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Original research article

Survival after radiation therapy for high-grade glioma

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ABSTRACT

Background: High-grade gliomas (HGGs) are a heterogeneous disease group, with variable prognosis, inevitably causing deterioration of the quality of life. The estimated 2-year overall survival is 20%, despite the best trimodality treatment consisting of surgery, chemotherapy, and radiotherapy.
Aim: To evaluate long-term survival outcomes and factors influencing the survival of patients with high-grade gliomas treated with radiotherapy.
Materials and methods: Data from 47 patients diagnosed with high-grade gliomas between 2009 and 2014 and treated with three-dimensional radiotherapy (3DRT) or intensity-modulated radiotherapy (IMRT) were analyzed retrospectively.
Results: Median survival was 16.6 months; 29 patients (62%) died before the time of analysis. IMRT was employed in 68% of cases. The mean duration of radiotherapy was 56 days, and the mean delay to the start of radiotherapy was 61.7 days (range, 27–123 days). There were no statistically significant effects of duration of radiotherapy or delay to the start of radiotherapy on patient outcomes.

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Conclusions: Age, total amount of gross resection, histological type, and use of adjuvant temozolomide influenced survival rate ($p < 0.05$). The estimated overall survival was 18 months (Kaplan–Meier estimator). Our results corroborated those reported in the literature.

1. Background and aim

High-grade gliomas (HGGs) are a heterogeneous disease group, both genetically and histologically, with variable prognosis, inevitably causing deterioration of the quality of life. The estimated 2-year overall survival is 20%, despite the best trimodality treatment consisting of surgery, chemotherapy, and radiotherapy. In our study, three-dimensional radiotherapy (3DRT) and intensity-modulated radiotherapy (IMRT) were used after surgery for HGG, with or without chemotherapy.

Radiotherapy for HGG can follow two protocols: the American Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC) – Table 1. Chemoradiation with concurrent and adjuvant temozolomide (TMZ) is the standard treatment for glioblastoma and will be further discussed below. Patients with anaplastic astrocytoma (AA) have poorer survival than those with oligodendroglial tumors. Their tumors often progress to grade IV, which justifies the intensification of treatment of these lesions with chemoradiation. However, the results of randomized studies (NCT00887146 and NCT00626990) to evaluate the benefit of adding concomitant chemotherapy or adjuvant radiotherapy for treatment of 1p19q codeleted tumors (CODEL) or not-codeleted tumors (CATNON) are not yet available.

2. Materials and methods

Patients diagnosed with primary HGG were selected by a search performed in our institution's database. The inclusion criterion was the treatment for anaplastic glioma or glioblastoma between 2009 and 2014 at the Hospital das Clínicas de Ribeirão Preto of the University of São Paulo (HCFMRP-USP). Patients who were under 18 years of age, had undergone radiotherapy in another facility, or had not completed radiotherapy were excluded.

The IMRT technique was implemented in the HCRP in 2010; previously, all patients were treated with 3DRT. The treatment was performed in a linear accelerator model Oncor Impression (Siemens) or Primus (Siemens), with 6 MV energy and a 1-cm thickness multileaf collimator or individualized protection for each course of treatment. All plans were non-coplanar, using the number of fields and sectors most suitable for a better compliance index and heterogeneity. Fractionation was 1.8–2.0 Gy per fraction (one fraction a day, 5 days a week) using total doses of 52–60 Gy in 26–30 fractions, following RTOG or EORTC guidelines. Quality controls were analyzed individually in IMRT with system ionization chamber arrangements (MATRIXX, MULTICube QA Software) (IBA Dosimetry, Bartlett, TN, USA). The treatment was permitted when the gamma function was below 3%.

Data collected included age, sex, histology, performance status, use of concomitant and/or adjuvant chemotherapy, surgical resection (total or subtotal macroscopic), date of treatment, final dose, treatment duration, irradiation technique (IMRT or 3DRT), first presenting symptoms, date of progression (if any) according to clinical and radiological magnetic resonance imaging (MRI) control, date of death, and date of last medical appointment (if the patient was alive at the time of data collection).

Data were analyzed with SAS software, version 9.2. Initially, an exploratory analysis of data was performed through measurements of central position and dispersion. Qualitative variables were described by absolute and relative

Table 1 – Target volume comparison between EORTC and RTOG guidelines.

EORTC (EORTC 22981/22961, 26071/22072 (Centric), 26981-22981, and AVAglio)	RTOG (RTOG 0525, 0825, 0913, and AVAglio)
Phase 1 (60 Gy/30 fractions)	Phase 1 (46 Gy/23 fr)
GTV = surgical cavity + contrast T1 enhancing tissue	GTV1 = surgical cavity + contrast T1 enhancing tissue + perilesional edema in T2 or FLAIR
CTV = GTV + 2-cm margin*	CTV1 = GTV1 + 2-cm margin (if no peritumoral edema, CTV is contrast enhancing area + 2.5-cm margin)
PTV = CTV + 3–5-mm margin	PTV1 = CTV1 + 3–5 mm margin
	Phase 2 (boost 14 Gy/7 fr)
	GTV2 = surgical cavity + contrast T1 enhancing tissue
	CTV2 = GTV2 + 2-cm margin
	PTV2 = CTV2 + 3–5 mm margin

Source: Adapted from Niyazi M et al. ESTRO-ACROP guideline.[29]

AVAglio; EORTC; RTOG; GTV, gross tumor volume; CTV, clinical target volume; PTV, planning target volume.
* Margins up to 3 cm were allowed in EORTC 22981/22961 and from 1 to 1.5 cm in EORTC 26981-22981.