



Treatment and Survival of Patients Harboring Histological Variants of Glioblastoma

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Introduction

It is unclear whether the survival difference observed between glioblastoma (GBM), giant cell glioblastoma (gcGBM), and gliosarcoma (GSM) patients is due to differences in tumor histology, patient demographics, and/or treatment regimens.

Methods

The National Cancer Database (NCDB) was utilized to evaluate patients diagnosed with GBM, gcGBM, and GSM between 1998 and 2011. Kaplan-Meier survival estimates and Cox proportional hazards models were utilized to estimate overall survival (OS).

Results

A cohort of 69,935 patients was analyzed; 67,509 (96.5%) of these cases had GBM, 592 (0.9%) gcGBM, and 1,834 (2.6%) GSM. The median age for GBM and GSM patients was 61 versus 51 years for gcGBM ($p < .0001$). Higher levels of resection ($p < .0001$) and radiation ($p = .001$) were observed in gcGBM patients compared to other histologies.

Multivariate analysis showed that gcGBM patients had a 20% reduction in the hazards of mortality (HR 0.80, 95% CI: 0.69-0.93) compared to GBM, while GSM patients had higher hazards of mortality (HR 1.04, 95% CI: 0.96-1.12) than the GBM cohort.

Results

Table 3
Kaplan-Meier median overall survival in months with 95% confidence intervals, and survival rates at 6, 12, 18, and 24 months

| Variable | All patients n = 41,037 | Tumor histologies | | |
|---------------------------|----------------------------|------------------------------------|---|---------------------------------|
| | | Glioblastoma n = 36,600 (89.2%) | Giant cell glioblastoma n = 229 (0.6%) | Gliosarcoma n = 1,834 (4.5%) |
| Median survival, months* | 9.8 (9.7-9.9) | 9.8 (9.7-9.9) | 13.4 (11.5-14.6) | 8.8 (8.3-9.4) |
| Survival rate, % (95% CI) | | | | |
| 6 months | 66.4 (66.0-67.0) | 66.2 (65.8-66.7) | 77.5 (72.5-81.7) | 65.7 (62.7-68.5) |
| 12 months | 41.1 (40.6-41.5) | 41.1 (40.6-41.6) | 54.3 (48.6-59.7) | 34.1 (31.2-36.9) |
| 18 months | 23.8 (23.4-24.2) | 23.8 (23.4-24.3) | 35.3 (29.6-41.7) | 18.4 (16.3-20.8) |
| 24 months | 15.3 (14.8-15.7) | 15.3 (14.8-15.6) | 30.2 (25.2-35.5) | 12.1 (10.2-14.2) |

Results

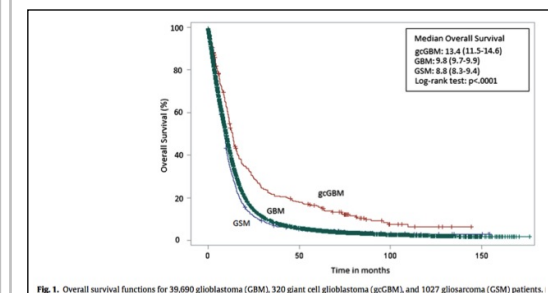


Fig. 1. Overall survival functions for 39,690 glioblastoma (GBM), 320 giant cell glioblastoma (gcGBM), and 1,027 gliosarcoma (GSM) patients.

Table 4
Adjusted hazard ratio of mortality with 95% confidence intervals for 41,037 glioblastoma patients

| Variable | Hazard ratio | 95% CI |
|---|--------------|-----------|
| Age at diagnosis | 1.38 | 1.37-1.40 |
| Race, white | 0.87 | 0.82-0.91 |
| Median household income, USD (ref: <\$30,000) | | |
| \$30,000-\$35,000 | 1.03 | 0.98-1.09 |
| \$35,000-\$45,999 | 1.01 | 0.97-1.06 |
| Greater than \$46,000 | 0.92 | 0.88-0.96 |
| Extent of resection (ref: biopsy) | | |
| Partial resection | 1.00 | 0.97-1.04 |
| Gross total resection | 0.79 | 0.76-0.81 |
| Tumor size | 1.00 | 1.00-1.00 |
| Tumor location (ref: temporal lobe) | | |
| Frontal lobe | 1.05 | 1.02-1.09 |
| Parietal lobe | 1.06 | 1.01-1.09 |
| Occipital lobe | 1.00 | 0.93-1.06 |
| Overlapping lobes | 1.16 | 1.11-1.21 |
| Intratentorial | 1.09 | 0.94-1.27 |
| Other | 1.28 | 1.21-1.35 |
| Radiation (ref: no) | | |
| Yes | 0.58 | 0.56-0.60 |
| Chemotherapy (ref: no) | | |
| Yes, single-agent | 0.73 | 0.71-0.76 |
| Yes, multi-agent | 0.71 | 0.68-0.75 |
| Histology (ref: GBM)** | | |
| Giant cell GBM | 0.80 | 0.69-0.93 |
| Gliosarcoma | 1.03 | 0.95-1.12 |

Conclusions

Previous studies have suggested a disparity in the survival of patients with glioblastoma tumors and their histological variants. Using a large cohort of patients treated at hospitals nationwide, this study found a 20% reduction in the hazards of mortality in gcGBM patients compared to GBM. Similarly, gcGBM patients had a 24% reduction in the hazards of mortality compared to the GSM cohort. Gliosarcoma patients had a 3% increase in the hazards of mortality compared to GBM.

Table 1
Demographics and tumor characteristics of patients diagnosed with glioblastoma tumors, 1998-2011

| Variable | All patients n = 69,935 | Tumor histologies | | | p value |
|------------------------------|----------------------------|------------------------------------|---|---------------------------------|---------|
| | | Glioblastoma n = 67,509 (96.5%) | Giant cell glioblastoma n = 592 (0.8%) | Gliosarcoma n = 1,834 (2.6%) | |
| Age at diagnosis, years | | | | | |
| Mean (SD) | 60.8 (12.95) | 60.8 (12.95) | 54.5 (15.3) | 60.4 (12.95) | <0.0001 |
| Median (IQR) | 61 (50-70) | 61 (50-70) | 56 (30-65) | 61 (50-70) | |
| Female | 29,225 (41.8) | 28,208 (41.8) | 251 (42.7) | 764 (41.7) | 0.89 |
| Race | | | | | |
| White | 63,842 (91.3) | 61,883 (91.4) | 528 (89.2) | 1,631 (88.9) | <0.0001 |
| Black | 3,662 (5.2) | 3,466 (5.1) | 32 (5.4) | 144 (7.9) | |
| Native American | 192 (0.3) | 190 (0.3) | 0 (0.0) | 2 (1.1) | |
| Asian | 1,097 (1.6) | 1,093 (1.6) | 22 (3.7) | 12 (0.7) | |
| Other | 488 (0.7) | 471 (0.7) | 5 (0.8) | 12 (0.7) | |
| Hispanic | 3,555 (5.1) | 3,424 (5.1) | 33 (5.6) | 97 (5.3) | 0.64 |
| Median household income, USD | | | | | |
| <\$30,000 | 7,976 (11.6) | 7,601 (11.6) | 71 (12.7) | 204 (11.9) | 0.02 |
| \$30,000-\$35,000 | 12,861 (18.3) | 11,600 (18.3) | 80 (14.3) | 233 (20.5) | |
| \$35,000-\$45,999 | 18,217 (27.7) | 17,581 (27.7) | 181 (32.3) | 455 (28.5) | |
| >\$46,000 | 27,564 (41.9) | 26,637 (41.9) | 229 (40.8) | 708 (41.2) | |
| Extent of resection | | | | | |
| Biopsy | 30,462 (44.2) | 29,501 (44.3) | 214 (38.7) | 747 (41.2) | <0.0001 |
| Partial resection | 18,501 (28.9) | 17,694 (28.9) | 141 (24.2) | 465 (28.2) | |
| Gross total resection | 19,952 (28.9) | 19,101 (28.7) | 228 (39.1) | 623 (34.3) | |
| Tumor size, cm | | | | | |
| Mean (SD) | 5.0 (6.6) | 5.0 (6.6) | 5.5 (1.6) | 5.2 (6.7) | 0.02 |
| Tumor location | | | | | |
| Frontal lobe | 18,881 (27.0) | 18,272 (27.1) | 180 (30.4) | 429 (23.4) | <0.0001 |
| Temporal lobe | 19,428 (27.8) | 18,571 (27.5) | 177 (28.8) | 680 (37.3) | |
| Parietal lobe | 11,886 (17.0) | 11,554 (17.1) | 97 (16.4) | 230 (12.8) | |
| Occipital lobe | 3,988 (4.4) | 3,773 (4.9) | 22 (3.7) | 71 (3.9) | |
| Overlapping lobe | 9,133 (13.4) | 9,022 (13.4) | 62 (10.5) | 240 (13.6) | |
| Intratentorial | 677 (1.0) | 599 (1.0) | 10 (1.5) | 29 (1.8) | |
| Other** | 4,692 (6.7) | 4,618 (6.7) | 49 (7.9) | 141 (7.7) | |

Table 2
Treatment of patients diagnosed with glioblastoma tumors, 1998-2011

| Variable | All patients n = 69,935 | Tumor histology | | | p value |
|--------------------|----------------------------|------------------------------------|---|---------------------------------|---------|
| | | Glioblastoma n = 67,509 (96.5%) | Giant cell glioblastoma n = 592 (0.8%) | Gliosarcoma n = 1,834 (2.6%) | |
| Radiation | | | | | |
| Yes | 51,937 (74.3) | 50,144 (74.4) | 469 (79.3) | 1,325 (72.6) | 0.001 |
| No | 17,998 (25.7) | 16,996 (25.1) | 123 (20.8) | 469 (27.2) | |
| Radiation modality | | | | | |
| External beam | 22,294 (68.9) | 21,571 (68.0) | 169 (28.1) | 554 (65.8) | <0.0001 |
| IMRT | 9,862 (38.3) | 9,456 (38.3) | 122 (41.9) | 282 (33.5) | |
| SEI | 229 (0.8) | 213 (0.8) | 0 (0.0) | 110 (5.9) | |
| Chemotherapy | | | | | |
| Yes | 42,369 (59.4) | 40,820 (59.4) | 385 (64.0) | 1,063 (58.8) | 0.06 |
| Single-agent | 14,715 (33.2) | 13,515 (33.2) | 323 (56.2) | 877 (68.1) | |
| Multi-agent | 5,520 (8.1) | 5,338 (8.2) | 45 (7.8) | 137 (7.7) | |