 4- to 5-fold increase in blood relaxivity at 1.5 T compared to extracellular contrast agents. We aimed to (a) assess the vascularity of newly diagnosed glioblastomas using gadofosveset high-resolution MR angiography, (b) correlate the findings with dynamic DSC and diffusion MR imaging (MRI) parameters for contrast-enhancing lesion (CEL) and surrounding non-CEL, and (c) determine whether high resolution MR angiography of tumor is useful in predicting survival.

Materials and Methods:

Before treatment, 33 patients (23 men; mean age, 63 years) with histologically proven glioblastoma underwent MRI including anatomical sequences, first-pass DSC images and postcontrast T1-weighted SE images after gadobutrol (Gadovist; Bayer Schering Pharma, Berlin, Germany) at 0.1 mmol/kg and, 48 hours later, high-resolution MR angiography acquired after gadofosveset (Ablavar, Lantheus Medical Imaging, North Bilerica, USA) at 0.03 mmol/kg with a 0.6 mm isometric voxel. Two independent observers evaluated presence of vessels on high resolution MR angiography. Volumes of interest for CEL, NCEL, and contralateral tissue were obtained for cerebral blood volume ratio (rCBV), cerebral blood flow ratio (rCBF), permeability constant (k2), mean temporal maximal intensity projection (tMIP), and apparent diffusion coefficient (ADC) using Olea Sphere V.2.0 software (Olea Medical, La Ciotat, France). Statistical analyses included Pearson correlation, linear regression analysis, and interclass correlation coefficients. Prognostic factors were evaluated by Kaplan-Meier survival and Cox proportional hazards analysis.

Results:

Eighteen (52.94%) glioblastomas were vascular and 16 (40.5%) avascular on high resolution MR angiography (Figure); interobserver reliability was good (K=0.745). In vascular glioblastomas, mean tMIP values were higher (p=0.024) and there was a trend to lower mean ADC values (p=0.068) (Table). Median survival for avascular and vascular glioblastomas treated with surgery and with radiotherapy plus chemotherapy was 15 months (95% CI, 4.5-30.2) and 8.5 months (95% CI, 2.9-14.1), respectively. When treatment was incomplete, median survival for avascular and vascular glioblastomas was 6.5 months (95% CI, 3.1-9.8) and 3.5 months (95% CI, 2.1-4.9), respectively. Vascular pattern was the best survival predictor for glioblastoma at 5.25 months (AUC 0.794, 81.2% sensitivity, 77.8% specificity, 76.5% positive predictive value, 82.4% negative predictive value). Vascular pattern yielded the highest hazard ratio (14.012; 95% CI: 2.436,80.579; P=0.003).

Conclusions:

High resolution MR angiography using gadofosveset can detect vascularity in glioblastoma. Vascularity is a useful imaging biomarker that correlates with worse survival in newly diagnosed glioblastoma.

Adult Brain:

Neoplasms

Anatomy - Secondary:

Brain

Keywords:

Glioblastoma

MR Imaging/MR Angiography

Outcome

	Contralateral gray matter	Non contrast-enhancing	

				lesion			Contrast-enhancing lesion		
	Avascular	**Vascular**	**p-value**	**Avascular**	**Vascular**	**p-value**	**Avascular**	**Vascular**	**p-value**
rCBF	18.3 (5.66)	16.58 (6.48)	0.429	20.81 (8.67)	18.14 (10.29)	0.432	44.65 (21.79)	55.53 (23.78)	0.193
rCBV	1.68 (0.63)	1.46 (0.7)	0.343	1.93 (0.71)	1.61 (0.99)	0.305	3.92 (1.82)	4.54 (2.25)	0.408
rCBVc	1.25 (0.49)	1.03 (0.52)	0.219	1.41 (0.5)	1.17 (0.8)	0.324	3.15 (1.52)	3.51 (1.55)	0.512
MTT	5.74 (1.31)	5.29 (1.07)	0.285	5.73 (1.59)	5.24 (2.02)	0.451	5.1 (1.19)	4.91 (1.3)	0.685
Tmax	3.06 (0.61)	3.11 (0.59)	0.81	5.32 (2.61)	6.91 (3.86)	0.184	5.59 (3.76)	5.21 (3.66)	0.775
TTP	38.12 (18.47)	42.47 (17.71)	0.495	38.09 (18.05)	41.85 (16.64)	0.539	39.81 (18.29)	41.8 (17.48)	0.756
K2	-46.75 (33.34)	-41.31 (18.08)	0.555	-48.32 (60.66)	-27.48 (36.07)	0.23	-62.96 (117.32)	-69.31 (87.32)	0.862
Cmax	0.12 (0.04)	0.12 (0.03)	0.676	0.13 (0.06)	0.13 (0.04)	0.948	0.29 (0.11)	0.41 (0.16)	**0.024**
ADC	79.6 (4.17)	82.05 (3.89)	0.091	130.18 (16.77)	134.59 (14.1)	0.417	120.86 (20)	109.73 (13.16)	**0.068**

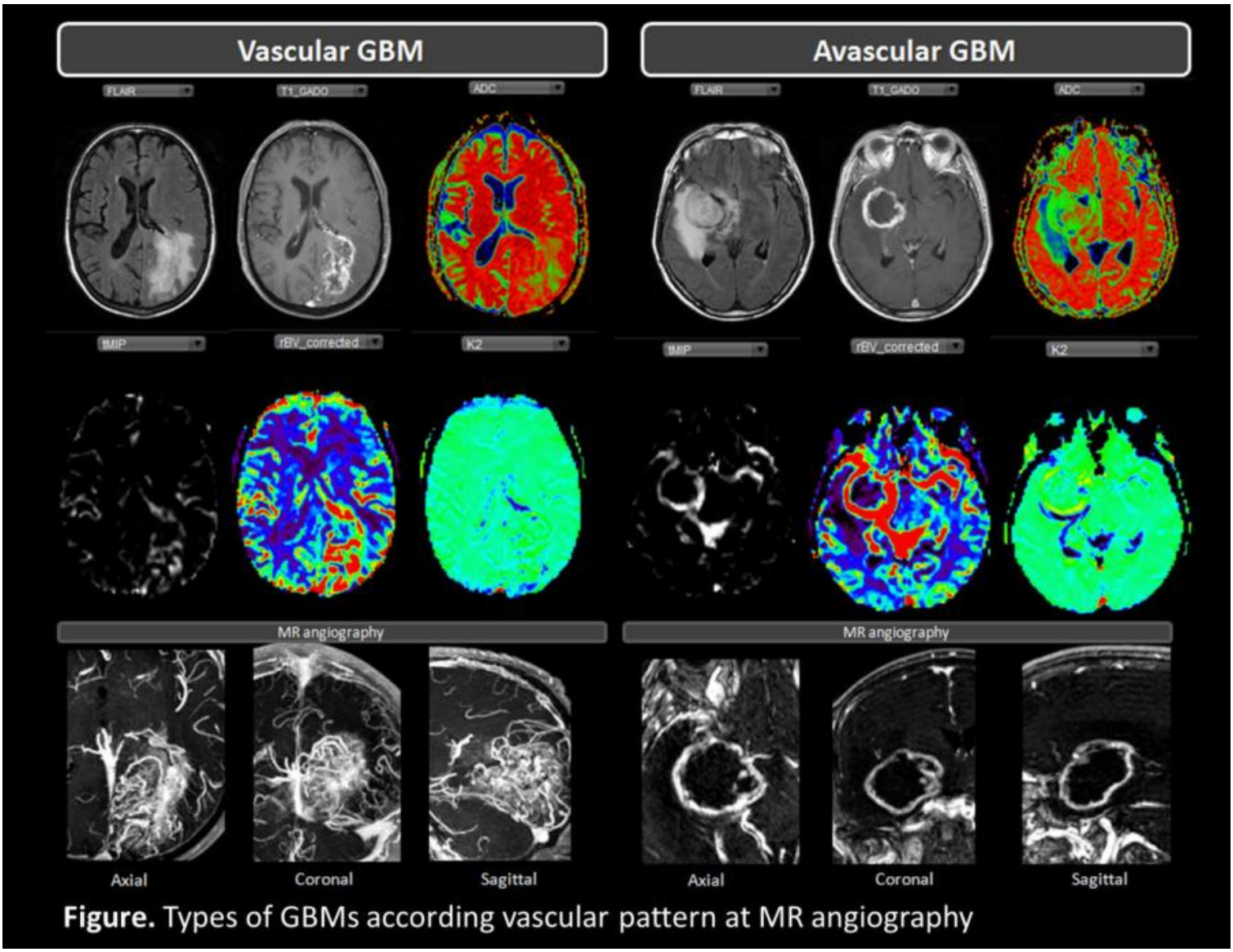

Figure. Types of GBMs according vascular pattern at MR angiography