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ORIGINAL ARTICLE

Pattern of care of brain tumor patients in the last months of life: analysis of a cohort of 3045 patients in the last 10 years

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Abstract

Background End-of-life in patients with brain cancer presents special challenges, and palliative care approach is underutilized. Patients with brain cancer, in the last months of life, receive frequent hospital readmissions, highlighting bad end-of-life care quality. Early integration of palliative care improves quality of care in advanced stage of disease and patient's quality of death.

Purpose We retrospectively analyzed a consecutive series of patients with brain cancer discharged after diagnosis to evaluate pattern of treatment and rate of hospital readmission in the last months of life.

Design Data were collected from the Lazio Region Healthcare database.

Setting Adult patients discharged with diagnosis ICD-9 191.* between January 1, 2010, and December 31, 2019 were included.

Results A total of 6672 patients were identified, and 3045 deaths were included. In the last 30 days 33% were readmitted to the hospital and 24.2% to the emergency room. 11.7% were treated with chemotherapy and 6% with radiotherapy. Most indicators of end-of-life care showed wide variability by hospital of discharge.

Conclusions Strategies to improve quality of care at the end of life and to decrease re-hospitalization and futile treatments are becoming increasingly important to improve quality of death and reduce healthcare costs. Variability observed by hospital of discharge indicates the lack of a standard approach to end-of-life care.

Keywords Brain tumors · End of life care · Palliative care · Outcome assessment · Pattern of care

Introduction

Despite the use of aggressive multimodality therapies that includes surgery, radiotherapy, and chemotherapy, the prognosis of patients with malignant brain cancer remains poor. Malignant gliomas have the worst prognosis, with a predicted median survival of 12 to 15 months for glioblastoma multiforme (WHO grade 4) and 2 to 5 years for anaplastic glioma (WHO grade 3) [1, 2].

The terminal phase of disease in patients with brain cancer presents special challenges in their ongoing needs, where the palliative care approach is often underutilized. Several studies reported that patients with brain cancer in the last months of life receive frequent hospital readmissions and emergency room accesses as a result of bad quality of end-of-life care [3].

Quality of end-of-life care in patients with brain cancer has been reported to be low. The available data show that despite the well-known bad prognosis in malignant gliomas patients referrals to hospice care within 7 days of death and acute hospitalization within 30 days of death are very frequent. Hospice utilization is often associated with poor quality end-of-life care [4]. Several indicators of end-of-life quality care have been proposed in the literature including early palliative care provision, the possibility to refuse treatments, the opportunity to avoid therapeutic obstinacy, and express advanced directives which are considered indicators of good quality of care. Instead, aggressive antitumor treatments, emergency room or intensive care access, and frequent re-hospitalization in the last

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weeks of life are considered indicators of bad quality of care [5, 6]. Unfortunately, data on healthcare utilization in cancer patients with short life expectancy showed that there has been a trend toward adopting more aggressive anticancer treatments in the last few years [7].

"Quality of death" in patients with brain cancer may also be suboptimal: a survey conducted in the Netherlands of 81 caregivers of patients with malignant gliomas who had died revealed that 25% of caregivers perceived that the patients had died without dignity (as measured on a 5-point Likert scale ranging from "very undignified" to "very dignified") [8]. Factors associated with positive perceptions of the quality of care in the final 3 months of life, according to a survey of 207 family caregivers of HGG decedents in the Netherlands, Austria, and Scotland, were dying in the preferred location, effective treatment of physical symptoms, and satisfaction with information provided [9, 10]. The need to improve quality of end-of-life care is necessary, but it is not clear which model of care for neuro-oncological patients is the most appropriate. Late referrals to palliative care and hospice stay in patients with brain cancers have been reported in some studies. Despite the need for hospice care in the end-of-life phase of patients with brain cancer, in a study evaluating timing of hospice referral in patients with brain cancer in the US, hospice enrollment was generally late: 22.5% of patients entered hospice care within 7 days of death, 35% entered within 14 days, and 59.4% entered within 30 days before death [4]. Similar data have been reported in another study carried out in 2017 showing that over 20–30% of patients with malignant brain cancer receive late or no hospice care. [11]. Moreover, transition to hospice care within 1 month of death was associated with undignified death in one study in patients with primary malignant brain cancer [4]. Late referral to hospice care and acute hospitalization in the last month of life are common, and these outcomes have been reported to be associated with poor health-related quality of life at end-of-life in other cancers [12].

Early integration of palliative care has been demonstrated to improve quality of care in advanced stages of disease and quality of death in cancer patients.

With the aim to evaluate quality of end-of-life care indicators, we retrospectively analyzed the patterns of treatment and the proportion of hospital readmission in the last months of life in a consecutive series of patients with brain cancer discharged after being diagnosed with brain cancer in the Italian Lazio region.

Methods

We conducted an observational retrospective cohort study based on data collected from hospital discharge records in Lazio, a central Italian region with a population of approximately 6 million inhabitants.

Data sources

The following regional health information systems were considered:

- Hospital information system collecting data from all regional hospitals, including patient demographic data, admission referral source, discharge status, up to six discharge diagnoses (International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)), up to six hospital procedures (ICD-9-CM), and the regional facility code.
- Health care assistance registry (approximately 97% of residents), including information about the date of birth, gender, date of registration in the regional healthcare system, and where applicable, date of death or deregistration.
- Healthcare emergency information system; collecting information on emergency department visits, including information on patient characteristics, triage, main diseases, treatments performed, and diagnoses at discharge.
- Regional drug-dispensing registry, including records for each medical prescription distributed in public and private pharmacies and also for the chemotherapy treatment supplied by the hospital's pharmacy at discharge. Chemotherapies are identified by the national drug register code. Individual patient data and date of CT dispensing are reported for every prescription.
- Outpatient diagnostic tests and specialist outpatient visit database, including tests or specific visit code, date of test, and name of laboratory where the test is carried out.

All regional health information systems include a unique person-based identifier, allowing deterministic record-linkage procedures.

Study population and statistical analysis

In the brain cohort, all patients were aged 18 years or older and discharged from hospital with a brain tumor diagnosis (ICD-9 code equal to 191*) between January 1, 2010, and December 31, 2019 were enrolled. Among those, only patients with an incident cancer (washout period of 5 years) and who died between 2 months to 3 years after discharge were considered.

Patient demographic characteristics and the interval between discharge and death were analyzed. To track the end-of-life care pathway, the following indicators in the last 30/60 days of life were calculated:

- the proportion of patients with a hospital admission with/without intensive care unit use;
- the proportion of patients with an emergency room visit;

- the proportion of patients who received chemotherapy;
- the proportion of patients who received radiotherapy.

Time trends in the use of end-of-life health care were analyzed by comparing indicators over two different periods, 2010–14 vs. 2015–19, through chi-square tests. Box plots were used to estimate and visualize hospital variability in the care model.

All statistical analyses were performed using SAS software, version 9.4.

Results

Of the 6672 patients discharged from hospital with a first diagnosis of brain cancer between January 1, 2010, and December 31, 2019, 3045 (45.6%) met the inclusion criteria and were enrolled in the present study. The mean age was 65 years; 1700 (55.8%) were males and 40.7% died within 6 months from discharge (Table 1).

Overall, in the last 2 months of life, 42.6% received hospital readmission (4.6% intensive care unit) and 37.9% had emergency department accesses (Table 2). In terms of treatment, 24.5% received chemotherapy and 12.1% radiotherapy. In the last 30 days, 33% were readmitted to hospital, and 24.2% were admitted to the emergency room. In total, 11.7% were treated with chemotherapy and 6% with radiotherapy. No differences were observed comparing the two study periods, 2015–19 versus 2010–14, except for a slight reduction in patients treated with chemotherapy at the end-of-life phase.

Table 1 Brain tumor cohort characteristics

	3045	
Sex		
Male	1700	55.8
Female	1345	44.2
Mean age (years)	65	
Median age (years)	67	
Range interquartile (IQR)	57–75	
Interval between discharge and death		
2–6 months	1239	40.7
6–12 months	819	26.9
13–24 months	762	25.0
25–36 months	225	7.4

Most indicators of end-of-life care showed a wide variability determined by hospital discharge (Fig. 1). The maximum proportion of patients with readmission to the hospital or admitted to the emergency department in the last month was 39.2 and 35.2%, respectively. The proportion of patients with an admission to an intensive care unit reached up to 7.7%, while the proportion of patients with a chemotherapy treatment reached up to 16.9%. The proportion of patients with the radiotherapy treatment ranged from 2.0 to 9.9% in the last 30 days of life.

Discussion

Quality of end-of-life care outcomes

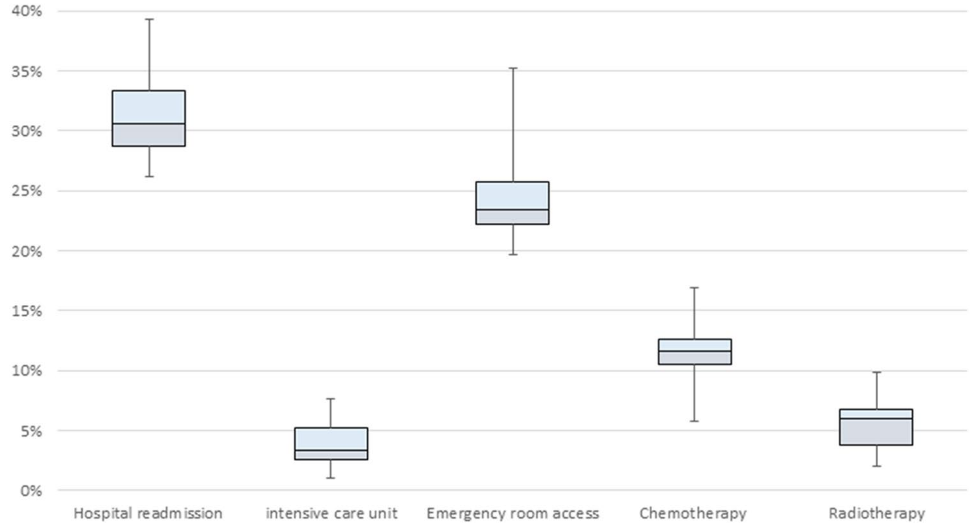
Our data represent the most extensive population study addressing quality of end-of-life indicators in a large group of patients with brain cancer. The results show that in the last 60 and 30 days before death, patients with brain cancer have a high rate of hospital readmissions, including emergency room and intensive care unit admissions. In addition, more than 10% of patients received aggressive treatment in the last 30 days, including chemotherapy (11.3%) and (about 6%) radiotherapy. Interestingly, looking at the last 5-year period with respect to the former period, this figure has not substantially changed during the long period of observation of the study (2010–2019), despite a statistically significant reduction in chemotherapy use in the last 5 years. Our analysis

Table 2 Claims-based indicators of end-of-life care of brain tumor by period

		Overall 2010–2019 3045		Period 1 2010–2014 1314		Period 2 2015–2019 1731		
Indicators	EOL window	*N*	%	*N*	%	*N*	%	*P*-value
Hospital readmission (ICU)	60 days	1298 (138)	42.6 (4.5)	570 (53)	43.4 (4.0)	728 (85)	42.1 (4.9)	0.4649
	30 days	1006 (113)	33.0 (3.7)	451 (45)	34.3 (3.4)	555 (68)	32.1 (3.9)	0.1890
Emergency room access	60 days	1137.0	37.3	490.0	37.3	647	37.4	0.9610
	30 days	732	24.0	311	23.7	421	24.3	0.6762
Chemotherapy	60 days	745	24.5	351	26.7	394	22.8	0.0120
	30 days	346	11.4	173	13.2	173	10.0	0.0063
Radiotherapy	60 days	369	12.1	164	12.5	205	11.8	0.5931
	30 days	182	6.0	87	6.6	95	5.5	0.1915

N = number of patients

Fig. 1 Hospital variability in pattern of care of brain tumor patients in the last 30 days of life



of the pattern of end-of-life care indicators, deriving from several hospitals in the Lazio region, shows a large variability in pattern of care received in the last 30 days before death in different institutions. This data may be related to the different strategies of care adopted in different hospitals and to the timing of palliative care services. For example, patients treated in hospitals delivering early palliative care and home care models of care seem to have better quality of end-of-life care with less hospital readmissions in the last months of life [13–15]. Several studies have proposed health information system data on health care service utilization at the end of life as quality indicators of end-of-life care in cancer patients. Particularly, hospitalization rate, emergency room visits, and intensive care unit admission are considered indicators of poor quality of end-of-life cancer care [5]. Moreover, aggressive cancer care in terminally ill cancer patients, including chemotherapy and other cancer treatments, has been reported to be increasingly utilized in the last few decades. To prolong chemotherapy with unknown benefits in the last stages of life in patients with poor performance when the aim of treatment is palliative care has been recognized as an unnecessary practice, thus influencing patients' quality of life at the end of life [16]. A recent study based on health information systems data relating to end-of-life care in cancer patients in a region of northern Italy confirms that the utilization of anticancer drugs within the last month of life is significantly higher in patients not receiving palliative care, while the rate of hospital readmission in the last months of life is significantly lower in patients receiving palliative care or hospice care. Authors concluded that palliative care services may have a role in preventing aggressive use of anticancer drugs and inappropriate hospital readmissions at the end of life [17]. Most of the data on the quality of end-of-life care has been reported in cancer patients, but little is known about the last treatment phase in neuro-oncological patients. Data in literature addressing end-of-life care in this population of patients is scarce. Most studies report retrospective, single-institution, small-size data [18–20]. In this field, an interesting contribution is provided by the retrospective study on a 5-year period by Harrison [16]. In this report, the authors found significantly less aggressiveness of end-of-life care in patients receiving early palliative care compared to late palliative care. Above all, in the group examined, palliative care was not implemented in an optimal way, since a small number of patients receive palliative care and often occurred too late in the disease trajectory. A recent systematic review on palliative care utilization in glioblastoma patients reported palliative care activation in 39–40% of cases, hospice referrals for 66–76% of patients, and hospitalizations at the end of life for 20–56% of patients, spending over 25% of their overall survival time hospitalized [21]. Among possible indicators of quality end-of-life care early provision of palliative care, timing of referral to hospice care, and place of death have been included in several studies [16, 22, 23]. Unfortunately, regional health information systems available for this study do not allow for the evaluation of palliative care and hospice care provision data. However, the reduction of aggressive anticancer treatments observed in the last 5 years may be influenced by the increased availability of palliative care services and hospice care in the Lazio region.

Our study, performed in a large cohort of patients with brain cancer evaluated over a long period of time (2010–1019), provides important data on the indicators of the quality of end-of-life care of this population of patients with brain cancer. Previous publications, reporting similar data in retrospective single-institution studies and in smaller populations, showed that quality of end-of-life care in patients with brain cancer seems to be very low in different countries with different healthcare systems [24].

According to several studies, early discussions on goals-of-care and integration of palliative care both in cancer and in patients with brain cancer may help to avoid undesired aggressive measures in the final days of life [22, 23, 25]. A recent systematic review of a small number of trials indicates that early palliative care provision may have more beneficial effects on quality of life and symptom intensity among patients with advanced cancer than among those given usual/standard cancer care alone [26]. Multiple clinical trials have demonstrated that earlier and longitudinal involvement of palliative care improves patients' quality of life, mood, and satisfaction with care received. In a randomized controlled trial study, early provision of palliative care improved symptoms and also survival of metastatic lung cancer, most likely due to the reduction of aggressive treatment in the last stage of disease [27].

Neuro-oncological literature in recent years highlights the need to improve the approach toward palliative care in patients with brain cancer and to identify delivery models to better answer the needs of patients and caregivers, particularly in the end-of-life stages of the disease [28, 29]. Patients with brain cancer have a poor prognosis and differ from other oncological and neurological diseases due to the very short life expectancy, the presence of specific symptoms related to neurological deterioration, and the complexity of supportive care needs [30].

Strategies to improve quality end-of-life care and decrease hospital readmission and futile treatments are becoming increasingly important to improve quality of death and to reduce costs of the healthcare system [31]. In this regard, the wide variability of outcomes by hospital discharge suggests that further research is needed to overcome the lack of an existing standard approach. The role of early palliative care in oncological patients has been well documented in the scientific literature. However, further studies are needed to evaluate the specific role of early PC in neuro-oncological patients and its efficacy in EoL quality of care. Also, dedicated tools to better evaluate the needs of palliative care during disease trajectory need to be validated in this population.

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Declarations

Ethics approval Not applicable.

Consent for publication This paper was not published elsewhere, and it is not submitted elsewhere for publication. All authors approved the manuscript and agree with its submission to Supportive Care in Cancer.

Conflict of interest The authors declare no competing interests.

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