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Characteristics of long-term glioblastoma survivors diagnosed from 2010 to 2016 in the United States

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Highlights

- Younger age (<60 years of age) at diagnosis is strongly associated with LTS in GBM.
- Gross total resection and radiation therapy improve odds of long-term survival.
- Female and living in a county with higher median income linked to longer survival.

Abstract

Background

Glioblastoma (GBM) is the most common malignant primary central nervous system (CNS) tumor, accounting for half (50.9 %) of all malignant tumors diagnosed in the US. We conducted a population-based analysis using Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) survival database investigate which patient- and tumor-level factors are characteristic of long-term survivors (LTS) of GBM.

Methods

Individual-level survival data containing diagnoses of primary GBM were obtained from the NPCR survival database for cases diagnosed during the period of January 1st, 2010 to December 31st, 2016, and followed through December 31st, 2019. Differences in LTS (>36-months) were investigated using χ^2 tests and multivariable logistic regression. Frequency of IDHmut-GBM by age was estimated in the same dataset from 2018 to 2021.

Results

Of the included GBM, 11.6 % met criteria for LTS. After adjustment for known prognostic factors, males (OR=0.78, $p < 0.001$) and age > 60 at diagnosis, were all significantly associated with decreased odds of LTS (70–79 years O =0.48, 80 + years OR=0.21, both $p < 0.001$). Frequency of IDHmut-GBM peaked from 25 to 34, with < 5 % of GBM in those > 50 having IDHmut-GBM. In a sensitivity analysis in those > 50 diagnosis, both male sex and age remained significant predictors of LTS

Conclusion

There are multiple patient- and tumor-level factors that are associated with improved survival in GBM, with the strongest effect sizes in the multivariable models being due to age. These results demonstrate substantial heterogeneity in GBM prognosis and emphasize the distinct survival advantage associated with age at diagnosis.

Introduction

Glioblastoma (GBM) is the most common malignant primary central nervous system (CNS) tumor; it accounts for 14.2 % of all tumors and 50.9 % of all malignant tumors [1]. The classical standard of care treatment is the Stupp protocol, which includes maximal safe surgical resection, followed by concurrent chemotherapy [2].In some cases, tumor-treating fields devices are included as a first line therapy and have been included into treatment guidelines and represent a key component of the multidisciplinary approach to GBM management [1], [3]. However, the prognosis for patients with GBM is still very poor, and with the median survival around nine months for those not receiving standard of care and 15–16 months for those receiving standard of care [4], [5], [6]. A small minority of GBM patients survived for more than five years. [1]. Identifying predictors of long-term survivorship in GBM has been a hot research topic in recent years [7], [8]. Most recent studies have focused on identifying molecular markers associated with prolonged survival. Several molecular alterations have been reported to be associated with improved prognosis [4], [7], including O^6-methylguanine-DNA methyltransferase (*MGMT*) promoter methylation status [9], mutations in isocitrate dehydrogenase 1 or 2 (*IDH1/2*)[10], and promoter-specific telomerase reverse transcriptase (*TERT*) mutations [11]. Nevertheless, no individual biomarker or clinical indicator has yet been established as an infallible predictor of long-term survival in GBM patients. Further research is essential to unravel this complex phenomenon and, as a result, potentially enhance the prognosis for those afflicted with GBM.

Herein we conducted a population-based analysis using data obtained from the Centers for Disease Control and Prevention's (CDC) National Program of Cancer Registries (NPCR) survival database, which aggregates information from population-based registries that cover an estimated ~82 % of the US population, in order to investigate which patient characteristics are more likely to be a feature of long-term survivors of GBM.

Section snippets

Study population

Individual-level survival data containing diagnoses of primary GBM (International Classifications of Diseases of Oncology, 3rd Ed. [ICD-O-3] histology codes 9440/3–9442/3 and 9445/3 for ICD-O-3 primary sites C71.0-C71.9) were obtained from CDC's National Program of Cancer Registries (NPCR) survival database for cases diagnosed during the period of January 1st, 2010 to December 31st, 2016, and followed through December 31st, 2019. While the current definition of glioblastoma (as of the 2021 WHO …

Results

Of the 55,745 GBM identified in the NPCR database that were diagnosed during the period of 2010–2016, only 11.6 % (6447) lived 36 months or greater (Table 1). This proportion did not

change significantly by year. Long term survivorship was most common among women, those that were ages 20–29 years old at diagnosis, and NH other (Fig. 1 and Table 1). The proportion of infratentorial and supratentorial GBM that were long-term survivors (proportion=12.2 % and 12.4 %, respectively) were both nearly …

Discussion

Over the last several decades, treatment options for GBM have significantly expanded [14], [15], [16], and several treatment advances have emerged, including tumor-treating fields (TTF), vaccine-based immunotherapeutics, and oncolytic viral therapy. Despite this, there have been minimal increases in survival since the introduction of the Stupp protocol, now deemed standard of care, in 2004. In the overall population, median survival remains at only nine months (regardless of treatment) and …

Conclusion

GBM is the most common malignant brain tumor and is uniformly lethal, with a median survival of ~1 year. A minority of individuals diagnosed with this disease are long term survivors who survive 3 or more years after diagnosis. Among a cohort of GBM patients diagnosed from 2010 to 2016, the strongest predictor of long-term survivorship was decreased age at diagnosis, followed by gross total extent of resection. These results demonstrate how, despite GBM being uniformly lethal, there is still …

Ethics Approval

Duke University School of Medicine Institutional Review Board deemed this study to not require ethical approval …

CRediT authorship contribution statement

Li Yunqian: Writing – review & editing, Writing – original draft, Project administration, Methodology, Conceptualization. **Barnholtz-Sloan Jill S.:** Writing – review & editing. **Ostrom Quinn T.:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Conceptualization. **Kruchko Carol:** Writing – review & editing, Funding acquisition. **Wang Yubo:** Writing – review & editing, Writing – original draft, …

Declaration of Competing Interest

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