Quality of Life of Brain Tumour Patients

Pace A, Villani V, Zucchella C
Maschio M

European Association of NeuroOncology Magazine 2012; 2 (3) 118-122
Introduction

Primary malignant brain tumours (BT) have a low rate of incidence: in developed countries, the annual incidence is 5.8 males and 4.1 females, respectively, per 100,000. Despite aggressive multimodality treatment with surgery, radiotherapy, and chemotherapy, the prognosis of patients with primary brain tumours remains poor. Malignant gliomas have the worst outcome with the median survival ranging from 12–15 months for glioblastoma multiforme (GBM) and from 2–5 years for anaplastic gliomas [1].

Considering the limited survival of BT patients, in the last decades growing interest has been dedicated to the impact of treatment on health-related quality of life (HRQOL) [2–4].

HRQOL has become an important endpoint in cancer studies and has been included in several trials as an outcome measure supplementing other traditional survival end points (overall survival and progression-free survival) [5–7].

The concept of HRQOL involves the patient’s subjective assessment or evaluation of important aspects of their well-being and is influenced by personal experience, beliefs, expectations, and perceptions. HRQOL measures should be patient-reported and are referred to as distinct areas exploring emotional, physical, cognitive, and social functioning as well as spiritual well-being [8, 9].

However, in brain tumour patients, HRQOL has long been a neglected issue. The objective of this review is to examine recent literature focusing on the most relevant HRQOL issues in neuro-oncology.

Quality-of-Life Assessment

Quality of life (QoL) is a complex entity that originates from the interaction between a person’s values and expectations and their actual experience [10]. Diseases and treatments constitute a new dimension that may change several domains of the pre-existing perception of QoL [11]. Several standard multidimensional HRQOL questionnaires have been utilized in BT patients. There is a general consensus that HRQOL evaluations should be patient-reported, given that they concern personal perceptions, but proxy-reported outcomes are still used to evaluate HRQOL as well [10, 11].

At present, no single gold standard tool exists to measure HRQOL. The most common tool in use was developed by the European Organisation for Research and Treatment of Cancer (EORTC) quality-of-life group: the EORTC QLQ-C30. The QLQ-C30 is a 30-item, self-reported questionnaire containing the following domains: physical functioning (5 items), role functioning (2 items), emotional functioning (4 items), cognitive functioning (2 items), social functioning (2 items), global quality of life (2 items), fatigue (3 items), pain (2 items), and nausea and vomiting (2 items) as well as single items for dyspnoea, insomnia, anorexia, constipation, diarrhoea, and financial impact. The EORTC QLQ-BN20, specifically validated for patients with brain cancer, includes 20 items assessing visual disorder, motor dysfunction, various disease symptoms, treatment toxicity, and future uncertainty [12]. Multidimensional measurements are time-consuming and reliable serial measurement of HRQOL in BT patients is difficult. Many factors may affect the quality of the collected data, mainly poor patient compliance, dropout bias, or methodological problems. Patient-related issues may affect particularly HRQOL measurements at progressive stages of disease and at the end of life, given cognitive problems and inability to repeatedly complete complex forms. Simpler and more sensitive instruments (such as cognitive function) are therefore needed to detect HRQOL changes at advanced stages of disease.

However, there are no clear data on the role of different determinants of HRQOL and their changes during the course of disease in BT patients [13].
HRQOL as Outcome Measure and Survival Predictor

HRQOL measures have recently become a secondary outcome indicator in several phase-II and -III clinical trials. Evaluating cancer treatments, the pattern of HRQOL may be used as an easy and cost-effective measure of clinical benefit or treatment toxicity [14, 15].

Although clinical cancer trials are usually centred on traditional endpoints such as overall survival or progression-free survival, in the last years models of quality-of-life-adjusted survival have been proposed to explore the clinical benefit of cancer treatments. Originally developed for evaluating breast cancer treatments [16, 17], Q-TWiST (“quality-adjusted time without symptoms of disease or toxicity of treatment”) analysis incorporates progression, survival, treatment toxicities and quality of life to better estimate the overall benefit for patients and evaluate both the quality and quantity of survival time.

HRQOL measures may not only be helpful in evaluating cancer care outcomes from the patients’ or family carers’ perspectives but have also been recently evaluated as early independent predictors of survival [18].

Only a few studies have addressed this issue in patients with primary brain tumours. Sehlin et al. showed that HRQOL as measured by the FACT-G total score was independently predictive of survival in a patient population with primary and secondary brain tumours [19]. Different results were obtained in other studies showing that HRQOL scores did not predict survival but cognitive functioning was a significant predictor of survival [20]. Also Bosma et al. [21] showed that baseline HRQOL evaluated by means of the Medical Outcomes Study Short Form 36 (SF-36) was not related to duration of survival. Mauer et al. [22], in a large series of newly diagnosed glioblastoma patients, showed that HRQOL and tumour-related symptoms, as measured by means of the EORTC-QLQ-C30 and BCM-20 questionnaires, added relatively little to prognostic factors of clinical survival such as age, performance status, extent of surgery, corticosteroids at entry, cognitive status, and MGMT promoter methylation status.

At present, it is difficult to compare these contradictory findings, given the different measures that were used and different populations of BT patients evaluated. The prognostic role of HRQOL has to be confirmed in larger studies.

Neurocognitive Impairment and HRQOL

It is well recognized that impairment of neurocognitive functioning resulting in behavioural, emotional, and intellectual difficulties occurs in nearly all patients with brain tumours and eventually compromises their independence.

Cognitive impairment associated with primary or metastatic brain tumours occurs in a significant proportion of patients, with 10% of patients developing progressive dementia and 50–90% showing deficits when evaluated with sensitive neuropsychological tests [23]. Cognitive deficits, mostly affecting information-processing speed, frontal-lobe executive functions, memory, attention, and language, can vary from mild dysfunction with good information-processing and good performance to severe impairment [24, 25]; such impairment is related to a combination of various factors, including the tumour itself, tumour-related epilepsy, treatment, and patient-related factors [26].

Cognitive functioning has a major impact on HRQOL, being related to the patient’s ability to perform activities of daily living, manage finances, recognize safe and unsafe behaviours, and comply with medication regimens. It has been suggested that neurocognitive impairment causes a decline in functional independence more often than physical disability; additionally, subtle cognitive deficits can prevent long-term brain tumour survivors from returning to premorbid autonomy, occupation, and social/familiar role [27–30]. Studies indicated that left-hemisphere localization and glioblastoma-multiforme-histological features represent principal predictors of neuropsychological deficits and reduced HRQOL in adults with newly diagnosed primary brain tumours [31].

Giovagnoli et al. [13] studied patients with recurrent high-grade gliomas with the aim of evaluating different facets of HRQOL and concluded that psychosocial aspects were the strongest determinants; Gustafsson et al. [24] reached the same conclusion in patients with low-grade gliomas, showing that HRQOL had a moderate relationship with emotional and cognitive functioning and a somewhat weaker relationship with physical performance. A recent study confirmed these findings, indicating that, in low-grade glioma patients, among factors significantly associated with the self-reported HRQOL, neurocognitive deficits were relatively prevalent [2].

Although information on neuropsychological performance and HRQOL in patients with primary central nervous system malignancies is becoming available, the relationship between the 2 in patients with brain metastases remains poorly studied [32]. In one study conducted in patients with brain metastases after whole-brain radiotherapy, deficits in neurocognitive functioning were evident before declines in patient ratings of HRQOL, with deterioration of performance on a memory test proving to be the strongest predictor of subsequent declines in patient-reported HRQOL [33].

Aware of the close relationship between cognitive functioning and HRQOL, researchers evaluated potential treatments for neuropsychological deficits. The first therapeutic agent used to reduce cognitive morbidity and improve HRQOL in irradiated brain tumour patients was the amphetamine methylphenidate [34, 35]. More recently, Shaw et al. [36] conducted a prospective, open-label study, administering an AChE for 6 month to survivors of partial or whole-brain radiation therapy, showing a significant improvement in cognitive functioning, mood, and HRQOL. A potentially positive impact of a bevacinumab-based therapy on neurocognitive function, performance status, and/or QoL has also started to emerge from reports of clinical studies among GBM patients [37]. At present, however, there are no proven pharmacological treatments for cognitive impairment following brain cancer, nor are there any known effective preventive strategies. Another alternative approach is represented by cognitive rehabilitation. Gehring
et al [38] conducted a randomized, controlled trial to evaluate the effects of a multifaceted cognitive rehabilitation programme (CRP) on cognitive functioning and selected quality-of-life domains in patients with gliomas, showing a salutary effect on short-term cognitive complaints and on longer-term cognitive performance and mental fatigue.

In summary, neurocognitive and HRQOL assessments are important endpoints for patients with primary brain tumours, increasingly incorporated in clinical studies. Even if their evaluation may be regarded as time-consuming and burdensome for both the patient and the clinician [3, 39], relying solely on survival or performance status does not adequately evaluate the often subtle impairments that can only be identified through multidimensional assessments. Future directions for research include longitudinal assessment to better characterize HRQOL and neurocognitive issues, determination of predictors of poor functioning, and potential cognitive and psychopharmacological interventions.

Mood Disorders and QoL

The prevalence and impact of mood disorders is not fully delineated in BT patients. The prevalence of depression in patients with glioma ranges from 0–93 % [40]. In a recent review on depression and glioma, Rooney et al reported that clinically diagnosable depression occurred in roughly 15 % of glioma patients [41].

The majority of studies on depression in adults with glioma are small, cross-sectional, and retrospective. Also, the instruments used to screen for depression appear to inflate depression frequency compared with the clinical interview.

Depression results are associated with functional impairment, cognitive dysfunction, reduced quality of life, and reduced survival [15, 42]. The association of depression with lowered HRQOL has been reported by several authors but, unfortunately, only a few studies have investigated the contemporary assessment of depressive disorder and HRQOL by means of clinically valid tools. Furthermore, longitudinal studies with repeated measurements during the evolution of disease are lacking. Pelletier et al [43] showed that the presence of depression was the most notable single predictor of overall worse HRQOL among BT patients. Litofsky et al, in a large population of 598 glioma patients [40], reported an impressive incidence of depression (93 %) in patients enrolled in the glioma outcomes project. The incidence of mood disorders and the efficacy of investigative methods in cancer patients are controversial. In the literature on cancer and depression, the main issue is the difficulty in distinguishing major from mild depression. Standard screening tools often fail to distinguish between demoralization and major depression. Situational or reactive depression should be considered a normal psychological response to the changes associated with the diagnosis of cancer. This type of depression is essentially psychological in nature, rather than physiological, and is more responsive to supportive psychotherapy than medication [44].

Thus, symptoms of depression should be considered as a part of coping strategies, in a physiological process of adaptation to the disease, at least in those patients whose depressive symptoms do not meet criteria for major depression.

Several authors reported that depression is not only a psychological reaction to cancer but may be related also to biological factors. However, the absence of strong associations with other variables (including tumour location, histology, and extent of resection) implies that depression in glioma is primarily a psychologically mediated response to losses, including the loss of health.

At present, according to a recent comprehensive review on depression and glioma, the impact of tumour biology on the pathogenesis of depressive and the emotional response to glioma diagnosis remain largely unknown [41]. Antidepressant medications and psychotherapy (particularly cognitive behavioural therapy) have been shown to be of comparable effectiveness in the treatment of major depression [45]. Earlier studies among depressive cancer patients have reported that treatment of depression increased their survival [46, 47]. However, Litofsky et al [40] did not observe significant impact on survival among high-grade glioma patients treated for depression.

Current evidence shows that many tumour- and patient-related factors may influence depression in BTs. Larger studies are needed to identify patients whose depression can be treated, as well as to find out what is the appropriate treatment of choice for depression in BT patients.

Epilepsy and HRQOL

Patients with brain-tumour-related epilepsy (BTRE) present a complex therapeutic profile and require a unique and multidisciplinary approach. Epilepsy in BT patients may have a negative impact on both cognitive functions and HRQOL, particularly in low-grade glioma patients. The cognitive deficits could primarily be ascribed to the use of AEDs, whereas the low HRQOL scores were mainly related to poor seizure control [48].

The presence of epilepsy is considered the most important risk factor for long-term disability in BT patients [48, 49]. Good seizure control can significantly improve the patient’s psychological and relational sphere (ie, social, personal, and professional) [50].

The evaluation of side effects (SE) of an AED is crucial in patients with BTRE due to the fact that SEs can affect the patient’s perception of QoL more than seizure frequency [51, 52].

Epilepsy may affect the HRQOL of brain tumour patients, causing possible long-term disability either because of factors related to epilepsy itself or to the drugs utilized for controlling seizures. The choice of AED therapy must take into consideration not only the drug’s efficacy for seizure control, but also possible effects of the drug on important aspects of the patient’s daily life, for example cognitive function, sexuality, efficacy of systemic therapies, and intensity of side effects [53].
End of Life and HRQOL

The relationship between palliative care and HRQOL at advanced disease stages of BT patients has been poorly evaluated, however there is growing concern about the quality of care given at the end of life (EoL) in these patients. Palliative care is now understood as an approach to care concerned with caring for the entire person faced with a range of physical, psychological, and social needs. The WHO definition of palliative care is "an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness" [54].

Existing data in BT patients suggest that too many patients do not receive adequate palliative care at the final stage of disease [54, 55]. However, increasing attention is being given to palliative care and end-of-life (EoL) issues in neuro-oncology. From diagnosis to the EoL, the care needs of BT patients are high and sometimes underestimated. Clinical symptoms (such as motor, visual, and communication impairment) and low quality of life are typical features of BTs already present during early phases of disease [56]. There is a wide consensus about the need to improve our knowledge of end-of-life care and to improve the quality of palliative care for patients dying from BTs. Patients and their caregivers should be assisted in adequate settings by well-trained, multidisciplinary, palliative neuro-oncology teams dedicated to the management of the most frequent symptoms. Recently, some studies have focused on supportive care needs of BT patients at the last stage of disease, reporting that the lack of symptom control often leads to re-hospitalization with increasing costs for the health care system and worsening of the patient’s quality of life [57]. Particularly, the occurrence of seizures at the end of life seems to influence quality of life of patients and their caregivers.

Recent studies reported that administrative data, and particularly hospital re-admission rates at the last stage of disease, may be considered a potential indicator of quality of EoL care [58].

In a recent paper of our group, we observed in a population of BT patients assisted until death with a neuro-oncologic palliative home care programme a high incidence of distressing symptoms influencing the quality of life during the course of disease and during the process of dying. We concluded that in order to allow the patient to experience a peaceful death, control of pain, confusion, agitation, delirium, or seizures by means of specific palliative interventions is needed [57].

The main goals of palliative care and end-of-life care in brain tumour patients are to offer adequate symptom control, relief of suffering, avoiding inappropriate prolongation of dying, and to support the psychological and spiritual needs of patients and families.

However, currently there is a lack of palliative-care provision for patients affected by advanced brain tumours with a negative impact on patient’s quality of life at the end of life. Nevertheless, there is a great need for education in palliative care and end-of-life care for brain tumour patients. Wider availability of palliative programmes and home-care models of assistance may represent an alternative to in-hospital care for the management of patients dying from a brain tumour and may improve the quality of end-of-life care.

Conclusions

The assessment of patient-reported outcomes in clinical trials and in clinical practice is likely to become a standard part of clinical management of BT patients. HRQOL has been reported to have a positive relationship with survival duration but, at present, there is no definitive evidence that baseline HRQOL scores have additional value with respect to clinical factors for predicting survival. However, considering their limited survival, the HRQOL assessment in patients with BTs is particularly important. It is increasingly recognized that the choice of treatment should also involve careful consideration of its effects on the health-related quality of life (HRQOL) during the remaining survival time. As survival is limited, patients optimally should be informed of the impact of all treatment options on their quality of life at the time of diagnosis. Relatively little is known about HRQOL during the disease course of patients with high-grade gliomas. The pattern of HRQOL may serve as an easy and cost-effective tool to recognize early changes in the subjective clinical condition of BT patients, and the relationship with disease progression.

Moreover, regular use of HRQOL measures in neuro-oncology practice may improve quality of care by facilitating doctor-patient communication and patient participation in treatment decisions at every stage of the disease.

Conflict of Interest

None.

References:

Quality of Life of Brain Tumour Patients


Eur ASSOC NEUROCINCOL MAG 2012; 2 (3) 122