Nomograms for predicting survival of patients with newly diagnosed glioblastoma: prognostic factor analysis of EORTC and NCIC trial 26981-22981/CE.3.


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BACKGROUND: A randomised trial published by the European Organisation for Research and Treatment of Cancer (EORTC) and the National Cancer Institute of Canada (NCIC) Clinical Trials Group (trial 26981-22981/CE.3) showed that addition of temozolomide to radiotherapy in the treatment of patients with newly diagnosed glioblastoma significantly improved survival. We aimed to undertake an exploratory subanalysis of the EORTC and NCIC data to confirm or identify new prognostic factors for survival in adult patients with glioblastoma, derive nomograms that predict an individual patient's prognosis, and suggest stratification factors for future trials.

METHODS: Data from 573 patients with newly diagnosed glioblastoma who were randomly assigned to radiotherapy alone or to the same radiotherapy plus temozolomide in the EORTC and NCIC trial were included in this subanalysis. Survival modelling was done in three patient populations: intention-to-treat population of all randomised patients (population 1); patients assigned temozolomide and radiotherapy (population 2, n=287); and patients assigned temozolomide and radiotherapy who had assessment of MGMT promoter methylation status and who had undergone tumour resection (population 3, n=103). Cox proportional hazards models were fitted with and without O6-methylguanine-DNA methyltransferase (MGMT) promoter methylation status. Nomograms were developed to predict an individual patient's median and 2-year survival probabilities. No nomogram was developed in the radiotherapy-alone group because combined treatment is now the new standard of care.

FINDINGS: Independent of the MGMT promoter methylation status, analysis in all randomised patients (population 1) identified combined treatment with temozolomide, more extensive tumour resection, younger age, Mini-Mental State Examination (MMSE) score of 27 or higher, and no corticosteroid treatment at baseline as independent prognostic factors correlated with improved survival outcome. In patients assigned temozolomide and radiotherapy (population 2), younger age, better performance status, more extensive tumour resection, and MMSE score of 27 or higher were associated with better survival. In patients who had tumours resected, who were assigned temozolomide and radiotherapy, and who had available MGMT promoter methylation status (population 3), methylated MGMT, better performance status, and
MMSE score of 27 or higher were associated with improved survival. Nomograms were developed and are available at http://www.eortc.be/tools/gbmcalculator.

**INTERPRETATION:** MGMT promoter methylation status, age, performance status, extent of resection, and MMSE are suggested as eligibility or stratification factors for future trials in patients with newly diagnosed glioblastoma. Stratifying by MGMT promoter methylation status should be mandatory in all glioblastoma trials that use alkylating chemotherapy. Nomograms can be used to predict an individual patient's prognosis, and they integrate pertinent molecular information that is consistent with a paradigm shift towards individualised patient management.

**Comment in**
Nomograms as clinicobiological predictors of survival in glioblastoma.  [Lancet Oncol. 2008]

PMID: 18082451 DOI: 10.1016/S1470-2045(07)70384-4

[Indexed for MEDLINE]