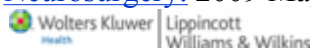




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1: [Neurosurgery](#). 2009 May;64(5):819-26; discussion 826-7.



Surrogate markers predict angiogenic potential and survival in patients with glioblastoma multiforme.

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OBJECTIVE: The neovascularization of malignant brain tumors is a poorly understood phenomenon. Radiographic and histological evidence of increased vascularity correlate with clinical grade of gliomas. However, a quantitative noninvasive assay to assess glioma vascularity and associated clinical aggressiveness has not been developed. Circulating endothelial progenitor cells are unique vascular precursors recruited from the bone marrow through the circulation to form new tumor blood vessels. These cells were measured in patients undergoing surgery for glioblastoma multiforme (GBM). We hypothesized that this might reflect the extent of tumor vascularity, predict prognosis, or be useful as an assay to assess response to antiangiogenesis therapies. In addition, we report on a novel in vitro assay to assess the proangiogenic activity within the plasma samples obtained from glioma patients. **METHODS:** Fifty-six patients with various-grade gliomas had peripheral venous blood collected at the time of surgery and at subsequent visits during the follow-up period. The blood was separated into plasma and cellular fractions. The plasma was utilized in a human umbilical vein endothelial cell-based angiogenic assay. The cellular fraction containing endothelial progenitor cells was isolated, and specific cellular phenotypes were immunologically separated and counted using flow cytometry. Pathological samples were reviewed at the time of initial resection, and each patient's clinical course was monitored until the time of manuscript submission. **RESULTS:** Plasma derived from peripheral blood of patients with GBM scored significantly higher on the functional angiogenic scale compared with plasma derived from patients with low-grade gliomas and from controls. In addition, all patients with GBM had measurable numbers of bone marrow-derived endothelial precursor cells coexpressing CD133 and vascular endothelial growth factor receptor 2 in their peripheral circulation at the time of tumor resection. These cells range from less than 0.1% to 1.6% of the entire circulating mononuclear white blood cell population, or approximately 200,000 cells in some patients. A statistically significant relationship was observed between the percentage of endothelial progenitor cells in the peripheral blood at the time of initial GBM resection and survival. **CONCLUSION:** These studies suggest that plasma and circulating CD133+ vascular endothelial growth factor receptor 2+ proangiogenic cells are present in the peripheral blood of patients with glioma and can be used as a surrogate biomarker to measure tumor angiogenicity. These cells can be measured at the time of diagnosis and monitored in the postoperative period. These assays can be used to predict tumor aggressiveness. Also promising is their potential to identify patients with increased angiogenic activity who might respond maximally to antiangiogenesis therapies or to assess tumor response in patients using those therapies as the use of these adjuvant molecular modalities becomes more prevalent in neuro-oncology.

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