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Hypofractionated conformal radiotherapy and chemotherapy in treatment of malignant gliomas

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Background: patients with high-grade gliomas are generally elderly patients with poor performance status and associated morbidities. We compared results of hypofractionated radiotherapy with standard fractionated radiotherapy. Hypofractionated radiotherapy with or without chemotherapy could be an appropriate treatment option for these patients with poor life expectancy.

Patients and Methods: Sixty-five patients with malignant gliomas, treated in our Institute between 2005 and 2010, have been identified for this study. Median age was 69 years (between 65 and 81 years). Karnofsky Index (KI) was more than 70% in 38 patients (58.46%) and equal or less than 70% in 27 patients (41.54%), better for patients under 74 years old. Most frequent associated morbidities have been high blood pressure, cardiovascular diseases and diabetes, 54 patients (83.1%). Depending on histological types there have been 44 patients with glioblastoma multiforme (67.69%) and 7 patients with anaplastic astrocytomas (10.77%) and 14 patients (21.46%) with less frequent histological types. Complete resection of tumor was performed in 50 patients (76.9%), partial resection in 13 patients (20%) and biopsy in 2 patients (3.1%). Postoperative treatment was performed as radiotherapy and chemotherapy in 41 patients (63.08%) and radiotherapy only in 24 patients (36.92%). Radiotherapy (RT) was performed as standard fractionated conformal radiotherapy (CRT) with median total dose of 58.5 Gy (minimum 40 Gy, maximum 60 Gy) with 2Gy/fr in 22 patients and hypofractionated CRT with median total dose 30.0 Gy, (minimum 16 Gy, maximum 45 Gy) with 2.66 to 4 Gy/fr, in 43 patients. Chemotherapy with temozolomide was performed in 41 patients (64.08%): concomitant and adjuvant in 22 patients (33.85%), concomitant only with RT in 15 patients (23.08%) and adjuvant to RT in 4 patients (6.15%). The following parameters have been observed: 1) KI, measured at the beginning and the end of treatment; 2) toxicity of RT, appreciated using RTOG scale and 3) toxicity of chemotherapy (hematological, digestive, renal and other) during concomitant and adjuvant phase, appreciated after CTCAE version 3.0. The end points of treatment have been overall survival and toxicities of treatment.

Results: The median follow-up was 32.6 months with 55 deaths and 10 patients alive. Overall survival (OS) at 36 months was 13% (CI: 7%-25%) for the entire group of patients. The OS depending on treatment type was: 20% for patients treated with RT and concomitant chemotherapy; 16% for those treated with radiotherapy only and 7% at 36 months for concomitant and adjuvant chemotherapy, $p=0.35$ (NS). The shortest survival was seen in patients treated with adjuvant chemotherapy to RT, less than 1 year. The OS versus type of RT was 20% for patients treated with standard fractionated RT and 9% for those with hypofractionated RT, differences not statistically significant ($p=0.02$). Toxicity of radiotherapy (RTOG scale) was 0 and 1 in 41 patients (63.07%) and 2 and 3 in 24 patients (36.92%) with no statistically significant differences between the two types of fractionation: $p=0.25$. OS depending on toxicities was between 16% and 11% at 36 months, $p=0.10$.

There have been 7 patients with grade 3 and 4 toxicities in chemotherapy treated group (41 patients): 4 in concomitant phase and 3 in adjuvant phase.

Conclusions: Hypofractionated radiotherapy was well tolerated with or without chemotherapy with acceptable toxicities and could be a good treatment option for elderly patients with high-grade gliomas. Important decisions factors for fractionation type and total dose administered are performance status, associated diseases and generally life expectancy of patients.

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