J Neurooncol. 2023 Jul 20. doi: 10.1007/s11060-023-04397-1. Online ahead of print.

Significance of O6-methyl guanine methyltransferase promoter methylation in high grade glioma patients: optimal cutoff point, CpG locus, and genetic assay

Murat Buyuktepe [1], Ibrahim Kaplan [2], Eyup Bayatli [3], Haldun Dogan [4], Hasan Caglar Ugur [3]

Affiliations

PMID: 37474746 DOI: 10.1007/s11060-023-04397-1

Abstract

Purpose: To evaluate O6-methyl guanine methyltransferase (MGMT) promoter methylation status in high grade glioma patients and to identify the best cutoff point as well as the most predictive CpG loci for patients survival.

Method: Consecutive high grade glioma patients treated with surgical gross total resection followed by concomitant radiochemotherapy and adjuvant chemotherapy were included in this retrospective observational study. Methylation status of MGMT promoter CpG island of resected tumor tissue were evaluated using next generation sequencing assay. The outcomes were grouped as CpG 70-78, CpG 79-83, CpG 84-87, CpG 70-87, and whole promoter. Quantitative analyses were dichotomized as methylated or unmethylated based on the cutoff points set to %10, and methylation was further graded as <%10 unmethylated, %10-30 low-methylated, and %30-100 high-methylated.

Results: Total of 95 patients with the mean age of 51.50 ± 12.36 years were included in the study. Overall survival (OS) and progression free survival (PFS) were 14.53 ± 1.92 (95% CI 10.77-18.30) and 10.90 ± 2.05 (95% CI 6.89-14.92) months, respectively. MGMT promoter was methylated in 38.2% of cases and high-methylated in 10.5% of cases. Methylation status of MGMT promoter was recognized as a very powerful predictor of OS and PFS. In particular, high-methylation of CpG 79-83 and CpG 84-87 islands at promoter region were strongly associated with better survival outcomes ($p < 0.05$).

Conclusion: Our outcomes support the prognostic value of MGMT promoter methylation in patients with high grade glioma. Sequencing of whole promoter CpG islands demonstrated that methylation of particular CpG sites might predict clinical outcomes more precisely.

Keywords: High grade glioma; Next-generation sequencing; O6-Methyl guanine methyltransferase; Promoter methylation; Survival.