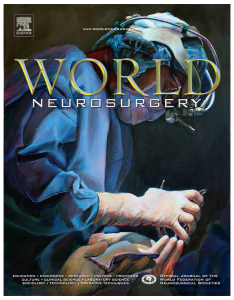

Caregivers’ Perspective and Burden of The End-of-Life Phase of Patients With Glioblastoma: A Multicenter Retrospective Study

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Title: **Caregivers' Perspective and Burden of The End-of-Life Phase of Patients With Glioblastoma: A Multicenter Retrospective Study**

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Abstract

Glioblastoma represents the most common aggressive primary brain tumour in adults. Changes in cognition, personality and in behaviour of patient as well as side effects of treatments cause unique challenges for providing care and may impact caregiver burden in different ways.

This retrospective study included 45 patients with diagnosis of glioblastoma treated between January 2022 and June 2023 in two Neurosurgical Departments. We investigated the quality of life and the experiences of glioblastoma patients caregivers on the end-of-life phase using a validated questionnaire consisting of 38 questions related to the caregiver's view of the patient's terminal phase and another 26 questions regarding caregiver's experiences and emotions during the last three months of the patient's life.

Fatigue, reduced consciousness and sadness were the most common patient's symptoms reported by their caregivers. The reported quality of life of caregivers was low and superimposable to the quality of life that they attributed to the patients. The burnout symptoms and feelings of insufficient information emphasize the urgent need for psychological support and training dedicated to caregivers.

The end-of-life phases of glioblastoma patient may represent a critical factor that significantly affects not only the patient but also caregiver burden, caregiving tasks, and caregiver time. A urgent multidisciplinary support program is needed to face and improve caregivers burden.

Introduction:

Glioblastoma represents the most common primary central nervous system (CNS) tumour in adults, representing approximately 57% of gliomas and 48% of all primary CNS tumours [1]. Treatment is still mainly palliative and consists of the maximum extension of a safe neurosurgical resection, and adjuvant treatment by radiotherapy and chemo-therapy [2]. Despite all recent advances in multimodality therapy, the overall prognosis remains poor, and long-term survival is un infrequent event.

In recent years, a lot of economic resources and scientific energy have been spent on the study of molecular biology of high-grade malignant brain lesions, focusing on diagnostic and prognostic aspects that are consistently evolving. Particularly, the 2021 WHO Classification of CNS tumours forces a detailed biological and molecular analysis to identify a grade IV glioma [1, 3], emphasizing DNA analysis as well as histology. Glioblastoma are further categorized into different subtypes based on the presence or absence of isocitrate dehydrogenase (IDH) mutations, 1p/19q codeletion, alpha-thalassemia/mental retardation syndrome X-linked (ATRX) mutations, among others. [4, 5, 6].

However, the scientific community has been paid poor attention to difficulties and desires of patients afflicted in their end-of-life phase of these incurable tumors, and the devastating impact on patients' family and caregivers. In this scenario, supportive and palliative care may be of paramount importance in the context of multimodal management, especially in designing the best path of supportive care with a beneficial impact on patients and healthcare system organization.

The end-of-life phases of patients with glioblastoma represents the time occurring immediately before death, with increase of symptoms and failure of antitumoral therapies [7]. In this phase, the rapid deterioration in physical, psychological and social functions of patients may represents a critical factor that significantly affects caregivers' burden, tasks, and time.

Moreover, especially after a surgical resection, glioblastoma patients are treated in daily treatment with oral or intravenous medications. In this scenario, the caregivers' role is strongly increased and may result into a devastating impact on their quality of life.

The quality of life may considered an extremely personal aspect, measurable only by the individual experiencing that life. It is difficult to establish the burden of a person's quality of life affected by a high-grade brain tumour. Quality of life embraces many dimensions such as physical health, mental competence, emotional stability, social integration, and life satisfaction [8, 9].

In this paper, we investigated the quality of life and the experiences of glioblastoma patients' caregivers during the end-of-life phase through a validated questionnaire to assess and discuss the end-of-life issues with glioblastoma patient and their families. The questionnaire analysed characteristics of the patients and caregivers, focusing on health-related problems, quality of care, education and living situation, end-of-life preferences and the preference place of death by the patients.

Methods:

Patients' and caregivers' data were retrieved from the medical records of two Neurosurgery Departments. The validated questionnaire used for this study was reported by Taphoorn and colleagues [10]. The survey test consisted of two parts (table S1). The first one contained 38 questions regarding the patients' terminal phase viewed from their caregivers' perspectives, particularly related to the last three months and last week before death. The second part consisted of 26 questions concerning psychological aspects of the caregivers during the last three months of the patients' life. Biographical and demo-graphic characteristics of the caregivers such as age, gender, date of surgery, post-operative treatments and date of death were collected.

The study was conducted at the Neurosurgical Clinic "Policlinico P. Giaccone", University of Palermo, Italy and at Neurosurgery Department, Villa Sofia Hospital, Palermo, Italy. We appointed caregiver as the person's closest living relatives through blood or legal relationships. The survey was administered by phone call. And if no other contact of the primary caregiver was achievable, we identified the caregivers as "not traceable". Figure 1 shows caregivers' selection for this study.

Statistical analysis

A descriptive statistics was performed for patients' and the caregivers' data. Microsoft Excel Software 16.82, 2024 was used for mean, median and standard deviation (SD).

Results:

We identified 45 patients with a diagnosis of glioblastoma treated between January 2022 and October 2023. 11 patients were not eligible because still alive and in 3 cases no contact with the phone number on the medical records was possible.

Finally, 31 caregivers were enrolled in this retrospective study and were contacted by telephone to join the survey, after the patient's death. A total of 24 of caregivers agreed (response rate = 77,41%). 3 out of 7 of those caregivers who denied the participation re-ported to feel emotionally overwhelmed. Moreover, 4 out of 7 decliners did not give any reasons or refused categorically.

The median period of time from diagnosis to death (time of caring) was from 1 to 22 months (7.6 ± 6.04 months), the median time elapsed from the patients' death to the date of study was 15.73 ± 6.69 months (table 1).

General Characteristics of Patients and Their Caregivers

Most of patients were male (66,6%) with a mean age of 67.9 years ± 9.17 years (Table 1). Mean Karnofsky Performance Status (KPS) was 68.75 ± 20.91, mean EcoG Performance Status Scale (PSS) was 2.2 ± 1.21. The mean age of the caregivers was 48.78 ± 10.9 years, with a female to male ratio of 2:1. The majority of caregivers were patients' sons (n = 13; 54.2%). Others included patients' partner (n = 6; 25%) and patients' brothers (n = 5; 20.8%). No other relatives or siblings were reported.

14 out of 24 of the patients (58.3%) were practising religious (Catholic) and in 70.8% of caregivers religion and faith were considered important in their life. 29.16% of patient and 16.7% of caregivers had a high grade of education, defined as secondary school or over.

Patients' Symptoms and Mobility

The caregivers were asked to quote the patient symptoms for two time points: the last three months and the last week of the patients' life (Figure 2). The highest symptom recorded was for fatigue (88.9%) during the last three months which increased slightly in the last week to 92.9%. Other symptoms frequently reported three months before death were reduced consciousness and drowsiness (71.4%), headache (69.2%), hemiparesis (64.3%), sadness (64.3%), aphasia (42.9%), dysphagia (38.4 %). During last week of life, aphasia was reported in 69.1%, dysphagia in 58.3%, behaviour 60.3% and concentration problems 63.3%.

The patients' mobility and degree of autonomy were generally reduced. Just 7.1% were self-sufficient during the last three months. Ambulatory assistive devices were necessary for 35.7% of the patients. 50% were confined to bed up to 86.4% in the last week of life.

Caregivers' Symptoms and Restrictions

The most frequently mentioned symptoms by caregivers were sadness (83.3%), followed by anxiety (46.2%) and irritation (41.1%). In 75% of caregivers a moderate job restriction and a limitation of social activities were detected. In 16 out of 24 cases, physical condition of their relative interfered with family life, with their social activities (58.3%) and caused financial difficulties (33.3%).

Quality of Life, Place of Death and End-of-Life Phase

The patients' quality of life (QOL) was quoted with a median of 4.0. This data is superimposable to the median QOL of 4.0 reported by caregivers on a scale of 1–7 (Figure 3). The patients' QOL during the last week decreased to a median of

3.0. The patients' median quality of care was 5.0 during the last three months and 3.0 in the last week of life.

50% of the patients died at home, 25% in hospices and 25% in a nursing home. 16 out of 24 patients (66.67%) wanted to die at home. In only one case a patient did not die at the place whished.

No formal advanced care directives were expressed from patients in this study. Furthermore, only 25% of caregivers received sufficient support for his relative from social environment, other than himself. The quantity of information provided by health care workers about patient illness was not sufficient in 25%, sufficient in 41.7% and satisfying in 33.3% of caregivers. The mental support provided by the health care professionals was not sufficient in 33% of cases. The 58.3% of caregivers reported that health care providers should have taken on a larger role in the care for their relatives.

Discussion:

This study used a survey [10] designed to assess caregivers' perspective in those people caring for patients with glioblastoma. Patients in this study were representative of the general glioblastoma patient population [11], with a predominance of males (2:1) and a median age of 67.9 years ± 9.17, superimposable to other reports [11, 12]. Moreover, the characteristics of caregivers of patients with glioblastoma in this study were mostly similar to those of other cancer caregivers [13] with a mean age of 48.78 years ± 10.9, and a female to male ratio of 2:1.

The rate of refusal (22.59% of caregivers) to take part in the study may be related to the sensitive nature of this topic might be due to the sensitive and potentially distressing nature of this topic, as reported by 42.86% of the deniers. However, a significant part of caregivers were well motivated and emotionally able to talk about their burden.

This supports the study of Lipsman et al [14], who reported that patients with terminal brain cancer and their caregivers' attitudes felt talking about these personal and distressing issues as constructive and positive.

Patients Quality of Life end End-of-Life Phase

During the end-of-life phase patients experience a rapid deterioration of their physical and social functions [15]. In this scenario, patient's quality of life may depends on the lack of symptoms control and adverse effects of the antitumoral therapy [14].

In accordance with literature findings [16, 17, 18], fatigue and drowsiness are frequent symptoms referred by high-grade glioma patients since diagnosis and significantly increase after radiotherapy. Comparing patients' symptoms during three months before death and during last week of life, caregivers reported that symptoms increasing in these two time points were aphasia (42.9% at three months before death up to 69.1% during last week of life), dysphagia (38.4 up to 58.3%), behaviour (35.7 to 60.3%) and concentration problems (53.9 to 63.3%). These data indicates that end-of-life care needs of a glioblastoma patients are unique, and thus differ from symptoms observed in patients with cancer not involving the CNS [21, 22, 23].

Residence of Care, Hospices and Home

Considering the complexity of these , there is a consensus amongst physicians that aggressive care at the end of life, including hospitalization or intensive care unit ad-mission, as well as the administration of chemotherapy in the end-of-life stage, may compromise the patient and caregivers health-related quality of life aspects, without significant proved benefit [24, 25]. Despite this, rates of hospitalization and ICU admission among patients with terminal malignant brain tumours remain high [24, 26]. In this scenario, hospice may represent a viable alternative to lighten the burden on hospitals and families, even if of patients with a malignant brain tumour are nonetheless enrolled in hospice late (i.e., within the last 3 days of life) or not at all [26, 27, 28, 29]. In our study, 53.8% of the patient lived ad home three months before death, 38.5% in hospital and 7.7% in a hospice. 50% of the patients died at home, 25% in hospices and 25% in a nursing home.

The rapid onset and progression of a brain tumour may result in a significantly adjust of lives and schedules of patients and caregivers, learning to prioritize, focusing on emotions, family, and especially home life. Not surprisingly, according to our founding, 16 out of 24 patients (66.67%) wanted to die at home. In only one case a patient did not die at the place whished, due to specific medical treatment.

Palliative teams and support programs should be encouraged not only for reduce burden on hospitals, but most importantly to grant the wishes of the patients to stay home with his family for last days of his life.

Advanced Care Directives

Advanced care directives has been demonstrated to represent an important element in improving end-of-life care of primary malignant brain tumours patients [30]. In our study none of the patient expressed a formal advanced care directives. If comparing the study of Sizoo et al conducted in Netherlands [10] a relevant difference is the lack of advance care directives in Italy if compared with the Dutch study, considering that 42% of Dutch patients had advance directives. This suggests that the possibility of euthanasia in Netherlands may provokes the need to plan an end-of-life decision.

Advanced care directives needs to be considered for improving decision-making by patients and family, increasing patient and family satisfaction, improving physician and patient relationship, and enhancing quality of life of the patient.

Caregivers' Needs

Considering caregivers needs for the management of their relatives, in our study, the quantity of information about patient illness provided by health care staff was not sufficient in 25%, sufficient in 41.7% and satisfying in 33.3% of caregivers. Effective communication and complete information about diagnosis and treatment, especially for transition from hospital to home-based care is crucial for the illness management. As suggested by Flechl et al [9] caregivers are often not able to manage the care at home at a certain point of disease and this could represent the cause of caregivers burnout problems. It was suggested that home-based visits from palliative teams would promote better patient care at home [30]. Indeed, caregivers referred that the mental support provided by the health care professionals was not sufficient in 33% of cases. The 58.3% of caregivers reported that health care providers should have taken on a larger role in the care for their relatives.

It is plausible to consider that an educational plan to develop communication skills may impact positively to the caregivers [31].
The patients' quality of care was reported with in a median of 5.0 in a 1-7 scale during the last three months and a median of 3.0 during the last week of life. As reported in two recent studies [32, 33], caregivers referred satisfaction with medical and nursing care, but psychological care was rated average to poor. Caring is both physically and mentally exhausting. Considering the symptoms reported by caregivers during all the illness course like sadness (83.3%), less interest in other (58.3%) and anxiety (46.2%), a psychological support group should be proposed to offer them a way out for distress and to improve communications and relations with the patient.

Limitations
Our group collected the responses of the caregivers that reflects the experiences at the two participating hospitals in Palermo. This little number of patient and caregivers enrolled may not express all the issues and need of patient with a high grade glioma, especially considering field such as advanced care directives and end-of-life plannings.

Conclusions

Despite incremental progress in the diagnostic and therapeutic approach to glioblastoma, improved palliative strategies are necessary to enhance a multidisciplinary holistic approach to these patients. Symptoms suffered by patient with glioblastoma may impact caregiver burden in different ways. It is vitally important to understand the mindset of these patients and their caregivers in order to provide them comprehensive and effective care. A urgent multidisciplinary support program is needed to face and improve caregivers burden.

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Figure Legend:

Figure 1 : A graphical view showing caregivers eligibility. Caregivers of patient not deceaded (n = 11); caregivers not traceble (n = 3); caregivers that refused to participate (n = 7); caregivers that agreed to participate (n = 24).

Figure 2 : Filled columns showing the symptoms reported by the caregivers during the last three months (3m) (in blue) and last week (1w) of life (in purple). X axis represents the reported symptoms, Y axis the percentage of the described symptoms. The most reported symptoms during three months before that were fatigue (88.3%), drowsiness (71.4%) and headache (69.2%). The most reported symptoms during the last week of life were fatigue (92.9%), drowsiness (75%) and sadness (69.3%). Symptoms frequently increased in these two time points were aphasia (42.9 up to 69.1%), disphagia (38.4 up to 58.3%), behaviour (35.7 to 60.3%) and concentration problems (53.9 to 63.3%).

Figure 3 : A 1-7 scale of quality of life rate of patients and caregivers in the three months before death. Caregivers were asked to rate their parent's (in blue) and their (in purple) quality of life through a 1-7 scale. 1 = very poor; 4 = neutral; 7 = excellent. The most rate (4 in a 1-7 scale) was reported by 11 caregivers when asked to rate their parent's quality of life. 8 caregivers reported a rate of 5 in a 1-7 scale when asked to rate their quality of life.

Figure 4 : A 1-7 scale of quality of care rate of patients and caregivers during last week of life. 1 = very poor; 4 = neutral; 7 = exellent. Caregivers were asked to rate their parent's (in blue) and their (in purple) quality of care through a 1-7 scale. 1 = very poor; 4 = neutral; 7 = excellent. The most rate (5 in a 1-7 scale) was reported by 7 caregivers when asked to rate their parent's quality of life. 9 caregivers reported a rate of 3 in a 1-7 scale when asked to rate their quality of care.

Abbreviations

CNS: central nervous system
QOL: quality of life

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