

## ABSTRACT

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Impact of Time to Diagnosis on Morbidity and Survival in Children With Malignant Central Nervous System Tumors.

Ronsley R(1), Crowell C, Irvine M, Kang M, Goldman RD, Erker C, Cheng S.

### Author information:

(1)Division of Hematology, Oncology and Bone Marrow Transplant, Department of Pediatrics, British Columbia Children's Hospital Clinical Research Support Unit, BC Children's Hospital Research Institute Faculty of Medicine, University of British Columbia Pediatric Research in Emergency Therapeutics Program (PRETx.org) and the Division of Pediatric Emergency Medicine, Department of Pediatrics, British Columbia Children's Hospital, BC Children's Hospital Research Institute, Vancouver, British Columbia Division of Hematology/Oncology, Department of Pediatrics, Dalhousie University and IWK Health Centre, Halifax, Nova Scotia, Canada.

**OBJECTIVE:** The aim was to determine the impact of time to diagnosis (TTD) on morbidity and mortality and to identify factors associated with overall survival (OS) in pediatric patients with malignant central nervous system (CNS) tumors.

**METHODS:** This is a retrospective review of all malignant CNS tumors presenting to 2 tertiary care pediatric hospitals from 2000 to 2019. Cox proportional hazard model analysis outcomes included TTD and OS as well as morbidity; stratified by tumor category, age, relapse, and presence of metastatic disease.

**RESULTS:** There were 197 children with malignant CNS tumors (mean age 8.7 y, 61% male). Tumors included medulloblastoma (N=58, 29.4%), ependymoma (N=27, 13.7%), high-grade glioma (N=42, 21.3%), germ cell tumors (N=47, 23.9%), and other embryonal tumors (N=23, 11.7%). Median TTD from symptom onset was 62 (interquartile range: 26.5 to 237.5 d) and 28% had metastatic disease. Three-year progression free survival was 55% and 3-year OS was 73.1%. Increased OS was associated with increased TTD (parameter estimate 0.12; confidence interval [CI]: 0.019-7.06; P=0.019), high-grade glioma (hazard ratio [HR]: 2.46; CI [1.03-5.86]; P=0.042), other embryonal tumor (HR: 2.84; CI [1.06-7.56]; P=0.037), relapse (HR: 10.14; CI: 4.52-22.70; P<0.001) and metastatic disease (HR: 3.25; CI: 1.51-6.96; P=0.002). Vision change (HR: 0.58; CI: 0.313-1.06; P=0.078), hearing loss (HR: 0.71; CI: 0.35-1.42; P=0.355), and cognitive impairment (HR: 0.73; CI: 0.45-1.19; P=0.205) were not associated with TTD in this model.

**CONCLUSIONS:** Increased median TTD is associated with higher OS in pediatric patients treated for malignant CNS tumors. Tumor biology and treatment modality are more important factors than TTD for predicting morbidity and long-term outcomes in pediatric patients with CNS tumors.

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