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Treatment of the elderly

Radiotherapy is effective in patients with glioblastoma multiforme with a limited prognosis and in patients above 70 years of age: A retrospective single institution analysis☆

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Abstract

***Background and purpose*: To evaluate the efficacy of radiotherapy in patients with glioblastoma multiforme (GBM) with a limited prognosis and in patients older than 70 years.**

***Patients and methods*: Retrospective analysis of 202 patients with GBM treated between 1990 and 2000 in a single institution. Patients (including patients $\geq$70 years) were assigned to RPA groups and their survival was compared with RTOG data.**

***Results*: Median survival was 8.0 months for the total group and 13.9, 10.6, 3.8, 2.1 months for RPA group III ($n=17$), IV ($n=87$), V ($n=60$) and VI ($n=38$), respectively. Median survival for patients $\geq$70 years was 3.6 vs. 8.1 months for 50–70 years and 11.0 months for $<$50. In each separate RPA group, patients $\geq$70 years had a similar survival compared to patients of 50–70 years. Irradiated patients (66%) survived significantly longer than non-irradiated patients: 10.6 vs. 1.9 months ($P<0.0001$).**

In RPA group V the median survival for irradiated patients was 9.4 vs. 2.1 months for non-irradiated patients. In a multivariate analysis, RT remained the only prognostic factor for survival (HR 8.9, $P<0.001$).

***Conclusions*: Prognosis for patients above 70 years of age is not different from younger patients, when analyzed for separate RPA groups. For patients with a poor prognosis (i.e. RPA group V), radiotherapy improves survival significantly.**
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Keywords: Glioblastoma multiforme; Radiotherapy; Survival; Recursive partitioning analysis; Elderly

Primary treatment of patients with a glioblastoma multiforme (GBM) or astrocytoma grade IV consisted, until recently of surgery followed by radiotherapy. The effectiveness of radiotherapy on survival was demonstrated in several trials [1]. Despite intense investigation of aggressive treatment with dose escalation [2,3], brachytherapy or the addition of chemotherapy [4], the prognosis for malignant glioma patients remains poor. Recently, a randomized trial demonstrated an increase in 2 years survival from 10 to 26% with the addition of temozolomide to radiotherapy [5]. At present, 60–66 Gy in 30 fractions is the most commonly used treatment schedule [1]. Because of the poor prognosis of most patients, the value of hypofractionated radiotherapy has been evaluated in order to reduce the treatment time of those patients. Recently, several groups have reported similar survival results with hypofractionated radiotherapy compared to conventional schedules [6–11]. So far, hypofractionated radiotherapy is mainly given to patients with a prognosis not exceeding 1 year.

In several studies, patient dependent prognostic factors have shown to be at least as important in predicting survival outcome as treatment characteristics [12–15]. The use of standardized criteria to assign GBM patients to prognostic groups allows meaningful comparison of treatment results and provides a system that can be used to determine the type of treatment for individual patients. Curran et al. developed a recursive partitioning model, by analyzing the association between survival and patient- and tumor-related characteristics, as well as treatment-related characteristics of 1578 irradiated patients with a malignant glioma [12]. Relevant prognostic factors were age, type of treatment, Karnofsky performance score, mental state and neurological

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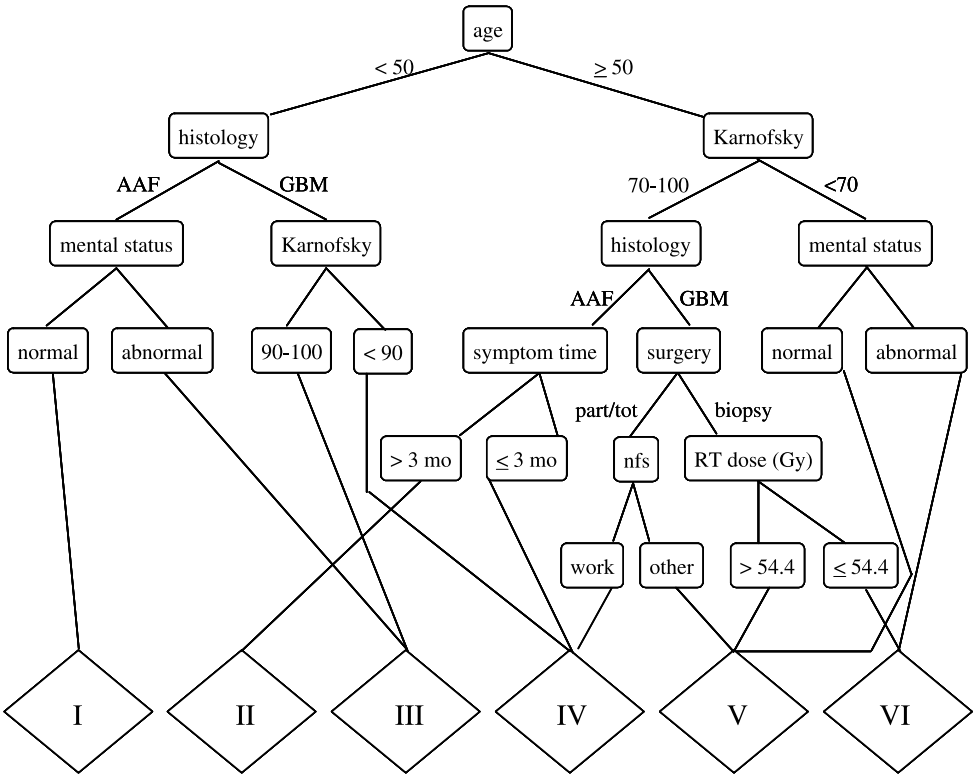

Fig. 1. Recursive partioning model according to Curran et al. [12]. Abreviations: AAF, anaplastic astrocytoma; GBM, glioblastoma multiforme; NFS, neurological function status.

functioning. Six prognostic subgroups were identified which significantly differed in survival rates (Fig. 1). For GBM, four groups are identified, with a median survival of 17.9, 11.1, 8.9 and 4.6 months, respectively. The reliability of the model was proven in a new dataset of patients treated for malignant glioma [16]. However, this recursive partitioning model is based on the results of three randomized RTOG trials, investigating different treatment options, and concerns only irradiated patients 18–70 years. With approximately 20% of the patients with a GBM being ≥70 years of age, identification of prognostic characteristics in this group is also important. We therefore retrospectively evaluated whether the recursive partitioning is applicable for all patients with a GBM, independent of age and treated in a single institution. In addition to this, the value of radiotherapy in patients with a very limited life expectancy has been studied.

Patients and methods

Patient population

Two hundred and eight patients with GBM (i.e. astrocytoma WHO grade IV) who were treated at Leiden University Medical Center (LUMC) between 1990 and the end of 2000 were indentified from the LUMC Tumor Registry. All tumors apart from one were histologically proven. Six patients were excluded because the relevant information could not be obtained: four patients received radiotherapy in another hospital, one patient was lost to follow-up and the medical records of one patient were lost.

Treatment

Surgery generally consisted of a gross total resection or a subtotal debulking of macroscopic tumor preserving neurological functions. Multifocal disease, bihemispheric involvement, a tumor location in a deep and/or eloquent area or a poor neurological condition of the patient could be reason to confine surgery to a biopsy.

During the period of investigation, radiotherapy was usually given in 2 Gy fractions to a total dose of 60 Gy, with a field reduction after 50 Gy. Patients with a poor performance status received 30 Gy in 10 fractions on a whole brain field or no radiotherapy at all.

Prognostic groups

Prognostic groups were identified by Curran et al. [12] using a recursive partitioning analysis (RPA) of the combined results of three randomized RTOG trials on malignant glioma. The decision tree is displayed in Fig. 1. Eligible for these studies were patients between 18 and 70 years of age, with a Karnofsky Performance Score (KPS) >40 with acceptable laboratory studies. In order to evaluate the treatment of patients ≥70 years of age, all patients were included and assigned to an RPA group according to the decision tree.

In the original RPA of the RTOG, the age of 50 years was important in the decision tree and patients ≥70 years were