

# Age as an Independent Prognostic Factor in Patients with Glioblastoma: a Radiation Therapy Oncology Group Analysis

M. Siker<sup>1</sup>, B. Berkey<sup>2</sup>, D. Nelson<sup>3</sup>, W. Curran<sup>4</sup>, J. Michalski<sup>5</sup>, L. Souhami<sup>6</sup>, A. Chakravarti<sup>7</sup>, W. Yung<sup>8</sup>, J. DeRowe<sup>9</sup>, C. Coughlin<sup>10</sup>, M. Mehta<sup>1</sup>

<sup>1</sup>University of Wisconsin School of Medicine and Public Health, Madison, WI. <sup>2</sup>Radiation Therapy Oncology Group, Philadelphia, PA. <sup>3</sup>Mayo Clinic, Rochester, MN. <sup>4</sup>Jefferson Medical College, Philadelphia, PA. <sup>5</sup>Washington University School of Medicine, St. Louis, MO. <sup>6</sup>McGill University, Montreal, QC. <sup>7</sup>Harvard Medical School, Boston, MA. <sup>8</sup>University of Texas M. D. Anderson Cancer Center, Houston, TX. <sup>9</sup>Montefiore Medical Center, Bronx, NY. <sup>10</sup>Dartmouth-Hitchcock Medical Center, Lebanon, NH.

## Introduction

Glioblastoma (GBM) is the most common and most malignant glial tumor presenting typically in the sixth decade. Prognosis for patients with GBM is determined by Radiation Therapy Oncology Group (RTOG) recursive partitioning analysis (RPA) class, which stratifies patients based on age, Karnofsky Performance Scale (KPS), and mental status (Curran et al, 1994). Because GBM is rare in younger populations, RTOG RPA is inadequate in defining outcome in young adults. There is currently a paucity of published data on GBM in this younger patient group. In a large co-operative group database retrospective review, we evaluated if very young age has an independent effect on survival, above and beyond RTOG RPA Class.

## Methods

We conducted a retrospective RTOG database evaluation of all eligible GBM cases from all treatment arms of 17 RTOG studies from 1974-2002. Age was evaluated as an independent continuous variable and we also divided patients into 3 cohorts: ages 18-30, 31-49, and 50 or greater. Patients were assessed for survival, as a function of age and as adjusted by RPA Class.

## Patient Characteristics

There were 3136 patients included in our study; 112 cases (3.6%) were 18-30 years old, 780 (24.9%) were 31-49, and 2244 (71.6%) were 50 or older. Younger patients tended to have a higher proportion with KPS 90-100, normal mental function, and total resection as shown in the table below.

	Age 18 - 30	Age 31 - 49	Age ≥ 50
N	112 (3.6%)	780 (24.9%)	2244 (71.5%)
KPS ≥ 90	63 (56%)	367 (47%)	730 (33%)
Total resection	31 (28%)	176 (23%)	476 (21%)
Good neurologic function	46 (41%)	342 (44%)	824 (37%)
Normal mental status	96 (86%)	499 (64%)	1197 (53%)

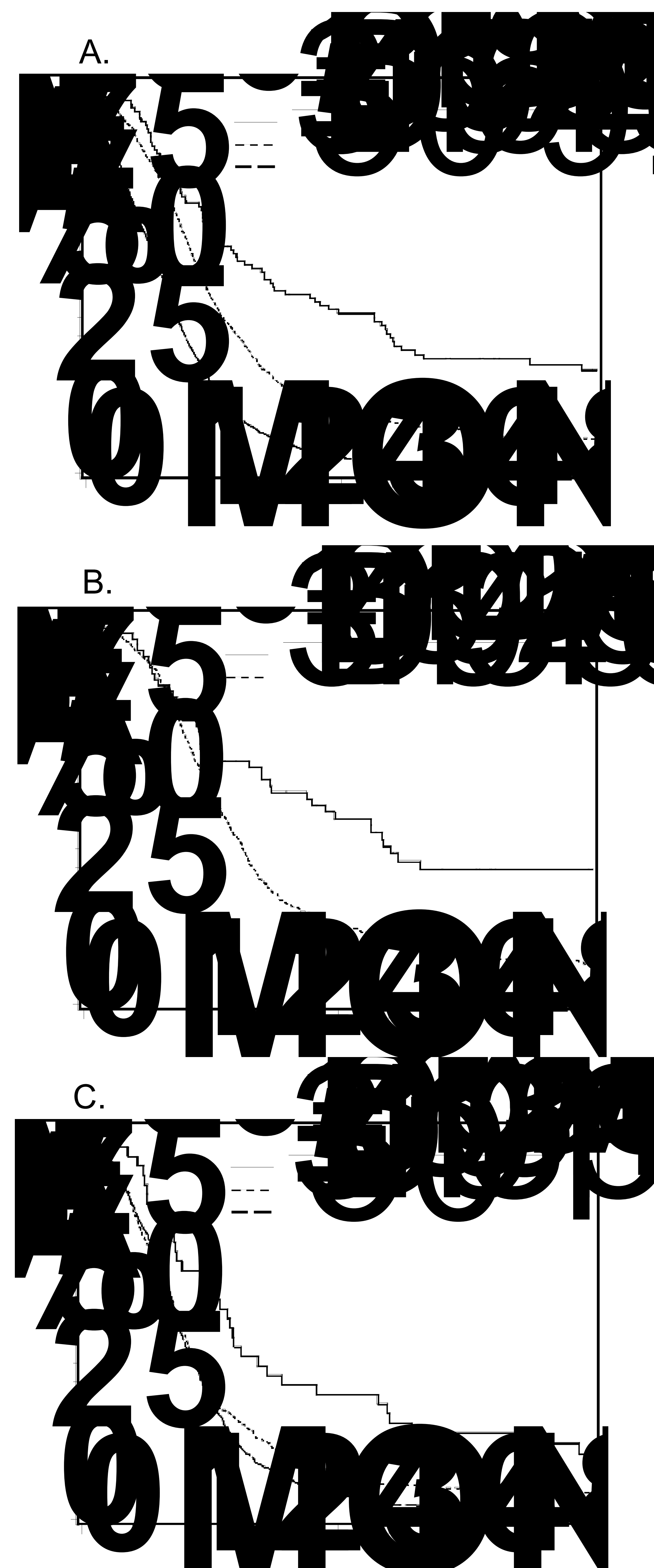


Figure 1. Overall survival by age for (A) all patients, and (B) RPA Class III, and (C) RPA Class IV.

## Results

Median survival times of the three groups were 21, 13.5, and 9.1 months ( $p < 0.0001$ ) (Fig. 1a). Patients in the age 18-30 group survived twice as long as those age  $\geq 31$  as shown in the table below. Significant improvement in survival for younger patients was demonstrated with adjustment for RPA Class. Of patients in RPA Class III, median survival for those aged 18-30 was 28.6 months compared to 16.2 months for those between 31-49 years ( $p < 0.0001$ ) (Fig. 1b). Median survival for patients aged 18-30 vs. 31-49 in RPA Class IV was 17.3 vs. 11.7 months ( $p = 0.0008$ ). RPA class IV patients aged  $\geq 50$  have very similar survival to the aged 30-49 patients (11.3 month median survival) for the first 18 months, but then the curves diverge for a statistically significant survival advantage for the 30-49 group ( $p = 0.017$ ) (Fig. 1c).

	Age 18 - 30		Age ≥ 31	
Months	% Alive	# at Risk	% Alive	# at Risk
0	100	112	100	3024
6	93	103	72	2137
12	69	75	40	1177
18	54	58	19	545
24	46	47	11	283
36	35	33	5	118
48	29	21	3	71
60	26	17	3	55
Median Survival	21.0 months		10.2 months	
P < 0.0001				

## Conclusions and Future Directions

GBM is very rare in young adulthood (age  $\leq 30$  yr), representing 3.6% of our patients. Patients diagnosed in young adulthood have significantly superior survival, a trend that has also been recently reported in a study including patients from a large national database. This finding persists even when adjusted for RPA Class. These results may imply that tumors arising in younger populations may demonstrate unique biologic characteristics which is the subject of future research.

## References

Curran WJ, Jr., Scott CB, Horton J, et al. Recursive partitioning analysis of prognostic factors in three Radiation Therapy Oncology Group malignant glioma trials. *J Natl Cancer Inst* 1993;85(9):704-10.