

A retrospective chart review to identify the involvement of palliative care with glioblastoma multiforme patients

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ABSTRACT

Background: Glioblastoma Multiforme is a deadly brain cancer that is very challenging for patients and their families. It is associated with rapid progression, cognitive decline, and a low survival rate.

Objective: To determine whether deceased Glioblastoma Multiforme patients had received follow-up service from the palliative care team before their death, whether invasive measures had been reduced, and whether the last antineoplastic treatment was given within 14–30 days before death.

Method: A retrospective study utilizing chart data from January 2020 to March 2022 from an institutional project. Data were gathered to reflect selected indicators of quality of care for palliative care patients.

Results: Of the 30 hospitalized patients with Glioblastoma Multiforme who had died while in hospital, 50% had received support from the palliative care team. Two patients (6.7%) had undergone antineoplastic treatment in the last 14 days of life and 13 (43.3%) had an order limiting invasive measures defined in the last two weeks of life.

Conclusion: In half of the patients monitored by a palliative care team, antineoplastic treatment and limitation of invasive measures occurred in the last 14 days of life. This may be associated with increased suffering of patients, family members, and professionals. Discussions about end-of-life care-related choices and goals of care need to be respected.

Keywords: oncology, palliative care, Glioblastoma Multiforme, end-of-life care

INTRODUCTION

Primary brain tumours represent about 2% of general cancer diagnoses, and more than 75% of them are high-grade gliomas, including Glioblastoma Multiforme (GBM) (Ford et al., 2012; Giammalva et al., 2018; Maugeri et al., 2016). GBM is a highly malignant primary brain tumour involving rapid progression and broad development of symptoms that encompass neurological, physical, psychological, and social symptoms, as well as changes in behaviour and personality (Golla et al., 2020). Its unique trajectory is often sudden and devastating, marked by an early cognitive decline that is challenging to cope with for family members and care teams (Ford et al., 2012; Giammalva et al., 2018; Philip et al., 2015; Philip et al., 2018).

Despite advances in treatment for this type of cancer over the past few decades, the five-year survival rate remains limited. The median survival period is around 14–18 months in younger, healthier patients, while in older fragile patients, the prognosis is worse (Catt et al., 2008; Giammalva et al., 2018; La Torre et al., 2009; Pompili et al., 2014; Tan et al., 2020).

As the disease progresses, patients display recurrent physical and neurological symptoms with greater frequency and intensity, which causes increased stress and suffering not only in patients, but also in the family members. The family members are dealing with care, finances, and domestic responsibilities in addition to patients' personality and behaviour changes (Crooms et al., 2020; McConigley et al., 2010; Schubart et al., 2008).

Due to the difficulties and needs of cancer patients with advanced diseases and their families, the American Society for Clinical Oncology (ASCO) implemented a program named Quality Oncology Practice Initiative (QOPI) in 2012 to help evaluate and improve the quality of care. The evaluation program contains 180 quality measures of oncology practices and quality of care indicators including items evaluating palliative and end-of-life care for cancer patients (Hemminger et al., 2017; ASCO, 2012).

In Hemminger et al. (2016), 117 patients diagnosed with GBM between January 1 and May 1, 2010, and who died before November 1, 2010, were evaluated through a retrospective cohort by following five ASCO/QOPI measures related to palliative and end-of-life care. The measures were: (1) emotional assessment at the second appointment, (2) advanced directive of will (ADW) documentation at third appointment, (3) no chemotherapy given in the last 14 days of life, (4) hospitalization

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in hospice more than seven days before death, and (5) involvement of palliative care and/or palliative care at the end of life. In that study, 37% of the patients had received at least one session with a palliative care team and most patients died with the involvement of a palliative care team at some point or at the end of life. Only 6% of the patients received chemotherapy in the last 14 days of life. An ADW, which declares a patient's end-of-life care preferences, was documented for 52% of the patients by the third appointment. However, 37.6% of the patients spent more than 80% of their life after diagnosis without an ADW. Meanwhile, the period from the first order limiting invasive measures to death was 27 days, and almost 25% of patients had no detailed order limiting invasive measures before the last week of life (Hemminger et al., 2017).

To clarify, limiting invasive measures refers to the point when a patient will not receive any advanced life support such as intubation, hemodialysis, vasoactive drugs, or cardiopulmonary resuscitation. The term "therapeutic obstinacy" refers to persisting in a certain behaviour when a treatment is considered "futile," not because it causes harm, but because it is of no clinically verifiable utility. Therefore, therapeutic obstinacy is defined as the continued and persistent use of measures that sustain the lives of patients with advanced diseases, with prolonged maintenance of vital biological systems and delay of death (Floriani, 2008; Campbell, 1995; Engelhardt, 2003). Therapeutic obstinacy is a grave ethics issue, especially in the modern age when technological progress has made it possible to prolong human life. Understanding therapeutic obstinacy and its reasons is crucial. Unfortunately, it is still not clearly understood by all health professionals, although some studies have already shown that nurses are beginning to understand and identify therapeutic obstinacy (Menezes et al., 2009; Silva et al., 2012).

In addition, palliative care exists in a conflicting field of interventions, which also includes therapeutic obstinacy, and may be underutilized. Conflict in intervention approaches can have repercussions on the quality of life of patients and their families, with undeniable ethical implications (Campbell et al., 1995; Engelhardt, 2022; Floriani & Schramm, 2008). In the hospital where this study occurred, the palliative care team is composed of one nurse, five doctors, and one psychologist. The request for palliative care services or referral to the palliative care team occurs according to the patient's primary physician. Factors associated with the inefficient use of palliative care services include the presumption of patients and their families that palliative care is appropriate only at the end of life; the stigma that palliative care diminishes hope; and health professionals' lack of knowledge or disagreement about criteria for referral (Hui et al., 2015; Kim et al., 2020; Perrin & Kazanowski, 2015).

Considering these problems and the importance of the subject, this study aimed to determine and discuss whether GBM patients admitted to an oncology inpatient unit received the palliative and end-of-life care recommended by ASCO for patients with advanced oncological diseases. This care would include follow-up with a palliative care team and not administering antineoplastic treatment in the last days of life.

METHODS

This is a retrospective study of patient data from January 2020 to March 2022. The quantitative analysis was carried out based on information contained in the institutional project database of oncology hospitalizations entitled, "Goal of Care Project." This study was approved by the Ethics and Research Committee of a multispecialty hospital in the city of São Paulo, Brazil.

Goal of Care Project

The Goal of Care Project aims to improve the quality of care for patients with advanced oncological disease. It equips teams with validated palliative care and communication strategies based on institutional policy. The project aligns care teams with the goals of care for hospitalized cancer patients and provides support for the team members in fulfilling the goals.

A descriptive analysis of the data was performed, and the quantitative data were represented by mean, standard deviation, median, or percentile. Categorical data were represented by absolute (n) and relative (%) frequency and expressed through contingency matrices and analyzed by Pearson's Chi-square test, or Fisher's Exact Test, when necessary. For all analyses, a $p \leq 0.05$ was considered significant.

RESULTS

A total of 991 patients were admitted to the oncology inpatient unit from January 2020 to March 2022, of which 47 had been diagnosed with Glioblastoma Multiforme. After a detailed analysis of the cases, we found that three of the patients were diagnosed with other primary diseases and had metastasis in the central nervous system, two were duplicated in the database, nine were still alive (and therefore, excluded from our sample) and three had follow-up discontinued due to service changes (e.g., referral to back-up clinics, impact of the COVID-19 pandemic, which was at its peak from March 2020 to December 2021). Thus, 30 patients remained as the final sample.

Among the study subjects, 12 (40.0%) were female and 18 (60.0%) were male, and the average age was approximately 57 years (See Table 1). The average time between diagnosis and death was 710 days (approximately two years). Twelve (40.0%) patients were referred to the ICU during their last hospitalization before death and six (20.0%) of these had an order limiting invasive measures defined there and died in the ICU. Eighteen (60.0%) patients were not referred to the ICU. In total, 24 (80.0%) patients had an order limiting invasive measures defined while in the inpatient unit. Twenty-three (76.7%) patients died in the inpatient oncology unit, and one patient (3.3%) was discharged from the hospital and died at home. Thirteen (43.3%) had their limitation of invasive measures defined in the last two weeks of life, five (16.7%) in the previous month of life, five (16.7%) in the last one to three months of life, and seven (23.3%) over three months before death while in hospital (see Table 1).

Of the 30 cases, 15 (50%) were referred to the palliative care team. Of these 15 cases, four (26.6%) were referred in the last two weeks of life, three (20.0%) in the last month of life,

Table 1

Characteristics of patients with Glioblastoma Multiforme who died while in hospital. São Paulo, 2022.

Characteristics of patients	Average	SD
Age	57 years	±17.40
Time from diagnosis to death	710 days	±599.13
Gender (N = 30 patients)		
Female	N = 12	40.0%
Male	N = 18	60.0%
Patient admitted to ICU (N = 30 patients)		
Yes	N = 12	40.0%
No	N = 18	60.0%
Death in Hospital vs hospitalization (N = 30 patients)		
Hospitalization	N = 23	76.7%
ICU	N = 6	20.0%
Home	N = 1	3.3%
Last line of antineoplastic treatment (N = 30 patients)		
1–2 line	N = 22	73.3%
3–4 line	N = 8	26.7%
PC team (N = 30 patients)		
Yes	N = 15	50.0%
No	N = 15	50.0%
Place of limitation of invasive measures while in hospital (N = 30 patients)		
ICU	N = 6	
Hospitalization	N = 24	
Time from palliative care consultation to death (N = 30 patients)		
< 14 days	4	26.6%
15–30 days	3	20.0%
30–90 days	4	26.6%
> 90 days	4	26.6%
Time from definition of limitation of invasive measures to death (N = 30 patients)		
< 14 days	13	43.3%
15–30 days	5	16.7%
30–90 days	5	16.7%
> 90 days	7	23.3%
Time from last antineoplastic treatment to death (N = 30 patients)		
< 14 days	2	6.7%
15–30 days	7	23.3%
30–90 days	12	40.0%
> 90 days	9	30.0%

Source: Author.

four (26.6%) between one and three months before death and four (26.6%) more than three months before death.

Two patients (6.7%) underwent chemotherapy in the last 14 days of life, seven (23.3%) in the last month of life, 12 (40.0%) between one and three months before death and nine (30.0%) over three months before death. Of these 22 (73.3%) underwent one to two lines of antineoplastic treatment and eight (26.7%) received three to four lines. Details of the patients who were referred to the palliative care team are shown in Table 2.

Of the patients monitored by the palliative care team, four (26.7%) were referred to the ICU ($p \leq 0.19$), four (26.7%) had their limitation of invasive measures defined in this sector, and one (6.6%) died in the ICU ($p = 1.0$). Four patients (26.7%) had their limitation of invasive measures defined in the last 14 days of life and seven (46.7%) in the last month of life ($p = 1.0$). The last antineoplastic treatment occurred in 1 patient (6.6%) in the last two weeks of life and in 3 (20.0%) in the last month of life ($p = 1.0$).

The definition time for limiting invasive and life-prolonging measures provided the results shown in Table 3. Thirteen patients (43.3%) had their limitation of invasive measures defined in the last 14 days of life; of these, four (30.8%) had this limitation defined in the ICU; and in nine (69.2%), it was defined in the hospital unit ($p \leq 0.21$). Six patients (46.1%) were referred to the ICU during the hospitalization that preceded

Table 2

Univariate analysis of patients monitored by the palliative care team (15 patients). São Paulo, 2022.

Variables	N (%)	P-value
Referred to the ICU	4 (26.7%)	$P \leq 0.19$
Death in the ICU	1 (6.6%)	$P \leq 0.19$
Place of definition of limitation of invasive measures		
Hospitalization	11 (73.3%)	$P = 1.0$
ICU	4 (26.7%)	
Limitation of invasive measures		
Last 14 days of life	4 (26.7%)	$P = 1.0$
Last month of life	7 (46.7%)	
Last antineoplastic treatment		
Last 14 days of life	1 (6.6%)	$P = 1.0$
Last month of life	3 (20%)	

Source: Author. Chi-square statistical analysis test was used.

Table 3

Univariate analysis of the time of definition of limitation of invasive measures before death. São Paulo, 2022.

Variables	Last 14 days of life (13 – 43.3%)		Last month of life (18 – 60.0%)	
	N (%)	P-value	N (%)	P-value
Patients who went to the ICU	6 (46.1%)	$P \leq 0.21$	6 (33.3%)	$P \leq 0.21$
Death in the ICU	4 (30.8%)		4 (22.2%)	
Place of definition of limitation of invasive measures				
Hospitalization	9 (69.2%)	$P \leq 0.21$	14 (77.8%)	$P \leq 0.21$
ICU	4 (30.8%)		4 (22.2%)	
Last antineoplastic treatment				
Last 14 days of life	2 (15.4%)	$P \leq 0.19$	2 (11.1%)	$P \leq 0.19$
Last month of life	6 (46.1%)		7 (38.9%)	

Source: Author. Chi-square statistical analysis test was used.

their death, and 4 (30.8%) died in this sector ($p \leq 0.21$). In addition, 2 patients (15.4%) received the last antineoplastic treatment in the last two weeks of life and 6 (46.1%) in the last month of life ($p \leq 0.19$).

Eighteen patients (60.0%) had their limitation of invasive measures defined in the last 30 days of life; of these, four (22.2%) had this limitation identified in the ICU and in 14 (77.8%) while they were in the hospitalization unit ($p \leq 0.21$). Six (33.3%) were referred to the ICU during the hospitalization that preceded their death, and four (22.2%) died in this sector ($p \leq 0.21$). In addition, two patients (11.1%) received the last antineoplastic treatment in the last two weeks of life and seven (38.9%) in the last month of life ($p \leq 0.19$).

Finally, we individually observed those patients who received antineoplastic treatment in the last month of life and show these data in Table 4. Of the patients who received antineoplastic treatment in the last month of life, six (66.7%) had their definition of limitation of invasive measures defined in the last 14 days of life and seven (77.8%) in the last month of life ($p = 1.0$). Three patients (33.3%) had this definition in the ICU and six (66.7%) in the hospitalization unit ($p = 1.0$), 5 (55.5%) were referred to the ICU in the last hospitalization, and three (33.3%) died in the ICU ($p = 1.0$).

Table 4

Univariate analysis of patients who received antineoplastic treatment in the last month of life. São Paulo, 2022.

Questions	Last month of life (9)	
	N (%)	P-value
Patients who went to the ICU	5 (55.5%)	$P = 1.0$
Death in the ICU	3 (33.3%)	
Place of definition of limitation of invasive measures		
Hospitalization	6 (66.7%)	$P = 1.0$
ICU	3 (33.3%)	
Time of definition of limitation of invasive measures		
Last 14 days of life	6 (66.7%)	$P = 1.0$
Last month of life	7 (77.8%)	

Source: Author. Chi-square statistical analysis test was used.

DISCUSSION

In this study, 60% of patients with GBM were male and 40% female, which is consistent with the prevalence found in the literature (Davis, 2016; Thakkar et al., 2014). GBM has a higher incidence in adults, especially at older ages (mean age: 64 years). The mean age in our sample was 57 years. Some studies point to differentiation between primary glioblastomas, where the average age of patients is 62 years, and secondary glioblastomas (which develop from low-grade astrocytomas or oligodendrogliomas), which are more frequent in younger patients, where the average age of patients is 45 years (Thakkar et al., 2014).

Several key indicators of quality of care in patients with advanced disease were the focus of this project. Data concerning these indicators ought to be incorporated into daily patient records and reviewed on a regular basis. Key indicators included referral to the palliative care experts, and discussion about goals of care and decisions about limitation of invasive measures were ones we could assess based on our medical records and allowed us to review our practices.

Although there are impasses and difficulties in approaching patients with GBM because it is a very distressing disease where the family has to deal with several burdens, behavioural changes, and physical symptoms, and even young patients have limited survival/life expectancy of mostly within two years with little possibility of disease-modifying treatments, most of the patients in the study received care as recommended by quality standards.

Patients referred to palliative care team

There is a growing awareness that patients benefit from the palliative care team monitoring their treatment throughout the course of the disease, with evidence that palliative care alleviates symptoms, decreases depression rates, reduces care costs, minimizes hospitalizations, reduces invasive measures at the end of life, and improves patient survival (Hemminger et al., 2017). Diamond et al. (2016) associated late referral for palliative care (e.g., less than seven days before death) with increased use of medical interventions at the end of life for patients with primary malignant brain tumours.

In a systematic review on the use of palliative care services and advanced care planning for adult patients with GBM, 38–86% of patients had received the service. However, in the studies selected for this review, patients were generally referred for palliative care close to the end of life, within an interval of 3 to 22 days before death (Wu et al., 2021).

Low rates for use of palliative care services, as well as late referrals to palliative care, may be a result of lack of knowledge about the utility of palliative care and the stigma arising from its name, as perceived by both patients/family members and health professionals. Fadul et al. (2009) evaluated the impact of the name “palliative care” versus “supportive care” through a survey among oncologists. When asked, “Does the name of the service decrease hope in patients and family members?”, 61% of oncologists answered “yes” for “palliative care” in contrast to 15% for “supportive care.” When asked if the “name of the service is a barrier to referring patients,” 44% answered affirmatively regarding the term “palliative care” compared to 11% for the term “supportive care.” Zimmerman, et al. (2016) also suggests the term palliative care carries a stigma, mainly in an initial outpatient setting and even after positive experiences with an early palliative care intervention. This stigma, along with the lack of well-defined criteria for referral to palliative care services, may be responsible for the low referral rates found in our study. The observation of low referral rates is corroborated in the literature, where it is reported that neuro-oncologists seldom refer patients with GBM for palliative care services at an early stage (Hemminger et al., 2017; Walbert et al., 2015).

As Hui and Bruera (2015) proposed, based on conceptual and clinical models, common themes have emerged regarding how we can integrate oncology and palliative care. However, even in the face of different approach models, there are still many divergent discussions for questions such as, “Who should receive a palliative care referral?”, “When should palliative care be introduced?”, “How much primary palliative care should oncologists and primary care physicians provide?” and “What setting is most appropriate for the delivery of palliative care?” The answers to these questions depend on the health system in which the service is offered, the patient population, resource availability, clinician training, and existing attitudes and beliefs about palliative care. Given such heterogeneity, individual institutions will likely need to define the optimal level of integration that would have the greatest acceptance and impact at their local level to improve the integration between these specialties (Hui et al., 2015).

How and when the definition and discussion of goals of care and limitation of invasive and life-prolonging measures take place

Most patients with GBM have impaired decision-making capacity in the last month of life (Hemminger et al., 2017). This cognitive impairment and lowered level of consciousness in the last 10 days of life was present in 95% of the patients in Thier et al. (2016), followed by symptoms such as fever (88%), dysphagia (65%), and seizures (65%). Being able to evaluate clinical signs and symptoms at the end of life is difficult for these patients and it is reported in the literature that these patients do not die with dignity.

Miranda et al. (2017) showed that patients with GBM have conversations about the severity of the disease relatively late, an average of 84 days before death. Most of these participants preferred life-prolonging care, but the instruments applied in the study did not describe which types of devices were used (e.g., dialysis, intubation, and cardiopulmonary resuscitation) or their consequences, and did not include patient goals/priorities. Our study shows that 13 patients (43.3%) had their limitation of invasive measures (i.e., dialysis, intubation, and cardiopulmonary resuscitation) defined only in the last 14 days of life; of these, the limitation occurred in the ICU for four (30.8%) patients. Having discussions about goals of care and, thus, limitation in invasive measures, ought to occur earlier in a patient’s care trajectory (ASCO, 2012). Pottash et al. (2020) reported that, in one neurological ICU, for 88% of the cases, the palliative care team was brought in to help define a patient’s goals of care. A similar result was reported by Tran et al. (2016), who described clarifying goals of care as the main reason for palliative care consultation, followed by providing family support, and assisting with decision-making and communication.

Boele et al. (2023) found that what matters most to patients and caregivers is having a relationship of trust with the team and being well-informed about treatment options. In turn, this allows the patient to be better able to participate in decision-making. Barriers to effective communication for individuals with GBM included rushing to start treatment, brain tumour-specific symptoms (e.g., memory loss and confusion), shock at the diagnosis, and patients/caregivers not knowing whom to ask their queries.

Forte (2018) proposes a framework with four steps to help align evidence-based practice (EBP) and person-centred care, and encourage communication about preferences and goals of care. It is based on a bioethical framework of situations. The first step is to know the body and its biology: the diseases and treatment options. The second step is necessary to know the person and biography: the patient’s values and views of suffering. In the third step, the focus is the healthcare multidisciplinary team and, in the fourth step, focuses on the patient-provider relationship. This framework is an example of the guide that the palliative care group in our hospital usually follows.

Last antineoplastic treatment close to death

It can be a challenge when the antineoplastic treatment is interrupted before the end of a protocol because the patient is too sick and/or the results of the blood tests are not good enough to continue, but the situation was not discussed as an option with the patient. The physician may have made the decision and the patient was only informed of the decision in the outpatient appointment.

Mack et al. (2010) found that patients who had end-of-life discussions with their physicians before the last 30 days of life were less likely to receive chemotherapy in the last 14 days of life (Philip et al., 2018). Patients who received “early palliative care” were less likely to receive chemotherapy in the last 60 days of life (Fadul et al, 2009). Early palliative care included patients meeting a member of a palliative care team shortly after diagnosis, and at least monthly thereafter in the outpatient clinic, until death. Guidelines for appointment with the palliative care team included five topics (i.e., understanding the illness, managing symptoms, decision-making, coping, and planning and referral) (Brom et al., 2016).

A considerable number of patients in our study received antineoplastic treatment in the last month of life and, despite their poor prognosis, more than half of the patients had a definition of limitation of invasive measures only in the last month of life. These situations may be associated with higher rates of suffering both for patients and their families, and for the professionals who were serving them. To us, this suggests that discussions about the goals of care should be carried out as early as possible.

Study limitations

This study has some limitations. Being unicentric, it allowed us to analyze the topic only in the specific context of the institution in which the research took place. The study results therefore, cannot be generalized. Whether other institutions and settings produce similar results needs to be explored in future studies.

Another limitation is the retrospective nature of the data compiled and analyses performed. This can increase the risk

of losing patients due to lack or loss of information. As the data were already defined and recorded, there was no possibility of changing the situation during the course of the study.

CONCLUSION

We found that although the time that elapsed between the diagnosis and death of the patients was approximately two years, only half of the patients were monitored by the palliative care team. The palliative care team involvement in our institution was by referral and maintained the follow-up of the patient according to the direct request made by the patient’s oncologist. In this way, it is necessary to encourage a sensitization of the oncologists to recognize the importance and benefits of the palliative care group follow-up.

We believe that our data will help the discussions with oncologists about the referral and importance of the palliative care team in management with their patients, as well the involvement of all care teams in discussions about goals of care, making them precocious and assertive. We anticipate, for example, having conversations about goals of care with patients early in the course of their illness could give the patients more opportunities to express their values and wishes, and discuss their preferences for care in a shared way.

From our point of view, palliative care works to ensure that patients do not receive inappropriate treatment at the end of life, but also allows patients and families to participate in making decisions about their care, so as to have care given in a way that protects the quality of life and dignity of the patient. As the disease progresses and a greater burden is felt by families and health professionals, the palliative care team can become a source of clarity, support, and guidance in a challenging situation.

Conducting an audit to assess indicators of quality palliative care can be helpful in providing understanding about practice patterns. However, it is important to conduct more studies on the discussion of end-of-life care for patients with GBM, in order to provide more sensitive care to such patients and their families while protecting patients’ dignity.

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