



Second surgery for recurrent glioblastoma: A concise overview of the current literature



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ABSTRACT

Optimal treatment for recurrent glioblastoma continues to evolve. Currently, however, there is no consensus in the literature on the role of reoperation in the management of these patients, as several studies provide evidence for a longer overall survival in selected patients with recurrent glioblastoma who underwent second surgery and other studies report a limited impact of second surgery in the clinical course. In this paper, a review of the current literature was performed to analyze the role of reoperation in patients with recurrent glioblastoma and to report the overall survival from diagnosis, progression-free survival and quality of life. Using PubMed and Ovid Medline databases, we performed a review of the literature of the last seven years, finding a total of 28 studies and 2279 patients who underwent second surgery, that were included in the final analysis. The median overall survival from diagnosis and the median survival from second surgery were 18.5 months and 9.7 months, respectively. Extent of resection at reoperation improves overall survival, even in patients with subtotal resection at initial operation. Preoperative performance status and age are important predictors of a longer survival, reason why younger patients with a good preoperative performance status could benefit from reoperation.

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1. Introduction

With a peak incidence between 50 and 70 years of age, glioblastoma multiforme (GBM) (WHO grade IV) is the most common primary intrinsic brain tumor of adulthood and the most malignant glioma subtype [7]. Despite advances in diagnostic technology, surgical techniques and adjuvant treatments, the prognosis remains poor and the median overall survival (OS) of patients has increased only 3.3 months (from 11.3 months to 14.6 months) over the past 25 years [33]. In order to prolong survival, treatment

strategies have become more aggressive, with an increasing number of patients who underwent second surgery and salvage chemotherapy or radiotherapy for recurrent GBM over the past 10 years. Surgery for recurrent GBM is possible with potential surgical and systemic complications and accepted morbidity [20,30,37].

As nowadays quality of life at the time of tumor recurrence is higher than in the past in a great number of patients, second surgery is increasingly considered a valid option [8]. The analysis of recent studies dealing with OS and progression-free survival (PFS) in patient who underwent second surgery could help to identify yet poorly appreciated clinical factors that are associated with a more favorable prognosis.

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2. Materials and methods

A MEDLINE search was performed for the key words “recurrent glioblastoma”, “glioblastoma”, “survival” and “glioblastoma reoperation” from 2007 to present. Only reports in English were used and articles referenced in other articles were also included. The search was limited to articles reporting survival from diagnosis or from second surgery and PFS in patients who underwent reoperation for recurrent GBM. Using these search methods, a total of 218 records were identified (Fig. 1). In addition, the abstracts of the identified studies were screened for relevancy and duplicate patient databases. Studies were excluded if 1) patients had malignant gliomas but not GBM; 2) the outcomes did not include survival analysis; 3) patients did not perform second surgery; 4) patients received locoregional chemotherapy after second surgery; 5) patients received gamma knife surgery before second surgery. Accordingly 190 records were excluded; leaving 28 records (Fig. 1). Collected data were used for the final analysis, whose endpoints were to evaluate the median OS (defined as the time from first diagnosis until death from any cause), the median survival from reoperation (SFR) (defined as the time from second surgery until death from any cause) and PFS (defined as the time from first diagnosis until recurrence). According to Macdonald criteria [25], all studies evaluated tumor progression as the appearance of new lesions, as an increase in tumor extension by 25% on computed tomography (CT) or magnetic resonance imaging (MRI), as a worsening in the clinical/neurological condition or a stable or increased use of corticosteroids. Arithmetic was performed for survival and tumor recurrence analysis.

3. Results

A total of 28 studies with significant data were identified using PubMed and Ovid Medline databases and included in our analysis, accounting for 5736 patients who underwent surgery for GBM [2–4,8,10,11,14,15,19,23,24,26–29,31–35,37,38,41–43,46–48]. Of these patients only 2279 (39.7%) underwent a second or more than two reoperations for recurrent GBM. Twenty-four of the 28 papers included in the analysis demonstrated a survival benefit from a second surgery [2–4,8,10,11,19,24,26–29,31–35,38,41–43,46–48]. Table 1 shows all details. Twenty-three studies provided details about OS, accounting for 1643 patients (Fig. 2). Survival data after second surgery were obtained from 19 studies, including 1433 patients. The median SFR and the median OS resulted 9.7 months and 18.5 months, respectively. Similarly, 13 studies, including 1017 patients, reported data regarding PFS, which was 9.2 months.

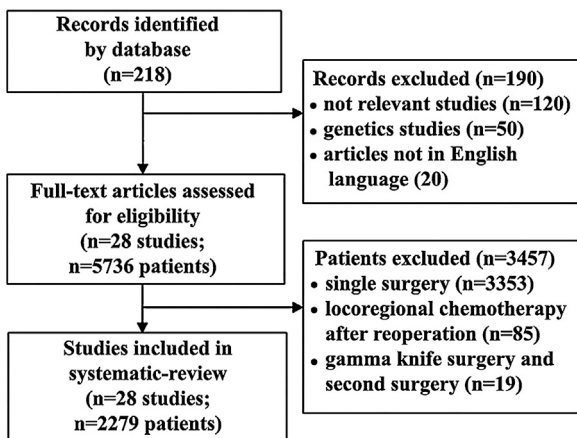


Fig. 1. Flow diagram of study selection.

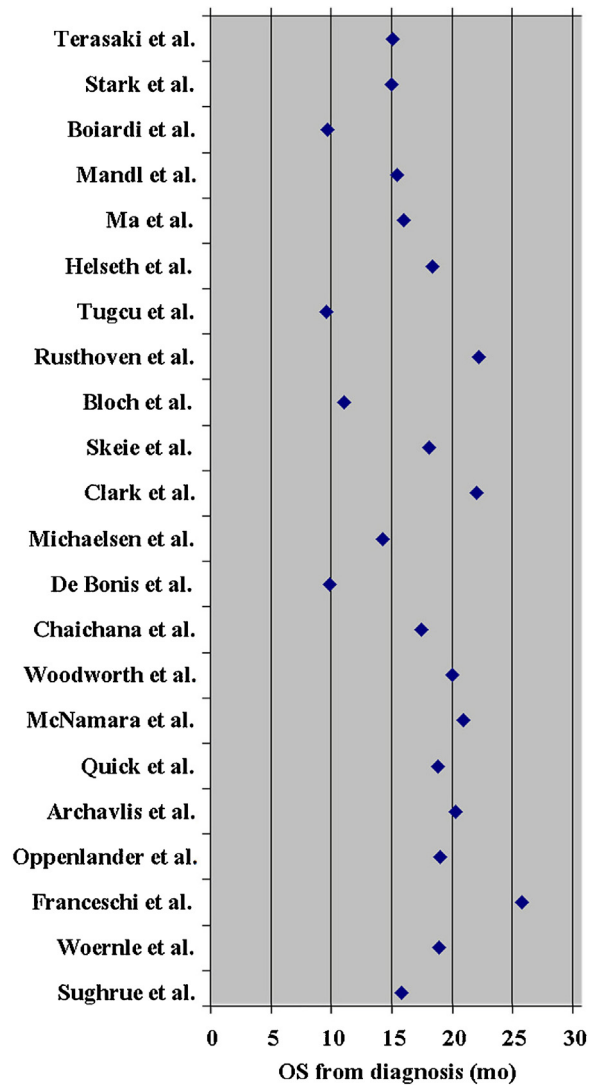


Fig. 2. Overall survival data from diagnosis of glioblastoma multiforme in patients who underwent second surgery, associated with adjuvant treatment, collected from the literature of the last seven years.

4. Discussion

Recurrence is a hallmark of GBM that eventually occurring in all patients, despite every kind of known therapy. Median OS of patients with GMB is still poor and this is largely the result of the recurrence of tumor after initial treatment with maximal safe surgical resection, radiotherapy and chemotherapy [33]. Radiation therapy in addition to surgery and chemotherapy showed to prolong survival from 3 to 4 months to 7–12 months in patients with GBM compared with surgery alone [40]. Treatment of recurrent GBM should be individualized, depending on patient’s clinical condition and performance status, age and quality of life. In our review 24 of the 28 studies included showed a survival benefit or improved functional status after reoperation followed by adjuvant treatments for recurrent GBM [2–4,8,10,11,19,24,26–29,31–35,38,41–43,46–48]. In contrast to these studies, Filippini et al. [14] found no benefit of reoperation on survival, as instead, chemotherapy did. Similarly, Franceschi et al. [15] showed, through a multivariate analysis, that second surgery did not affect survival and had a limited impact in the clinical course of patients with recurrent GBM patients. Skeie et al. [37] reported that median survival after treatment for patients who

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