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Extent of Resection Thresholds in Molecular Subgroups of Newly Diagnosed Isocitrate Dehydrogenase–Wildtype Glioblastoma

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Abstract

Background and objectives: Maximizing the extent of resection (EOR) improves outcomes in glioblastoma (GBM). However, previous GBM studies have not addressed the EOR impact in molecular subgroups beyond IDH1/IDH2 status. In the current article, we evaluate whether EOR confers a benefit in all GBM subtypes or only in particular molecular subgroups.

Methods: A retrospective cohort of newly diagnosed GBM isocitrate dehydrogenase (IDH)-wildtype undergoing resection were prospectively included in a database (n = 138). EOR and residual tumor volume (RTV) were quantified with semiautomated software. Formalin-fixed paraffin-embedded tumor tissues were analyzed by targeted next-generation sequencing. The association between recurrent genomic alterations and EOR/RTV was evaluated using a recursive partitioning analysis to identify thresholds of EOR or RTV that may predict survival. The Kaplan-Meier methods and multivariable Cox proportional hazards regression methods were applied for survival analysis.

Results: Patients with EOR ≥88% experienced 44% prolonged overall survival (OS) in multivariable analysis (hazard ratio: 0.56, P = .030). Patients with alterations in the TP53 pathway and EOR <89% showed reduced OS compared to TP53 pathway altered patients with EOR>89% (10.5 vs 18.8 months; HR: 2.78, P = .013); however, EOR/RTV was not associated with OS in patients without alterations in the TP53 pathway. Meanwhile, in all patients with EOR <88%, PTEN-altered had significantly worse OS than PTEN-wildtype (9.5 vs 15.4 months; HR: 4.53, P < .001).

Conclusion: Our results suggest that a subset of molecularly defined GBM IDH-wildtype may benefit more from aggressive resections. Re-resections to optimize EOR might be beneficial in a subset of molecularly defined GBMs. Molecular alterations should be taken into consideration for surgical treatment decisions in GBM IDH-wildtype.