

ABSTRACT

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Determining venous thromboembolism risk in patients with adult-type diffuse glioma.

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Venous thromboembolism (VTE) is a life-threatening condition that is common in patients with adult-type diffuse gliomas, yet thromboprophylaxis is controversial because of possible intracerebral hemorrhage. Effective VTE prediction models exist for other cancers, but not glioma. Our objective was to develop a VTE prediction tool to improve glioma patient care, incorporating clinical, blood-based, histologic, and molecular markers. We analyzed preoperative arterial blood, tumor tissue, and clinical-pathologic data (including next generation sequencing data) from 258 patients with newly diagnosed World Health Organization (WHO) grade 2-4 adult-type diffuse gliomas. Forty-six (17.8%) experienced VTE. Tumor expression of tissue factor (TF) and podoplanin each positively correlated with VTE, though only circulating TF and D-dimers, not circulating podoplanin, correlated with VTE risk. Gliomas with mutations in IDH1 or IDH2 (IDHmut) caused fewer VTEs; multivariable analysis suggested that this is due to IDHmut suppression of TF, not podoplanin. In a predictive time-to-event model based on LASSO, the following predicted increased VTE risk in newly diagnosed glioma patients: (1) prior history of VTE; (2) hypertension; (3) asthma; (4) white blood cell count; (5) WHO tumor grade; (6) patient age; (7) body mass index. Conversely, IDHmut, hypothyroidism, and MGMT promoter methylation predicted reduced VTE risk. These ten variables were used to create a web-based VTE prediction tool which was validated in two separate cohorts of adult-type diffuse glioma patients from other institutions. This study extends our understanding of the VTE landscape in these tumors, and provides evidence-based guidance for clinicians to mitigate VTE risk in glioma patients.

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