Original Research

The Impact of Inpatient Rehabilitation on Function and Survival of Newly Diagnosed Patients With Glioblastoma

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Objective: To examine the impact of an inpatient rehabilitation program on functional improvement and survival among patients with newly diagnosed glioblastoma multiforme (GBM) who underwent surgical resection of the brain tumor.

Design: A retrospective cohort study of newly diagnosed patients with GBM between 2003 and 2010, with survival data updated through January 23, 2013.

Setting: An urban academic nonprofit medical center that included acute medical and inpatient rehabilitation.

Participants: Data for newly diagnosed patients with GBM were examined; of these patients, 100 underwent inpatient rehabilitation after resection, and 312 did not undergo inpatient rehabilitation.

Main Outcome Measurements: Overall functional improvement and survival time for patients who participated in the inpatient rehabilitation program.

Results: A total of 89 patients (93.7%) who underwent inpatient rehabilitation improved in functional status from admission to discharge, with the highest gain observed in mobility (96.8%), followed by self-care (88.4%), communication/social cognition (75.8%), and sphincter control (50.5%). The median overall survival among inpatient rehabilitation patients was 14.3 versus 17.9 months for patients who did not undergo inpatient rehabilitation ($P = .03$). However, after we adjusted for age, extent of resection, and Karnofsky Performance Status Scale scores, we found no statistical difference in the survival rate between patients who did and did not undergo inpatient rehabilitation (hazard ratio [HR], 0.84; $P = .16$). Among the patients who underwent inpatient rehabilitation, older age (HR, 2.24; $P = .0006$), a low degree of resection (HR, 1.67; $P = .02$), and lack of a Stupp regimen (HR, 1.71; $P = .05$) were associated with greater hazard of mortality.

Conclusions: Patients who undergo inpatient rehabilitation demonstrate significant functional improvements, primarily in the mobility domain. Confounder adjusted multivariate analysis showed no survival difference between patients who did and did not undergo inpatient rehabilitation; this finding suggests that a structured inpatient rehabilitation program may level the survival field in lower-functioning patients who otherwise may be faced with a dismal prognosis.

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INTRODUCTION

Glioblastoma multiforme (GBM) is the most common primary brain cancer and among the most lethal, accounting for approximately 1% of all cancer diagnoses and 2% of cancer deaths in the United States [1]. The number of new diagnoses made annually is 2-3 per 100,000 people in the United States and Europe. GBM accounts for 12%-15% of all intracranial tumors and 50%-60% of astrocytic tumors. The median survival of patients with GBM even after optimal treatment continues to be less than 15 months [2].

Patients with brain tumors who undergo inpatient rehabilitation have demonstrated functional improvements across multiple diagnostic categories, including GBM, astrocytoma,

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metastatic disease, and meningioma [3-6]. These functional improvements are found in patients with tumor recurrence and are comparable with other illness conditions such as traumatic brain injury and cerebrovascular accident [7-11]. Patients diagnosed with brain tumors have been found to require decreased lengths of stay and have comparable rates of discharge to the community compared with other patient groups [4,8,10,12]. Patients who participate in an inpatient rehabilitation program also demonstrate a significant increase in quality of life after discharge, an area identified as crucial to the survival of this group beyond the hospital stay [13,14]. Moreover, significant improvement during inpatient rehabilitation has been associated with longer survival after discharge. Patients with GBM and brain metastases who made high functional gains from admission to discharge (with a change in functional independence measure [FIM] scores) demonstrated longer survival compared with patients who had little change in functional status [6].

Although some data are available, authors of most previous studies have grouped many different types of brain tumors together. No investigators have specifically examined outcomes of newly diagnosed patients with GBM who entered into inpatient rehabilitation immediately after undergoing the initial resection of their tumor. Although in one study the authors included a number of patients with GBM after the first resection of their tumor [10], these patients were grouped together with other patients who had all types of glial cell—based forms of tumor in a single cohort. No specific information was provided with regard to how patients with GBM performed from admission to discharge explicitly, distinct from glioma as a general category. Other investigators who have examined inpatient rehabilitation outcomes in patients diagnosed with GBM did not examine patients who were newly diagnosed; include details concerning the extent of resection; describe tumor characteristics (eg, size and location); or include other oncologic treatments that were provided [9,11]. Other common limitations of existing studies assessing this population include small sample sizes [3,6,11,14] and heterogeneous diagnostic groups comprising histologically mixed tumor types [3,14].

Conflicting evidence exists regarding improvements that occur after participation in inpatient rehabilitation and factors that may be associated with survival. Investigators have reported improvements in FIM cognition scores [4], FIM mobility scores [5-7], and functional gains in all areas, including activities of daily living, mobility, and cognition [9]. Furthermore, although functional gain after discharge has been associated with longer survival in a small cohort of patients with GBM, the sample of patients with GBM who were examined included those with tumor recurrence and patients who did not undergo resection, in addition to patients who were newly diagnosed [6]. To our knowledge, no investigation has been conducted that singularly (1) compares newly diagnosed patients with GBM who did and did not undergo inpatient rehabilitation after their tumor was resected or (2) examine factors that may be associated with survival for a homogeneous group of patients newly diagnosed with GBM who underwent inpatient rehabilitation.

The present study examined the impact of an inpatient rehabilitation program on functional improvement and survival for patients newly diagnosed with GBM who underwent surgical resection. The primary hypothesis was that patients participating in the inpatient rehabilitation program would experience functional improvements. The key secondary end point was that responders would experience a survival benefit compared with patients who did not respond as well to the rehabilitation program. The aim of the study is to evaluate functional improvement and survival benefit from an inpatient rehabilitation program.

METHODS

Patient Population

We retrospectively reviewed 440 newly diagnosed patients with GBM who were treated between 2003 and 2010 at one academic institution. Twenty-five patients were excluded because they died within 30 days of surgery, and 3 were excluded because their surgery dates were not available (and thus survival time could not be calculated). After exclusion of these 28 patients, our analysis included 412 patients. Each patient's age, gender, extent of resection, type of treatment (radiation, temozolomide, radiation plus temozolomide, vaccine, chemotherapy, Avastin, or gamma knife), tumor size/location, date of death, and last follow-up data were extracted. Mortality dates and follow-up dates were updated from the cancer registry database as of January 23, 2013. The extent of resection was defined as gross total (ie, the entire enhancing tumor was resected), near gross total (>95% of the enhancing tumor was resected), partial (<95% tumor resection), and biopsy only. The extent of resection variable was further considered as a binary variable: (1) high resection if near/gross total resection was achieved or (2) low resection if biopsy or partial resection was documented. Demographic and functional variables including specific FIM scores for patients who underwent inpatient rehabilitation were collected at admission and discharge (eg, the average amount of therapy such as the 3-hour rule). Survival was defined as the period from the time of surgery to the date of death or the last follow-up date for patients who were still alive. Overall survival time was calculated in months for all patients.

Inpatient Rehabilitation Program

The inpatient rehabilitation program consisted of medical and functional management from an interdisciplinary team in a hospital environment (personnel from physiatry, rehabilitation nursing, physical therapy, occupational therapy,