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Review article

Ten-year survival in glioblastoma. A systematic review

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ABSTRACT

Glioblastoma (GBM) is among the most deadly neoplasms associated with one of the worst 5-year overall survival (OS) rates among all human cancers. The aim of this systematic review is to present all cases with OS of a decade or more and to perform a descriptive analysis of the group.

This systematic review was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline. A comprehensive search for relevant articles was performed on PubMed, Embase and Google Scholar for a period until June 10, 2016, using the following search words: glioblastoma multiforme, glioblastoma, GBM, long-term survival/survivors. Reports containing cases with the long-term survival of 10 years or longer were included in the review.

The search produced 36 studies with 162 cases published in the years 1950–2014. The rate of long survivors in the cohort studied was established 0.76%. Mean age at diagnosis, OS and PFS were 31.1 ± 11.1, 15.9 ± 6.3, 11.9 ± 5.6 years respectively. Total and subtotal resections were found in 82 and 58 patients respectively. Nine cases received a biopsy alone. No statistical differences were found in a comparison of PFS, OS and age between total and subtotal resection groups. A regression analysis showed a significant correlation between PFS and OS, with an inverse relationship stated between age at diagnosis and OS.

The 10-year survival rate in the cohort studied with GBM was estimated 0.71%. OS was positively correlated with the length of PFS and inversely related with age at diagnosis.

1. Introduction

Glioblastoma (GBM) is among the most deadly neoplasms and continues to be regarded as incurable and universally fatal with a 5-year overall survival (OS) rate, which is one of the worst among all human cancers. The median OS, despite aggressive treatment, remains about 15 months [1–4]. A literature review shows there has been a consistent, but somewhat slow improvement in OS over the last decades [5]. However, 3–5% of patients survive for more than 3 years and are referred to as long-term survivors [6–8]. Unfortunately, the vast majority of patients will have an early tumor progression or recurrence despite applying aggressive multimodality approaches. GBM recurs most often (in 75–90% of patients) within 2 to 3 cm from the border of the original lesion and multiple lesions are seen in 5% of cases after treatment [9–11].

Long-term survival might be correlated with a long progression-free survival (PFS), a multimodal therapy and extensive, multiple tumor resections [6]. Based on the population-based outcome data from the Alberta Brain Tumor registry it can be stated that only 2% of patients with GBM survived three years or longer [12]. Interestingly, the probabilities of surviving an additional year after 1, 2, 3, 4 and 5 years of prior survival were 35%, 49%, 69%, and 93%, respectively [13]. A 10-year survival after GBM diagnosis has been described in individual cases. Smoll et al. found that the cure fraction of young adults with GBM is expected to be 12% and occurs at a minimum time of 10 years after the diagnosis [14]. In the report of Ostrom at al. presenting results from the Central Brain Tumor Registry (CBTRUS) of the United States in the years 1995–2011, the rate of 5- and 10-year survival in GBM was estimated at 5% and 2.6% respectively [15]. This data gives a more promising view on the prognosis and survival in GBM.

The aim of this systematic review was to provide qualitative and quantitative literature analysis of a 10-year survival in GBM.

2. Material and methods

2.1. Search strategy

A search was carried out using PubMed, Embase and Google Scholar for time period until June 10, 2016. Subsequently, a review of articles obtained from such a search and any relevant references

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cited in the articles was conducted. The search strategy involved both keywords and the MeSH term searches for: glioblastoma multiforme, glioblastoma, GBMM, long-term survival/survivors, which were combined with the appropriate Boolean connectors. Only clinical reports were included in the analysis.

2.2. Inclusion and exclusion criteria

Only clinical studies and case reports containing full characteristics on each patient's medical history with the long-term survival of 10 years or longer were included in the review. The selection process has been illustrated in Fig. 1. From 263 records found, 151 articles were excluded because they presented either survival shorter than 10 years, or patients with a diagnosis other than GBM. Reports, which did not present a full characteristics of cases, but only reported cumulative results on cases of survival longer than 10 years in the cohort of patients were also excluded. 78 records were eliminated due to replicated data. Finally, 36 studies, published in the years 1950–2014, met the inclusion criteria.

A further analysis of the reports showed that some of the descriptive characteristics of patients were missing in articles, therefore a total number of cases in subgroup analysis may be lower than the number of the entire group included in the study. A distinction was made between reports published before and after the date of publishing the second edition of classification of nervous system tumors in 1993 by Kleihues [16].

A separate analysis was performed for 10 studies with a large number of all GBM cases and the rate of 10 years survivors was calculated for each study. Finally, a cumulative rate of 10 years survivors for all 10 studies was calculated.

2.3. Statistical analysis

All the results were statistically analysed using the computer software STATISTICA (StatSoft, Inc.) and MedCalc (MedCalc Software). Statistical significance was assumed at $p < 0.05$. The Shapiro–Wilk test was used to evaluate the normal distribution of data. Continuous data was expressed as means ± SD. The *t*-test and one-way ANOVA were used to conduct a test for differences among groups.

3. Results

A review process has been presented in the flow diagram (Fig. 1). A total of 36 reports [1,12,14,17–49] comprising 162 patients were included in this review (Fig. 2). There were 17 single-case reports and 3 studies with more than 10 cases. There were 51 female and 43 male patients analyzed, however in 68 cases gender could not be established.

A descriptive analysis showed a mean age at diagnosis of 31.1 ± 11.1 years (range: 4–69 years) (Fig. 3). An average OS was calculated at 15.9 ± 6.3 years, 50% of cases had OS of more than 13.8 years and the longest survival case was 34 years (Fig. 4). A mean PFS was estimated at 11.9 ± 5.6 years and no progression was found in 31 patients who were alive at the time of the report (Table 1). There were no statistical differences for OS, PFS and

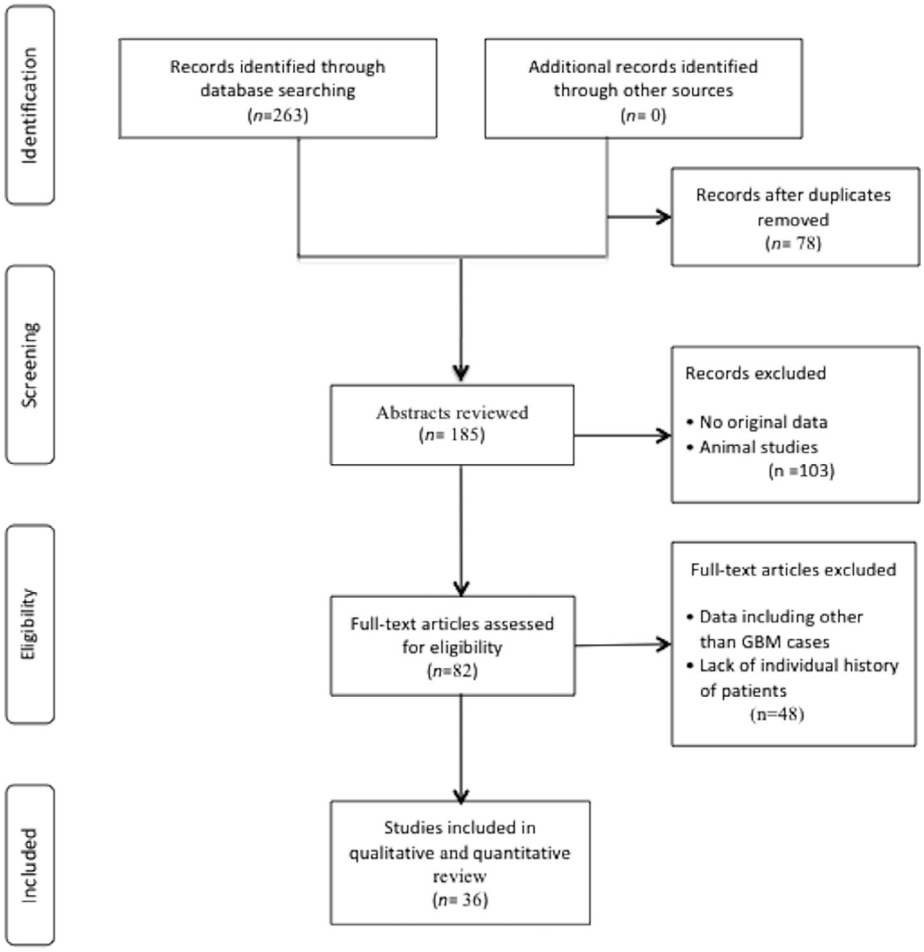

Fig. 1. Flow diagram presenting study selection in the review.

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