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# A comparative analysis of IDH-mutant glioma in pediatric, young adult, and older adult patients

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## Abstract

**Background:** The frequency and significance of IDH mutations in glioma across age groups is incompletely understood. We performed a multi-center retrospective age-stratified comparison of patients with IDH-mutant gliomas to identify age-specific differences in clinico-genomic features, treatments, and outcomes.

**Methods:** Clinical, histologic, and sequencing data from patients with IDH-mutant, grade 2-4 gliomas, were collected from collaborating institutions between 2013-2019. Patients were categorized as pediatric (<19y), YA (19-39y) or older adult (≥40y). Clinical presentation, treatment, histologic, and molecular features were compared across age categories using Fisher's exact test or analysis-of-variance. Cox proportional-hazards regression was used to determine association of age and other covariates with overall (OS) and progression-free survival (PFS).

**Results:** We identified a cohort of 379 patients (204 YA) with IDH-mutant glioma with clinical data. There were 155 (41%) oligodendrogliomas and 224 (59%) astrocytomas. YA showed significantly shorter PFS and shorter median time-to-malignant transformation (MT) compared to pediatric and adult groups, but no significant OS difference. Adjusting for pathology type, extent of resection, and upfront therapy in multivariable analysis, the YA group was independently prognostic of shorter PFS than pediatric and adult groups. Among astrocytomas, CDK4/6 copy number amplifications were associated with both shorter PFS and shorter OS. Among oligodendrogliomas, PIK3CA and CDKN2A/2B alterations were associated with shorter OS.

**Conclusions:** IDH-mutant glioma YA patients had significantly shorter PFS and time to MT but did not differ in OS compared to pediatric and adult groups. Treatment approach varied significantly by patient age and warrant further study as addressable age-associated outcome drivers.