Role of MGMT methylation status and IDH1 mutation in glioma patients

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BACKGROUND:

O6-methylguanine-DNA-methyltransferase (MGMT) has emerged as a relevant predictor of therapeutic response and good prognosis in patients with glioblastoma (GBM). Transcriptionally active MGMT rapidly removes the alkyl adducts, preventing the formation of cross-links and thereby causing resistance to alkylating drugs. Studies with pyrosequencing (PSQ) showed that this technique has a higher reproducibility and sensitivity than other techniques. However, the definition of a prognostically relevant threshold for the percentage of MGMTmethylation remains one of the most critical issues in the use of PSQ analysis. Objective: The aim of this study was to define the cut-off value correlated with good favourable prognostic outcomes.

RESULTS: The Receiver Operating Characteristics analysis showed that the best possible criteria for PSQ-detected percentage of MGMT methylation that predicted progression free survival (PFS) and overall survival (OS) were 31% and 24%, respectively. Patients with 31% of PSQ-detected MGMT methylation had a shorter survivals. A multivariate analysis for PFS showed that patients GBM with MGMT methylation >31% and urderwent a surgery has a better prognosis. Conversely, in non GBM patients is more important the age, and elderly has the worst prognosis. The percentage of MGMT methylation status in our population did not results predictive of OS. In patients affected by grade II and III glioma a worst prognosis was significantly associated with IDH1 wild type and old age.

METHODS:

We retrospectively analyzed 177 patients (102 males, 75 females) with glioma (GBM 124 and 53 glioma Grade II or III) who underwent surgery or biopsy.

CONCLUSIONS

Our study reinforces the importance of MGMT methylation status in the management of GBM patients and also the role of IDH1 mutation in grade II and III gliomas

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