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Evaluating the prognostic factors effective on the outcome of patients with glioblastoma multiformis: does maximal resection of the tumor lengthen the median survival?

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Abstract

Background: The ETR that should be undertaken in patients with GBM remains controversial. This study aims to reiterate some independent predicting factors and to underscore the role and the ETR in increasing the survival of patients in the situation of developing countries, that is, without preoperative MRI or tractography. The authors submit additional information to be added to the list of CTRs in the management of malignant brain tumors.

Methods: The authors prospectively analyzed a cohort of 35 consecutive patients with histologically proven GBM who underwent tumor resection in surgically amenable areas for the first time at Sina Hospital, Tehran, between 2003 and 2005. Demographic data, volumetric measurements, and other characteristics identified on preoperative and immediate postoperative MR imaging as well as intraoperative and postoperative clinical data were collectively analyzed by SPSS for Windows, version 11.5 (SPSS, Chicago, Ill).

Results: Cox proportional hazards model multivariate analysis identified the following independent predictors of survival: Karnofsky performance scale ≥80 (P = .01), ETR (P = .01), tumor location in functionally silent prefrontal area (P = .002) vs tumor location in corpus callosum (P = .001), postoperative RT (P = .004), and postoperative chemotherapy (P = .001)

Conclusion: Maximal resection of the tumor volume is an independent variable associated with longer survival times in patient with GBM. Gross total resection should be performed whenever possible, although not at the expense of increased morbidity.

Keywords: Controlled trials; Developing country; Glioblastoma multiformis; Prognosis; Resection; Survival

1. Introduction

Glioblastoma multiforme is the most common primary CNS tumor. Glioblastoma multiforme comprises almost 25% of primary CNS tumors and 50% to 55% of adult gliomas [30]. The optimal treatment for patients with GBM still remains a controversy. Continued refinements in microsurgical techniques and the use of adjunctive technologies have reduced major neurologic morbidity to 8.5% and mortality to 1.7% for patients undergoing craniotomy, respectively [30]. Extensive resection of the primary tumor may lead in a better short-term outcome, but there has been little scientific evidence so far to give maximal tumor resection a credit to prolong survival of the cases. Despite recent advances in surgical techniques and adjunctive therapies, the prognosis for GBM still remains poor with a median survival of approximately 1 year [23]. The results of a critical and comprehensive review of the literature

Abbreviations: CNS, central nervous system; CTR, controlled trial; ETR, extent of tumor resection; GBM, glioblastoma multiforme; GCS, Glasgow Coma Scale; ICU, intensive care unit; KPS, Karnofsky performance score; MRI, magnetic resonance imaging; RT, radiotherapy; TUMS, Tehran University of Medical Sciences; WHO, World Health Organization

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performed by Sanai and Berger [23] proved the lack of class 1 evidence confirming the unbiased effect of ETR on the outcome of patients undergoing surgery for GBM.

Radical resection of malignant gliomas carries the risk of injuring the adjacent vital structures in the brain due to the infiltrative nature of the neoplasm, especially when it is located within the eloquent areas. The major role of surgery is to extirpate the tumor along its macroscopic boundaries and debulk it as completely as possible [12,22,33]. Studies have shown that tumor cells may invade far beyond the main tumor mass into the brain due to the infiltrating nature of the malignant gliomas. Although many authors stress the consistent finding of a variable zone of microscopic tumor infiltration of the brain outside of the enhancing area, extending at least as far as the abnormal T2 signal intensity, a great deal of evidence confirms the presence of the tumor cells centimeters beyond the presumed tumor margin [7,10,22]. As volumetric data were collected to determine the amount of residual tumor mass as accurately as possible based on pre- and postoperative imaging techniques, maximal resection emerged as a strong predictor of survival [3,8,9], whereas high-quality imaging is necessary and should include MRI [1,27,29]. Early studies have shown that even hemispherectomy is inadequate for the control of malignant gliomas [12]. In the situation in developing countries wherein several high-technology instruments are used in a restricted way, this requires the operating physician having a grasp of knowledge in the anatomy of the region and paying meticulous attention to changes in color and consistency of the tissue while working in the vicinity of the tumor. With significant reduction in the mass effect of the tumor, the patient may tolerate RT better and experience fewer side effects [9].

Several factors can affect the survival of patients with GBM, the more prominent of which are age, preoperative performance status according to the KPS, tumor location, preoperative imaging characteristics, the extent of tumor excision, and finally, postoperative RT [17]. Performing a prospective multivariate analysis in a cohort of patients operated by a single group of surgeons (FA and AA), we may reliably identify the independent significant predictors of survival of such patients. In this study, we tried to create a multivariate analysis and to overcome the possible selection biases affecting the outcome demonstrated by other authors [28].

Hereby, it is not intended to illustrate a new event but only to present a correctly designed and managed prospective surgical cohort performed by a group of young investigators (FA, MRZ, MA) so that their findings may be added to the literature for possible meta-analysis in the future.

2. Clinical material and method

Thirty-five consecutive patients with GBM who underwent craniotomy by a single group of surgeons (FA and AA) at Sina Hospital, TUMS, between 2003 and 2005 were enrolled in this study. All cases were classified from the histopathology point of view to GBM or grade 4 astrocytoma, according to the classification of the WHO. The demographic data, clinical manifestations, KPS score on admission, and history of previous head and neck RT were all prospectively recorded.

Volumetric assessments were performed in all patients based on preoperative and postoperative MR images obtained within 72 hours after operation. If there was any contraindication in performing MRI, patients would then be followed with CT scan.

Tumor mass was measured on the globoid scale (ie, A × B × C/2) [1,3,18]. We were not furnished with any computer software program.

Deep lesions were defined as those involving the insula, thalamus, basal ganglia, or third ventricle. In our institute, the rationale for treatment of deep-seated gliomas has been to obtain biopsy samples to confirm the pathology, followed by appropriate adjuvant therapy; therefore, we had to discard them and focus on the superficial lesions.

Tumor proximity to the eloquent brain cortex was graded according to Table 1, suggested by Sawaya et al [25]; and to clarify the analysis of the correlation between different variants, each case had a specific functional grading number regarding this classification. Patients were followed from the time of the surgery until the final event (ie, death) occurred.

3. Statistical techniques

χ^2 test was used to identify the significance of a given variable ($P < .05$). Cumulative survival duration was measured by the Kaplan-Meier curve. Cox proportional hazards model was used to perform univariate and multivariate analysis and identify independent predictors of

Table 1
Grading of the intraparenchymal tumors according to the functional location of the lesion according to Sawaya et al [25]

Grade	Functional location
I: noneloquent brain = 5 cases	Frontal or temporal pole
	Right parieto-occipital lobe
	Cerebellar hemisphere
II: near eloquent brain = 16 cases	Near sensory or motor cortex = 13 cases
	Near calcarine fissure
	Near speech center
	Corpus callosum = 3 cases
	Near dentate nucleus
	Near brain stem
III: eloquent brain = 14 cases	Motor or sensory cortex
	Visual center
	Speech center
	Internal capsule
	Basal ganglia
	Hypothalamus and thalamus
	Brain stem
	Dentate nucleus