Gliomas and quality of life

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Abstract

Introduction: According to the World Health Organization, health is not merely the absence of disease but a state of complete physical, mental, and social well-being. To measure health and the effects of health care implies to assess changes in the frequency and severity of diseases and an estimation of well being. This can be done by measuring the improvement in the patient's quality of life. Quality of life is a broad and complex concept that involves the individual's perception of their life and is affected by the person's physical health, psychological state, personal beliefs, social relationships and their interaction with the environment. Objectives: To review articles on QOL assessment in patients with glioma. Material and method: A critical analysis of the literature was made. Conclusion: There are many QOL instruments available but very few designed for brain tumor patients. Brain tumors have an impact on someone's life that goes beyond physical impairment. Characteristics of the tumor itself and its treatment affect not only cognition but also social and emotional aspects of the patient's life. QOL assessment complements neurological and cognitive examination and provides valuable information for the development of new treatment.

Key words
Quality of life, brain tumor, glioma

Sinopse

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Introdução: A Organização Mundial de Saúde, saúde não é apenas a ausência de doença, mas sim, um estado de completo bem-estar físico, mental e social. Avaliá-la, e os efeitos dos tratamentos, implica avaliar as mudanças na freqüência e gravidade das doenças e uma estimativa do bem-estar. Isto pode ser feito por meio da avaliação da melhoria na qualidade de vida do paciente. Qualidade de vida é um conceito amplo e complexo que envolve a percepção do indivíduo sobre sua vida e é afetada por sua saúde física e psicológica, suas crenças pessoais, seus relacionamentos sociais e sua interação com o ambiente. Objetivo: Fazer uma revisão bibliográfica sobre a avaliação da qualidade de vida de pacientes com glioma. Material e método: Foi feita uma análise crítica da literatura. Conclusão: Existem muitos instrumentos para avaliar qualidade de vida, mas, são poucos os criados para pacientes com tumor cerebral. O impacto de um tumor cerebral na vida de alguém vai além do físico. As características do próprio tumor e seu tratamento afetam a cognição e também aspectos sociais e emocionais da vida do paciente. A avaliação da qualidade de vida completa o exame neurológico e cognitivo, além de oferecer importante informação para o desenvolvimento de novos tratamentos.

Palavras-chave
Qualidade de vida, tumor cerebral, glioma.

Introduction

The burden of being diagnosed with cancer and its impact on the person’s life is well known. Besides this negative impact brain tumour patients have to deal with specific symptoms that may further hinder their quality of life, such as cognitive deficits. Depending on the histological grade of the tumour, they differ in the way they spread, rate of growth, extend of oedema surrounding them and location. Each one of these aspects will have a different effect on the patient’s subjective QOL. The assessment of Health Related Quality of Life (HRQOL) in cancer patients has developed in the last decades, primarily aiming to a better understanding of the impact of a specific tumour or treatment on the functional, psychological and...
social health of the individual, particularly in situations where the treatment aims symptom control or where the probability of cure is low and intervention is directed mainly at palliation and restoration of function rather than cure. The assessment of HRQOL in primary brain tumors though needs further studying.

Assessment of health related quality of life in cancer

The importance of QOL measurements lies on the value of a wide range of issues related not only to the illness per se but also to emotional and social functioning. Furthermore, the use of HRQOL questionnaires provides patient information that is neither assessed by neurological examination nor by cognitive testing.

The World Health Organization presents a system for classifying impairments, disabilities, and handicaps with the aim of improving information on the consequences of disease:

1. Impairments are classified according to abnormalities of body structure and appearance or disturbances of organ or system function resulting from any cause. It is the effect of the tumour and its treatment on the function of the brain, which is assessed by neurological and neurocognitive evaluations;

2. The classification of disabilities reflects the consequences of impairment on the patient's ability to function in activities of daily living (ADL), often assessed by performance status measures, such as the Karnofsky Performance Scale (KPS);

3. Handicaps cover the disadvantages experienced by the individual in social and vocational roles and on life satisfaction as a result of impairments and disabilities (interaction of the individual with the environment). It is often assessed by QOL measures.

According to the Constitution of the World Health Organization (WHO), health is a state of complete physical, mental, and social well-being not merely the absence of disease. The measurement of health and the effects of health care must include an indication of changes in the frequency and severity of diseases and an estimation of well being. This can be assessed by measuring the improvement in the quality of life related to health care. Quality of life is a broad and complex concept that involves the individual's perception of their life and is affected by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment.

Many are the instruments available to assess the QOL but very few designed for brain tumor patients. Some used with oncological patients are:

1. European Organization for Research and Treatment of Cancer (EORTC): it contains 30 items in five functioning domains (physical, role, emotional, social, and neurocognitive), a global QOL domain, three symptom domains (fatigue, pain, nausea and vomiting) and six single items: (dyspnea, diarrhea, constipation, anorexia, insomnia, and financial impact).

2. Functional Assessment of Cancer Therapy-General (FACT-G), which measure physical, social, family, emotional, and functional well-being and the quality of the relationship with the physician.

3. Short-Form Health Survey (SF-36), a self-report questionnaire, composed of 36 items, organized into eight multi-item scales assessing physical functioning, role limitations caused by physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations caused by emotional problems, and general mental health. Raw scores are converted linearly to 0 to 100 scales, with higher scores representing better levels of functioning.

4. Functional Living Index-Cancer (FLIC), a visual analogue scale with five domains: psychological well being, role/social/interpersonal, inner experience of disease, isolation/sharing and nausea. A higher total score indicates a better QOL.

Kemmler et al. (1997) compared the EORTC QLQ-C30 with the Fact-G for cancer patients, two hundred forty-four patients completed both questionnaires during the same session. The results showed that the EORTC QLQ-C30 and the FACT-G measure markedly different aspects of QOL, despite considerable overlap, this implies that neither of the two QOL instruments can be replaced by the other and that a direct comparison of results obtained with the two instruments is not possible.

Although many studies include the Karnofsky Performance Scale (KPS), which measures a patient's ability to perform their own activities of daily living (ADLs), it has limitations, since it focuses on assessment of the physical domain of QOL and is not sensitive to areas like personality changes or neurocognitive impairment. Others find that the use of a multidimensional approach or a global index of well-being that also reflects psychosocial and cognitive aspects proved to be more appropriate than traditional functional instruments (such as the KPS) in assessing the QOL of brain tumor patients and in detecting the extent of the disease. The KPS is also less sensitive than other measures in detecting change in functional status and certain QOL dimensions: depression, cognition, psychosocial status and relationships since it does not take into account mental, emotional and social functioning or the impact of symptoms and medications on the patient's life.

Quality of life assessment in brain tumor

Based on the EORTC QLQ-C30 and the Fact-G questionnaires, QOL measures were developed and validated specifically for the brain tumor population:

1. Brain Cancer Module (BCM 20) developed by Osoba et al. It contains five multi-item scales (future uncertainty, visual disorder, motor dysfunction, communication deficit, and emotional distress) and seven single items asking about headaches, seizures, drowsiness, hair loss, itching, weakness in the legs, and difficulties with bladder control. The BCM 20 raw scores are linearly converted to 0 to 100 scales, with higher scores representing lower levels of functioning.
2. Functional Assessment of Cancer Therapy-Brain (FACT-Br) is a 54-item scale designed to assess various QOL aspects in brain tumor patients. Responses are based on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much). Five major QOL components are assessed: physical, social, emotional, functional well-being, and patient-physician relationship, plus other ADLs (e.g., driving, reading).

Due to the lack of brain-tumor-specific instruments for measuring QOL studies are carried out in order to produce such instruments. Rogers et al. studied the use of a modified self-administered 10-Point Likert self-assessment quality of life scale on 430 patients with brain tumors ranging from meningiomas to high-grade gliomas.

The original scale was initially designed for patients receiving treatment for advanced breast cancer and consisted of an analog scale scored from 1 to 10 separated in the following items: feeling of well-being, mood, level of physical activity, pain, nausea, appetite, ability to do housework or job, social activities, level of anxiety, and "is treatment helping?". This scale was adapted for the use in patients with brain tumors by adding scales for six more items: level of self-care, level of social support from family or friends, quality of sleeping, concentration ability, memory, and energy level. The results showed that five of the nine original functional status questions were significantly related to tumor severity: well-being, physical function, pain, house/job performance, and social activities. Also four of the six questions that were added to be brain-tumor specific were significantly related to tumor severity: self-care, concentration, memory, and energy.

Although the study has limitations the modified instrument itself may be useful for patients with limited tolerance for the completion of long forms, it may be used in a repeated fashion to follow the clinical course of the patient and his or her response to treatment and it is more specific for brain tumor patients than the original scale. From the sample studied the authors found no differences between bilateral, midline, or left versus right-sided lesions. Patients with brainstem tumors had significantly lower self-care and concentration scores, with a trend to poorer energy scores. Lowered quality of life strongly predicts mortality. More specifically, poor scores on well-being, mood, physical function, house/job performance, self-care, concentration, and energy all predicted higher mortality risk. In addition, being male, receiving chemotherapy, having bilateral disease, and being older were all significant risk factors for mortality.

Another study used HQOL instruments and other baseline measures to predict survival, the Linear Analog Self Assessment, FACT-Br, Mini-Mental State Examination (MMSE) and the Symptom Distress Scale assessment of fatigue. Among the patient characteristics, age, performance score, tumor location, and extent of resection were significantly associated with survival. Younger age (P < 0.0001), gross total resection (P = 0.05), anticonvulsant therapy (P = 0.04), higher MMSE score (P = 0.01), and tumor in the frontal lobe (P = 0.03) all tended to predict a better overall survival. In contrast, patients who required corticosteroid treatment (P = 0.03), had an ECOG performance score of 2 (P = 0.0004), or had a tumor in the occipital lobe (P = 0.02) tended to have worse survival. There was no difference in survival between patients who completed at least one QOL assessment and those who did not complete any (P = 0.60). Two QOL measures had a statistically significant association with survival: SDS-fatigue (P = 0.003) and FACT-Br (P = 0.01). Patients who were less fatigued and those with higher overall QOL tended to survive longer.

The use of baseline measures of functional capacity and performance in order to predict survival in adults following the diagnosis of brain tumors was also studied by McCarter et al. The QOL of 93 patients was measured using the Health Utilities Index (HUI) system by a self-assessment questionnaire, KPS and MMSE. Each patient completed a 15-item self-administered health status questionnaire and their usual health status were classified according to both the HUI Mark 2 (HUI2) and HUI Mark 3 (HUI3) systems. Together they measure the following attributes, divided in four to six descriptive levels: sensation (vision, hearing, speech), mobility/ambulation, emotion, cognition, self-care/dexterity, and pain. The constructs for emotion, cognition, and pain differ across the two systems. HUI2 emotion is focused on worry and anxiety, cognition on learning new information, and pain on frequency of pain and analgesic use. HUI3 emotion focuses on happiness and interest in life, cognition on memory and thinking, and pain on severity and frequency of disruption of activities. Compared to the general population a significantly higher proportion of patients reported problems in sensation (vision, hearing, and speech), ambulation, dexterity, and cognition. The attributes most frequently reported to be affected were vision (72% of patients), cognition (51% of patients) and pain. There were no important size differences in mean scores for KPS and MMSE between the patients who underwent total or subtotal resection and those who had a partial resection or biopsy only. But the mean HUI2 overall HRQL utility score was statistically significantly and clinically importantly higher in the group that underwent biopsy only. The results showed that a decrease of 0.1 units in HUI2 self-care single-attribute utility score was associated with an increased hazard of death of 30% for patients with low-grade tumors (25). For patients with high-grade tumors (56), a 10 unit decrease in the KPS, a 5 unit decrease in MMSE, and a 0.1 decrease in HUI3 speech and dexterity single-attribute scores were associated with an increased hazard of death of 20%, 26%, 36%, and 18%, respectively. The median survival duration was 16.4 months, and 69% of the patients died within 5 years after assessment. Of the 56 patients with high-grade gliomas, 94.6% died; while of the 25 patients with low-grade gliomas, 32.0%.

The authors conclude that scores derived from the measurement of HRQL following diagnosis can predict survival in adults with brain tumors.

QOL and radiotherapy

Although studies on the impact of radiotherapy on QOL show that this treatment may be the cause of neuropsychologi-
Cal deficits: the risk of long-term cognitive dysfunction after irradiation is low when administered alone in young adults and it may be related to other factors such as the disease itself and treatment rather than standard focal RT.

Jason et al. studied the QOL in patients being treated with radiotherapy using the Functional Living Index: Cancer (FLIC) in the assessment of cognitive and other quality of life measures in 29 patients with supratentorial malignant astrocytomas before and after high-dose (8000 cGy) multiple daily fractionated radiotherapy. Patients also commented a neuropsychological evaluation and the spouses completed the Family Environment Scale and the Profile of Mood States. Cognitive abilities generally improved over the course of radiotherapy. Occasionally, deterioration of potential clinical importance was observed on functions associated with the tumour site. Quality of life was stable in most cases and improved in five, but deteriorated in three patients.

Taphoorn et al. carried out a randomised controlled trial of radiotherapy alone versus radiotherapy with concomitant and adjuvant temozolomide for patients with glioblastoma. The results showed that survival was higher for patients assigned combination treatment compared with those assigned standard radiotherapy alone without a detrimental effect on QOL. In fact there were moderate improvements in both groups although during first follow-up there was a significant increase in fatigue, nausea and vomiting, appetite loss, and constipation in those allocated radiotherapy and temozolomide.

Jagannathan assessed QOL in 20 patients with a two-year survival rate after gamma knife radiosurgery (GKS) for primary and metastatic brain tumors. All patients had a well-controlled primary tumor site and good tumor control at the site of their GKS treatment. Despite the high incidence of radiation necrosis (64%) QOL was at a high level for nearly all patients indicating that radiosurgery provides a noninvasive and effective way of controlling brain tumors, while preserving quality of life.

Low grade gliomas (LGG)

Low grade gliomas are frequently associated with epilepsy. Klein et al. studied the impact of epilepsy and antiepileptic drug treatment on cognitive function and QOL in 156 patients and compared it with healthy controls. The results showed that glioma patients had significant reductions in information processing speed, psychomotor function, attention functioning, verbal and working memory, executive functioning, and QOL. Other study points out that besides the tumor-related epilepsy, cognitive deficits in LGG patients may be caused by the tumor itself, tumor treatment (surgery, radiotherapy, medical therapy), psychological stress, or a combination of these.

Gustafsson studied the quality of life and coping in 39 patients with low-grade gliomas (LGG) using the EORTC-QOL-C30 and the Ways of Coping Questionnaire (WQ). The results showed that nearly all patients were capable of self-care, but less than half were able to carry out normal activities without restriction.

Problems with fatigue, sleep disturbances and pain were most frequent. The scores indicated that 45% of the patients had low overall quality of life. Most difficulties were reported in the domains, Role, Cognitive and Emotional functioning. Ratings of overall quality of life and fatigue had the strongest relationship. The results also suggest that mental problems have a stronger impact on quality of life than physical ones. There was a significant relationship between coping by escape-avoidance and lower level of emotional functioning. The authors conclude that a multidisciplinary team is needed for assessment and treatment of the different problems in patients with LGG and special attention should be paid to patients who use coping by escape-avoidance, as this is associated with emotional distress.

Popin et al. assessed QOL in 20 adults who had been surgically treated for pilocytic astrocytoma in childhood and compared the results with 20 healthy control subjects of matching age and sex. At the time of surgery the average age of the patients was 8 years and at the time of assessment it was 27 years. None received cranial irradiation. The QOL questionnaire used assessed 12 dimensions: energy, leisure, cognition, socializing, work, sex life, symptoms, depression, well-being, memory, family and adolescence. The results showed that although the patients appeared to lead a normal life a more in-depth evaluation of their life experience demonstrates that they differ significantly from the larger population, especially regarding the cognition, well-being, memory, socializing and adolescence dimensions.

In a pilot study Taphoorn et al. assessed QOL in 14 adult patients without clinical or CT signs of tumour recurrence that were treated for LGG with surgery and radiotherapy at least one year previously. A neurological examination was performed and the KPS determined, attentional, mnestic, verbal, visuo-spatial and executive functions were evaluated using standardized tests. The patients answered questions in a structured interview that focused on social-economic status; physical complaints; problems with DLA, including cognitive functioning; social functioning and perceived social support; evaluation of the overall health status and well-being; treatment experiences and outlook. Affective status was measured using the Affect Balance Scale (ABS) and the Profile of Mood States (POMS). The ABS consists of 10 yes/no questions and measures "happiness", defined as an experience of more positive than negative affect over the past three weeks. The POMS is a mood-adjetive checklist used in studies on subjective well-being consisting of 32 items divided in 5 dimensions: depression, anger, fatigue, tension and vigour. The results showed concentration and memory impairments, sleepiness, increased emotional reactivity and lowered tolerance for stressful situations, high scores on depression, anger, fatigue and tension and low scores on vigour.

High-grade gliomas (HGG)

These are the most serious and aggressive types of malignant brain tumors. Despite intensive treatment with surgery, radiotherapy, and chemotherapy, patients with these brain cancers
invariably experience tumor recurrence, often within a year after completion of first-lineltherapy, with median patient survival times ranging from less than 1 year to 3 years from initial diagnosis.

Osoba et al. assessed the QOL in patients with recently-diagnosed (n = 41) and recurrent (n = 64) malignant glioma at baseline and several weeks later (follow-up). The instruments used were the EORTC QLC-C30, BFM20, KPS, Barthel Activities of Daily Living Index (BADLI) besides a standard neurological examination. Patients with recurrence and those with a KPS of 50–70 had significantly worse physical, role and cognitive functioning and global quality of life with more visual, motor and communication problems as well as more weakness of both legs and trouble controlling the bladder than did those who were recently-diagnosed and those with a KPS of 80–100. Patients capable of independent activities of daily living had higher functioning scores and less fatigue than did those who were not independent. Patients with dysphasia, mental confusion or motor deficit on neurological examination had significantly more symptoms and reported significantly lower levels of physical, role, cognitive, emotional and social functioning and global quality of life than those who did not have these difficulties. In patients with deteriorating neurological status between baseline and follow-up, there was an increase in fatigue and a marked decline in cognitive, physical, role, emotional and social functioning and global quality of life.

Meyers and Hess evaluated cognitive function, QOL, and ability to perform activities of daily living in 56 patients with recurrent glioblastoma or anaplastic astrocytoma who were recruited on phase 1 and phase 2 clinical trials and at intervals coinciding with monthly MRI scans. All patients had previously undergone surgical resection, radiation therapy, and front-line chemotherapy. They were seen for baseline evaluations prior to beginning the specific clinical trial for recurrent/relapsed tumor and were receiving similar medication regimens (including anticonvulsants and steroids) that did not change significantly over the course of the study. Cognitive deterioration occurred 6 weeks before MRI evidence of tumor progression while declines in subjective QOL or ability to perform ADL tended to occur after tumor progression. These findings were supported by other study confirming that attention and memory deficits represent indices of tumor progression marking both QOL and survival of patients with brain tumors.

Giovagnoli used the FLIC to evaluate QOL in 57 patients with HGG with stable disease after combined treatments (surgery, radiotherapy and chemotherapy) in comparison to 24 patients with other chronic disabling disorders of the central or peripheral nervous system. The results indicated that QOL was satisfactory in the glioma group and similar to the QOL in patients with other chronic neurological diseases. Mood, physical performance, and mental speed appeared as major predictors of QOL in patients with stable brain tumour.

Bampoe et al. compared QOL in patients with newly diagnosed glioblastoma multiforme who received conventional external radiation therapy alone (50 Gy in 25 fractions) to patients who received conventional radiation therapy plus a brachytherapy boost (minimum peripheral tumor dose of 60 Gy). QOL was assessed with a previously developed and validated questionnaire derived from the Sickness Impact Profile and complemented with single independent items based on the authors' clinical experience. The questionnaire was presented in a linear-analog self-report format and completed by patients on randomized entry into the study and thereafter at intervals of three months. The results showed no differences between either group in KPS and QOL scores during the first year of follow-up. However, compared to baseline scores, there was a significant deterioration in KPS as well as the following QOL items: self care, speech, concentration, cognitive functioning and physical experience (symptoms).

Cognitive functioning and QOL in the postneurosurgical period were evaluated by Klein et al. in 68 newly diagnosed HGG patients and compared with that of 50 patients with non–small-cell lung cancer and to matched healthy controls. QOL in both patient groups were similar but significantly lower than that of the healthy controls. Glioma patients reported significantly more neurological symptoms and poorer objective and subjective neuropsychological functioning than the lung cancer patients. Cognitive impairment was observed in all glioma patients and 52% of the lung cancer patients. The neurosurgical intervention (biopsy or resection) or the time elapsed since neurosurgery were not related significantly to neuropsychological functioning. Corticosteroid use was associated with better recognition memory, whereas antiepileptic drug use was correlated negatively with working memory capacity.

Hahn et al. also evaluated QOL and cognitive functioning in 68 newly diagnosed HGG patients, and their caregivers. Patients with left hemisphere tumors presented more depressive symptoms, memory problems, and poorer attention, verbal fluency and verbal learning. Patients with glioblastoma multiforme demonstrated poorer psychomotor speed and visual tracking than patients with non–glioblastoma multiforme histologic features. Patients and caregivers perceived QOL similarly, which can be improved with medical therapy or tailored rehabilitation programs. Caregiver assessments can predict patient QOL, which may be useful in patients with declining status.

Conclusion

The need to understand the impact of brain tumor and its treatment on the patient’s life has lead to the development of QOL instruments for this population but they are still few and more studies should be carried out to produce more QOL measures. Brain tumors affect each patient differently but most of them present cognitive deterioration, physical symptoms, and emotional dysfunction that may interfere with their activities of daily living. Due to the complexity of these impairments a thorough investigation should be performed which includes QOL assessment and neuropsychological evaluation besides the neurological examination.

QOL assessment is an important tool that not only provides valuable information for the development of new treatment but can also be used to predict the survival of brain tumor patients.
References


