Comparative Study J Neurooncol. 2026 Jun 9;178(2):55. doi: 10.1007/s11060-026-05612-5.

Survival after hypofractionated radiation versus standard radiation in glioblastoma by MGMT promoter methylation status and age: an analysis of the national cancer database

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PMID: 42265433 DOI: 10.1007/s11060-026-05612-5

Abstract

Purpose: Hypofractionated radiotherapy (HFRT) is recommended by NCCN and EANO guidelines for elderly patients with glioblastoma, but large real-world comparisons with standard fractionated radiotherapy (SFRT) are limited. We evaluated the association between HFRT and survival among patients with glioblastoma, stratified by elderly status and MGMT promoter (MGMTp) methylation, in a national cancer registry.

Methods: In this retrospective cohort study of the 2022 National Cancer Database, we identified 2,401 elderly (≥ 70 years) and 4,944 non-elderly (< 70 years) patients with histologically confirmed glioblastoma. Overall survival was compared between HFRT (40 Gy/15 fractions) and SFRT (60 Gy/30 fractions) with Kaplan-Meier and multivariable Cox proportional hazards analyses stratified by age, MGMTp methylation, and chemotherapy status. Covariables included demographic variables, Charlson-Deyo score, extent of resection, and tumor size.

Results: Among elderly patients, 1,432 received HFRT and 969 received SFRT. Kaplan-Meier analysis indicated a survival advantage for elderly individuals who received SFRT plus chemotherapy compared to those who received HFRT plus chemotherapy (15.01 versus 10.71 months, $p < 0.001$), regardless of MGMTp methylation. However, multivariable analyses revealed no survival difference between HFRT and SFRT in elderly individuals across all chemotherapy and MGMTp subgroupings. Among non-elderly patients (557 HFRT; 4,387 SFRT), both Kaplan-Meier and multivariable analyses demonstrated shorter survival with HFRT across chemotherapy and MGMTp subgroups.

Conclusion: SFRT was associated with longer survival in non-elderly patients, possibly reflecting selection of poorer-risk patients for HFRT. In elderly patients, HFRT was noninferior regardless of MGMTp status, supporting its use as a less intensive approach with comparable survival and reduced treatment burden.

Keywords: Chemoradiation; Elderly; Glioblastoma; Hypofractionated radiotherapy; MGMT; NCDB; Survival.