

## Evaluation of Health-Related Quality of Life in Lithuanian Brain Tumor Patients Using the EORTC Brain Cancer Module

**Adomas Bunevičius<sup>1,2</sup>, Šarūnas Tamašauskas<sup>1</sup>, Arimantas Tamašauskas<sup>1,3</sup>, Vytenis Deltuva<sup>1,3</sup>**

<sup>1</sup>Department of Neurosurgery, Medical Academy, Lithuanian University of Health Sciences,

<sup>2</sup>Behavioral Medicine Institute, Medical Academy, Lithuanian University of Health Sciences,

<sup>3</sup>Neuroscience Institute, Medical Academy, Lithuanian University of Health Sciences, Lithuania

**Key Words:** brain tumor; health-related quality of life; validity; reliability.

**Summary.** *Background and Objective.* Health-related quality of life (HRQoL) is considered an important outcome measure in neuro-oncology. The aim of this study was to evaluate the psychometric properties of the brain cancer-specific Quality of Life Questionnaire (QLQ-BN20) of the European Organization for Research and Treatment of Cancer (EORTC) in Lithuanian brain tumor patients.

**Material and Methods.** One hundred consecutive patients (71% of women; mean age,  $58 \pm 14$  years) admitted for elective brain tumor surgery were evaluated for HRQoL using the QLQ-BN20, QLQ-C30 (a core EORTC questionnaire for cancer patients), and SF-36 scale; for motor dysfunction (clinical examination); for cognitive dysfunction (Mini-Mental State Examination); and for disability (Barthel Index).

**Results.** The QLQ-BN20 subscales had an adequate internal consistency (Cronbach  $\alpha$ , 0.75–0.90). Motor dysfunction on neurological examination was associated with greater motor dysfunction on the QLQ-BN20; greater disability, with greater future uncertainty, motor dysfunction, communication deficits, headaches, seizures, drowsiness, itchy skin, weakness of legs, and poor bladder control on the QLQ-BN20; and cognitive dysfunction, with greater future uncertainty, visual deficits, motor dysfunction, communication deficits, headaches, drowsiness, and weakness of legs symptoms on the QLQ-BN20, suggesting an adequate clinical validity of the QLQ-BN20. A score for motor dysfunction on the QLQ-BN20 correlated with a score for motor dysfunction on the QLQ-C30 and SF-36 scales; a score for headache on the QLQ-BN20, with a score for pain on the QLQ-C30 and SF-36 scales; and a score for drowsiness symptoms on the QLQ-BN20, with a score for fatigue on the QLQ-C30.

**Conclusions.** The Lithuanian version of the EORTC-QLQ-BN20 scale has acceptable psychometric properties and can be reliably used for the assessment of HRQoL in brain tumor patients.

### Introduction

Brain tumors are a rare disease with an incidence rate of 18 per 100 000 person-years for primary brain tumors and with an estimated overall prevalence rate reaching 222 per 100 000 persons (1). The prognosis of brain tumor is often devastating with an estimated 5-year survival rate reaching approximately 20% for all ages and all tumor types (2–4). In addition, brain tumor patients are subjected to a severe neurological impairment and the increased risk for mental distress and psychiatric comorbidities that can consequentially contribute to deteriorated quality of life (5–8).

Traditional outcome measures in clinical trials evaluating the efficacy of brain tumor treatment include overall survival and progression-free survival among others. However, these classic endpoint measures do not provide with information regarding

the burden that brain tumors impose on patients' functional status and health-related quality of life (HRQoL). Patient-centered outcomes are particularly important in patients with incurable diseases, such as certain brain tumors (7). Hence, the routine assessment of HRQoL is becoming increasingly important as a secondary outcome measure in neuro-oncology (9, 10).

The brain cancer-specific Quality of Life Questionnaire (QLQ-BN20) of the European Organization for Research and Treatment of Cancer (EORTC) (11) was specifically designed for the assessment of HRQoL in brain tumor patients and remains the most widely used HRQoL measure in brain tumor patients (7). A recent study in 17 Eastern and Western European countries reported the adequate psychometric properties of the QLQ-BN20 scale, suggesting that this instrument can be reliably applied for the evaluation of HRQoL in international clinical trials (12). However, to the best of our knowledge, the psychometric properties of the Lithuanian version of the QLQ-BN20 remain to be assessed.

Correspondence to A. Bunevičius, Department of Neurosurgery, Medical Academy, Lithuanian University of Health Sciences, Eivenių 2, 50028 Kaunas, Lithuania  
E-mail: a.bunevicius@yahoo.com

The evaluation of the Lithuanian version of the QLQ-BN20 instrument would provide with more evidence regarding the cross-cultural validity of the QLQ-BN20 instrument and would enable participation in international clinical trials when the QLQ-BN20 is used as a secondary endpoint measure.

Hence, in the current study, the validity and reliability of the QLQ-BN20 in Lithuanian brain tumor patients were evaluated.

### Material and Methods

**Patients.** In a period from May 2010 until December 2010, consecutive patients admitted for elective brain tumor surgery at the Clinic of Neurosurgery, Hospital of Lithuanian University of Health Sciences, Kaunas, Lithuania, were invited to participate in this cross-sectional study. Patients were not included in the study if they were younger than 18 years, did not speak Lithuanian fluently, or were unable to comprehend study assignments. A total of 126 patients were invited to participate in the study. However, 24 patients (19%) refused to participate in the study, and 2 patients (2%) did not complete all the study assignments and were excluded from further analyses. Hence, our final study sample consisted of 100 patients (71% of women; mean age,  $58 \pm 14$  years). There were no differences in sociodemographic and clinical characteristics between patients who did not agree to participate in the study and those who were studied (all  $P > 0.05$ ).

The study and its consent procedures were approved by the Ethics Committee for Biomedical Research at the Lithuanian University of Health Sciences, Kaunas, Lithuania. Written informed consent was obtained from each study patient.

**Study Design.** The patients were approached within 3 days of admission to the inpatient unit. During the same visit, the patients were assessed for the following: 1) HRQoL using the QLQ-BN20 (11, 12), the QLQ-C30 (version 3.0) (13), and the 36-Item Short Form Medical Outcome Questionnaire (SF-36) (14); 2) symptoms of depression and anxiety using the Hospital Anxiety and Depression scale (HADS) (15); 3) disability using the Barthel Index (BI) (16); and 4) cognitive functions using the Mini-Mental State Examination (MMSE) (17). Medical records were reviewed for the presence of motor dysfunction on neurological examination and for the brain tumor pathology reports. The Lithuanian version of the QLQ-C30 was obtained from the EORTC, and the Lithuanian translation of the QLQ-BN20 was performed according to the EORTC standards.

**Questionnaires.** The QLQ-C30 was established for the evaluation of functional status and symptoms in different populations of cancer patients and is a core EORTC questionnaire (13). The QLQ-C30

contains 30 items that comprise 9 multi-item and 6 single-item scales designed to assess for global health status (2 items); functional status (5 items); role functioning (2 items); emotional functioning (4 items); cognitive functioning (2 items); social functioning (2 items); fatigue (3 items); nausea and vomiting (2 items); pain (2 items); dyspnea (1 item); insomnia (1 item); appetite loss (1 item); constipation (1 item); diarrhea (1 item); and financial difficulties (1 item). Items and scale scores are linearly transformed to a 0–100 scale with higher scores indicating better HRQoL on global health status and functional status scales, and worse HRQoL on symptom scales.

The QLQ-BN20 was specifically designed as the QLQ-C30 supplement for the evaluation of HRQoL in brain tumor patients (11). The QLQ-BN20 is a 20-item self-rating instrument that aggregates into 4 multi-item scales of future uncertainty (4 items), visual disorder (3 items), motor dysfunction (3 items), communication deficits (3 items); and 7 single-item scales of headaches, seizures, drowsiness, itchy skin, hair loss, weakness of legs, and bladder control. All scale scores and items are linearly transformed to a 0–100 scale with higher scores indicating more severe symptoms. The 11-scale structure of the QLQ-BN20 was previously confirmed using the multitrait scaling analysis in large samples of brain tumor patients (11, 12).

The MMSE, BI, and the motor deficits on neurological examination were chosen as anchors against which the known-group validity of the QLQ-BN20 and QLQ-C30 was tested. The MMSE (17) is widely used in clinical practice for the assessment of cognitive functions (18) with total scores ranging between 0 and 30. Greater scores indicate better cognitive function. In the current study, good cognitive function was considered as an MMSE score of  $> 24$ , and poor cognitive function was considered as an MMSE score of  $\leq 24$ .

The BI (16) is routinely used in clinical practice for the assessment of disability in neurologic patients (19). The BI contains 10 items that evaluate daily functions of dressing, bathing, feeding, grooming, transfers from bed to chair and back, bladder and bowel control, toilet use, mobility, and climbing stairs. Each item is scored as 0, 5, 10, or 15, depending on the person's ability to perform the activity. The global BI score ranges from 0 to 100 points with higher scores indicating lesser disability. In the current study, patients were dichotomized according to the median BI scores in our cohort as optimal functional status (BI score, 100) and suboptimal functional status (BI score,  $< 100$ ).

Finally, the SF-36 (14) and the HADS (15) were chosen for the assessment of construct validity of the QLQ-BN20. The SF-36 is a multi-item self-rating

instruments designed for the assessment of HRQoL across different populations of patients. The SF-36 evaluates physical functioning, physical limitation, bodily pain, general health, vitality, social functioning, emotional limitation, and mental health with higher scores indicating better HRQoL. The Lithuanian version of the SF-36 (20) is widely used for research purposes in Lithuania (21).

The HADS (15) is a 14-item, self-rating scale designed for the assessment of depressive (HADS-D) and anxiety (HADS-A) symptoms in somatic patients and is well-validated in Lithuanian inpatients and outpatient somatic patients (22–24). Possible scores on both subscales range from 0 to 21 with higher scores indicating more severe respective symptoms.

**Statistical Analysis.** First, the internal consistency of the QLQ-BN20 and QLQ-C30 multi-item subscales using the Cronbach  $\alpha$  was evaluated. Next, by using the independent-sample *t* test, we assessed the clinical validity of the QLQ-BN20 by evaluating the ability of the questionnaire to distinguish between known subgroups of patients with respect to motor dysfunction on neurological examination, disability, and cognitive functions. We hypothesized the following: 1) patients with motor dysfunction when compared with patients without motor dysfunction would have a greater symptom severity on the QLQ-BN20 scales of motor dysfunction and weakness of legs; 2) patients with suboptimal functional status (BI score of <100) when compared with patients with optimal functional status (BI score of 100) would have greater future uncertainty and physically oriented symptoms on the QLQ-BN20 scales; and 3) patients with poor cognitive functions (MMSE score of <24) when compared with patients with good cognitive functions (MMSE score of >24) would have greater communication deficits and drowsiness as well as more symptoms related to increased intracranial pressure, such as headaches and visual deficit, on the QLQ-BN20. Finally, the construct validity of the QLQ-BN20 was evaluated by calculating Spearman correlation coefficients ( $\rho$ ) of QLQ-BN20 scores with QLQ-C30 scores, SF-36 scores, and HADS scores. We expected stronger correlations (Spearman  $\rho$  of >0.4) between the scores of subscales with a significant conceptual overlap (i.e., motor dysfunction with physical functioning and headache with bodily pain) and much weaker correlations between the scores with a lower conceptual overlap.

Data were analyzed using the PASW for Windows (IBM Corporation, Chicago, Illinois). Data were expressed as mean (standard deviation) and as median and interquartile range (IQR) for quantitative variables and as a number (percentage) for qualitative variables. A two-tailed *P* value of <0.05 was considered significant.

## Results

**Baseline Characteristics.** The demographic and clinical characteristics of study patients are presented in Table 1. The majority of patients were diagnosed with meningiomas (46%), followed by high-grade gliomas (19%), and pituitary tumors (16%). Nearly one-fifth (18%) of patients had motor dysfunction on neurological examination, 25% had a BI score of <100, and 21% had a MMSE score of <24.

**Descriptive Statistics and Internal Consistency.** The descriptive statistics of the QLQ-BN20 and QLQ-C30 scores are presented in Table 2. Scores on the majority of the QLQ-BN20 and QLQ-C30 subscales and items were skewed toward the direction of better HRQoL, since the majority of patients reported “not at all” or “little” for most symptoms and dysfunctions. On the average, QLQ-BN20 symptoms of headache and drowsiness and items evaluating future uncertainty received the highest scores. With respect to the QLQ-C30 scores, insomnia and fatigue were the highest rated symptoms. The internal consistency was adequate of all QLQ-BN20 multi-item scales with the Cronbach  $\alpha$  ranging from 0.75 to 0.90. All but one QLQ-C30 multi-item scale of cognitive functioning had adequate internal consistencies with the Cronbach  $\alpha$  ranging from 0.73 to 0.96. The Cronbach  $\alpha$  of the QLQ-C30 cognitive functioning scale was 0.64.

**Clinical Validity.** The known-group comparisons are presented in Table 3. As expected, motor dysfunction on neurological examination was associated with significantly greater motor dysfunction on the QLQ-BN20 scale and with a trend for higher scores for weakness of legs on the QLQ-BN20 subscale. The patients with a BI score of <100 when

Table 1. Demographic and Clinical Characteristics of Study Patients (n=100)

| Demographic Characteristic     | Value               |
|--------------------------------|---------------------|
| Age, mean (SD), median (IQR)   | 58 (14), 59 (21)    |
| Gender, n (%)                  |                     |
| Men                            | 29 (29)             |
| Women                          | 71 (71)             |
| Clinical characteristic        |                     |
| Tumor type, n (%)              |                     |
| Meningioma                     | 46 (46)             |
| High-grade glioma              | 19 (19)             |
| Low-grade glioma               | 2 (2)               |
| Pituitary tumor                | 16 (16)             |
| Acoustic neuroma               | 7 (7)               |
| Other                          | 10 (10)             |
| Motor dysfunction, n (%)       | 18 (18)             |
| Barthel index                  |                     |
| Score, mean (SD), median (IQR) | 97.3 (7.0), 100 (0) |
| Score <100, n (%)              | 25 (25)             |
| Mini-Mental State Examination  |                     |
| Score, mean (SD), median (IQR) | 26.4 (4.4), 28 (4)  |
| Score <24, n (%)               | 21 (21)             |

IQR, interquartile range.

*Table 2.* Descriptive Statistics and Internal Consistency of the EORTC QLQ-BN20 and QLQ-C30 Subscales

|                                       | Number of Items | Mean (SD)   | Median (IQR) | Cronbach $\alpha$ |
|---------------------------------------|-----------------|-------------|--------------|-------------------|
| <b>QLQ-BN20 scales/ single items*</b> |                 |             |              |                   |
| Future uncertainty                    | 4               | 22.8 (22.5) | 17 (40)      | 0.75              |
| Visual disorder                       | 3               | 16.0 (24.3) | 0 (33)       | 0.76              |
| Motor dysfunction                     | 3               | 20.4 (27.0) | 11 (33)      | 0.77              |
| Communication deficit                 | 3               | 15.3 (26.7) | 100 (33)     | 0.90              |
| Headaches                             | 1               | 38.3 (38.9) | 33 (67)      | –                 |
| Seizures                              | 1               | 12.7 (25.9) | 0 (0)        | –                 |
| Drowsiness                            | 1               | 23.3 (31.2) | 0 (33)       | –                 |
| Hair loss                             | 1               | 16.3 (31.6) | 0 (33)       | –                 |
| Itchy skin                            | 1               | 8.7 (22.0)  | 0 (0)        | –                 |
| Weakness of legs                      | 1               | 18.0 (28.2) | 0 (33)       | –                 |
| Bladder control                       | 1               | 5.7 (17.1)  | 0 (0)        | –                 |
| <b>QLQ-C30 scales/single items</b>    |                 |             |              |                   |
| Global health status†                 | 2               | 56.3 (24.1) | 58 (33)      | 0.92              |
| <b>Functional scales†</b>             |                 |             |              |                   |
| Physical functioning                  | 5               | 76.7 (25.0) | 80 (40)      | 0.81              |
| Role functioning                      | 2               | 76.7 (25.0) | 80 (40)      | 0.96              |
| Emotional functioning                 | 4               | 70.8 (26.4) | 75 (42)      | 0.90              |
| Cognitive functioning                 | 2               | 74.8 (28.4) | 83 (33)      | 0.64              |
| Social functioning                    | 2               | 78.3 (27.8) | 92 (33)      | 0.73              |
| <b>Symptoms scales/items*</b>         |                 |             |              |                   |
| Fatigue                               | 3               | 32.9 (30.0) | 22 (44)      | 0.89              |
| Nausea and vomiting                   | 2               | 7.8 (18.9)  | 0 (0)        | 0.77              |
| Pain                                  | 2               | 29.3 (32.4) | 17 (50)      | 0.80              |
| Dyspnea                               | 1               | 9.0 (22.1)  | 0 (0)        | –                 |
| Insomnia                              | 1               | 44.0 (40.4) | 33 (92)      | –                 |
| Appetite loss                         | 1               | 16.3 (28.6) | 0 (33)       | –                 |
| Constipation                          | 1               | 16.0 (27.4) | 0 (33)       | –                 |
| Diarrhea                              | 1               | 5.7 (17.8)  | 0 (0)        | –                 |
| Financial difficulties                | 1               | 22.7 (31.7) | 0 (33)       | –                 |

IQR, interquartile range.

\*Higher scores indicate a higher level of symptoms. †Higher scores indicate better quality of life and better functioning.

*Table 3.* Clinical Validity of the EORTC-QLQ-BN20 Scale

| Item                  | Motor Dysfunction |             |       | Barthel Index |             |       | MMSE        |             |       |
|-----------------------|-------------------|-------------|-------|---------------|-------------|-------|-------------|-------------|-------|
|                       | Yes               | No          | P     | <100          | 100         | P     | <24         | >24         | P     |
| Future uncertainty    | 23.1 (23.3)       | 22.7 (22.5) | 0.94  | 39.1 (23.7)   | 17.3 (19.4) | <0.01 | 31.7 (27.2) | 20.4 (20.6) | 0.04  |
| Visual disorder       | 11.7 (20.3)       | 16.9 (25.1) | 0.41  | 25.3 (28.8)   | 12.9 (21.9) | 0.06  | 32.3 (28.5) | 11.7 (21.2) | 0.01  |
| Motor dysfunction     | 44.4 (34.5)       | 15.1 (22.0) | <0.01 | 45.6 (33.1)   | 12.0 (18.3) | <0.01 | 33.9 (32.3) | 16.8 (24.4) | 0.03  |
| Communication deficit | 14.2 (26.4)       | 15.6 (26.9) | 0.84  | 32.9 (31.0)   | 9.5 (22.3)  | <0.01 | 38.6 (33.8) | 9.1 (20.6)  | <0.01 |
| Headaches             | 40.7 (38.9)       | 37.8 (39.1) | 0.77  | 54.7 (38.3)   | 32.9 (37.8) | 0.02  | 52.4 (41.6) | 34.6 (37.5) | <0.01 |
| Seizures              | 11.1 (22.9)       | 13.0 (26.6) | 0.78  | 25.3 (35.1)   | 8.4 (20.6)  | 0.03  | 23.8 (35.2) | 9.7 (22.1)  | 0.09  |
| Drowsiness            | 25.9 (31.4)       | 22.8 (31.4) | 0.70  | 42.7 (34.0)   | 16.9 (27.6) | <0.01 | 38.1 (32.1) | 19.4 (30.0) | 0.01  |
| Hair loss             | 20.4 (34.6)       | 15.4 (31.1) | 0.55  | 17.3 (33.5)   | 16.0 (31.2) | 0.86  | 28.6 (42.5) | 13.1 (27.4) | 0.13  |
| Itchy skin            | 9.3 (25.1)        | 8.5 (21.5)  | 0.90  | 20.0 (33.3)   | 4.9 (15.2)  | 0.04  | 19.0 (30.9) | 5.9 (18.3)  | 0.07  |
| Weakness of legs      | 31.5 (33.3)       | 15.0 (26.3) | 0.06  | 37.3 (29.4)   | 11.6 (24.8) | <0.01 | 34.9 (34.1) | 13.5 (24.8) | 0.01  |
| Bladder control       | 1.9 (7.9)         | 6.5 (18.5)  | 0.10  | 17.3 (27.4)   | 1.8 (9.3)   | 0.01  | 14.3 (24.9) | 3.4 (13.7)  | 0.07  |

MMSE, Mini-Mental State Examination. Bold indicates significant differences.

compared with the patients with a BI scores of  $\geq 100$  reported significantly greater future uncertainty, motor dysfunction, communication deficits, headaches, seizures, drowsiness, itchy skin, weakness of legs, and poor bladder control on the QLQ-BN20. A score of  $\leq 24$  on the MMSE was associated with greater future uncertainty, visual deficits, motor dysfunction, communication deficits, headaches, drowsiness, and weakness of legs on the QLQ-BN20 scale.

*Construct Validity.* A score for future uncertainty on the QLQ-BN20 scale correlated strongly with

the scores for physical functioning and role functioning on the QLQ-C30 ( $\rho=-0.63$ ,  $P<0.001$ ) and with the HADS-A ( $\rho=0.47$ ,  $P<0.001$ ) and HADS-D ( $\rho=0.53$ ,  $P<0.001$ ) scores. A score for motor dysfunction on the QLQ-BN20 correlated well with a score for physical functioning on the SF-36 ( $\rho=-0.60$ ,  $P<0.001$ ) and scores for fatigue ( $\rho=0.59$ ,  $P<0.001$ ), physical functioning and role functioning ( $\rho_{\text{sf}}=-0.58$ ,  $P_{\text{sf}}<0.001$ ) on the QLQ-C30. A score for communication deficit on the QLQ-BN20 correlated with the scores for

cognitive functioning ( $\rho= -0.55$ ,  $P<0.001$ ) and global health status ( $\rho= -0.53$ ) on the QLQ-C30; a score for headache on the QLQ-BN20, with the scores for pain on the QLQ-C30 scale ( $\rho=0.80$ ) and bodily pain on the SF-36 ( $\rho=0.74$ ,  $P<0.001$ ); and a score for drowsiness symptoms on the QLQ-BN20, with the global health status score on the QLQ-C30 ( $\rho= -0.52$ ,  $P<0.001$ ). The scores for visual disorder, seizures, hair loss, itchy skin, and bladder control on the QLQ-BN20 scale correlated weakly with all QLQ-C30 and SF-36 scores (all  $\rho$  coefficients less than 0.4).

## Discussion

The results of the present study suggest that the QLQ-BN20 scale has acceptable psychometric properties in Lithuanian brain tumor patients; hence, it can be reliably applied for the evaluation of HRQoL in clinical practice and research studies. In addition, our findings provide further evidence regarding an adequate transcultural validity of the QLQ-BN20.

The completion rate of the QLQ-BN20 was high, since only 2 patients did not complete the questionnaire, suggesting an adequate Lithuanian translation of the scale with respect to the ability to comprehend the QLQ-BN20 items. The majority of patients rated their HRQoL at the lower end of the questionnaires, indicating a relatively mild level of symptoms on admission for surgery. A trend for lower ratings on the QLQ-BN20 scales was previously reported in a large international sample of glial brain tumor patients (12). The QLQ-BN20 symptoms of headache and drowsiness and items evaluating future uncertainty as well as the QLQ-C30 symptoms of insomnia and fatigue were rated highest. These findings are not surprising since our sample was mixed with respect to a brain tumor type, and the latter symptoms are not brain tumor type specific, but rather suggest deterioration in general well-being. The QLQ-BN20 symptoms of bladder control, itchy skin, and seizures as well as the QLQ-C30 symptoms of dyspnea and diarrhea received the lowest ratings. Again, these findings can be partially explained by a diverse population with respect to a diagnosis of brain tumor because seizures are more likely to occur in glial brain tumor patients, and itchy skin together with diarrhea are the expected side effects of radiation therapy and chemotherapy, respectively, which are applied only to the selective subgroups of brain tumor patients.

Importantly, we found the acceptable internal consistencies of all QLQ-BN20 multi-item scales and of all QLQ-C30 multi-item scales with one exception of the cognitive functioning scale. These findings are in line with previous studies and confirm the reliability of the proposed factor structure of the QLQ-BN20 and QLQ-C30 (11–13, 25). Lower

than expected internal consistency of the QLQ-C30 cognitive functioning scale (Cronbach  $\alpha=0.63$ ) can be partially explained by the fact that the 2 items of the scale target concentration (“Have you had difficulty in concentrating on things, like reading a newspaper or watching television?”) and memory (“Have you had difficulty remembering things?”), which can represent different manifestations of cognitive dysfunction, can be present in the absence of cognitive dysfunction and can represent the intermittent side effects of brain tumor treatment (26). Thus, we suggest retaining the original structure of the QLQ-BN20 and QLQ-C30.

The known-group validity analyses confirmed an adequate clinical validity of the QLQ-BN20 scale. In line with our hypotheses, the patients with motor dysfunction on neurological examination reported the higher levels of motor dysfunction and weakness of legs on the QLQ-BN20, suggesting that the QLQ-BN20 reliably identified patients with impaired motor functions. As expected, the lower BI scores were associated with greater future uncertainty and with a greater severity of physically oriented symptoms on the QLQ-BN20. Furthermore, patients with lower BI scores reported more communication deficits, headaches, seizures, and drowsiness, suggesting that these symptoms can significantly interfere with the activities of daily living of brain tumor patients. In addition, poor cognitive function was associated with more communication deficits, drowsiness, and greater symptoms related to increased intracranial pressure. Poor cognitive function was also related to more motor dysfunction and more future uncertainty. The latter findings can be explained by the fact that cognitive dysfunction usually occurs in the advanced stages of the disease when there are ample neurological symptoms (26, 27).

The structural validity of the QLQ-BN20 was adequate because the QLQ-BN20 scores for motor dysfunction, headache, and drowsiness were associated with the greater levels of respective symptoms assessed using the SF-36 and the QLQ-C30. In addition, a score for future uncertainty on the QLQ-BN20 was associated with decreased physical and role functioning and with higher levels of mental distress, suggesting that physical functioning and mental distress are important determinants of how patients perceive their future. It was previously shown that future uncertainty was associated with a decreased survival of brain tumor patients (28). Hence, interventions targeting physical functioning and mental health might consequentially improve the prognosis of brain tumor patients. Moreover, a score for communication deficits on the QLQ-BN20 was associated with poor cognitive functioning. Indeed, it is well established that the deterioration of cognitive functions leads to communication deficits

(28), and a communication deficit is among clinical diagnostic criteria for dementia (29, 30, 31). A poor correlation of scores for visual disorders, seizures, hair loss, itchy skin, and bladder control on the QLQ-BN20 with the QLQ-C30 and SF-36 scores can be explained by the fact that the abovementioned symptoms are characteristic of neurological disorders or are the common sequelae of brain tumor treatment. The QLQ-C30 and SF-36 scales are generic HRQoL scales designed for use in different patients' populations and different populations of cancer patients, respectively, and therefore tap the broader domains of HRQoL rather than brain tumor-specific symptoms. Hence, in brain tumor patients, we recommended using the QLQ-BN20 for the assessment of HRQoL instead of generic HRQoL scales.

The major strength of the current study was the use of widely available and well-validated scales (BI, MMSE, and SF-36) against which the construct and clinical validities of the QLQ-BN20 scale were established. Moreover, an official Lithuanian translation of the QLQ-C30 was obtained from the EORTC, and the Lithuanian translation and validation of the QLQ-BN20 were performed under the EORTC guidance. However, a moderate sample size is a major limitation of our study. In addition, the QLQ-BN20 was applied at one time point; therefore, the test-retest reliability of the QLQ-BN20 was

not evaluated. In addition, we and others have previously reported that perceived health status, such as HRQoL and psychological distress symptoms, can change in response to brain tumor treatment (7, 11, 14, 32); hence, further studies should explore the feasibility of the QLQ-BN20 in detecting such changes in Lithuanian brain tumor patients.

### Conclusions

The results of the current study indicate the acceptable psychometric properties of the EORTC QLQ-BN20 HRQoL scale in Lithuanian brain tumor patients. These findings allow a participation in international clinical trials involving brain tumor patients when the QLQ-BN20 is used as an endpoint measure. Our findings also contribute to the growing body of evidence regarding the transcultural validity of the QLQ-BN20 scale.

### Acknowledgments

This research was partially funded by a grant (MIP-10315) from the Research Council of Lithuania.

We thank Augustinas Tumėnas, Deividas Stukas, Kristina Lukšyté, and Rūta Remeikaité for their help in data collection.

### Statement of Conflicts of Interest

The authors state no conflict of interest.

### References

- Porter KR, McCarthy BJ, Freels S, Kim Y, Davis FG. Prevalence estimates for primary brain tumors in the United States by age, gender, behavior, and histology. *Neuro Oncol* 2010;12(6):520-7.
- Davis FG, Freels S, Grutsch J, Barlas S, Brem S. Survival rates in patients with primary malignant brain tumors stratified by patient age and tumor histological type: An analysis based on Surveillance, Epidemiology, and End Results (SEER) data, 1973-1991. *J Neurosurg* 1998;88:1-10.
- Greenlee RT, Murray T, Bolden S, Wingo PA. Cancer statistics, 2000. *CA Cancer J Clin* 2000;50:7-33.
- Deltuva V, Bunevicius A, Jurkiene N, Kulakiene I, Tamasauskas A. Perioperative single photon emission computed tomography in predicting survival of malignant glioma patients. *Oncol Lett* 2012;4:739-44.
- Bunevicius A, Deltuva V, Tamasauskas S, Tamasauskas A, Laws ER Jr, Bunevicius R. Low triiodothyronine syndrome predicts poor outcomes in patients undergoing brain tumor surgery: a pilot study. *J Neurosurg*. In press.
- Bunevicius A, Deltuva VP, Deltuviene D, Tamasauskas A, Bunevicius R. Brain lesions manifesting as psychiatric disorders: eight cases. *CNS Spectr* 2008;13(11):950-8.
- Taphoorn MJ, Sizoo EM, Bottomley A. Review on quality of life issues in patients with primary brain tumors. *Oncologist* 2010;15:618-26.
- Olesen J, Gustavsson A, Svensson M, Wittchen HU, Jönsson B; CDBE2010 study group; European Brain Council. The economic cost of brain disorders in Europe. *Eur J Neurol* 2012;19(1):155-62.
- Bottomley A, Flechtner H, Efficace F, Vanvoorden V, Coens C, Therasse P, et al.; European Organisation for Research and Treatment of Cancer (EORTC) Data Center and Qual-
- ity of Life Group. Health related quality of life outcomes in cancer clinical trials. *Eur J Cancer* 2005;41(12):1697-709.
- Klein M. Health-related quality of life aspects in patients with low-grade glioma. *Adv Tech Stand Neurosurg* 2010; 35:213-35.
- Osoba D, Aaronson NK, Muller M, Sneeuw K, Hsu MA, Yung WK, et al. The development and psychometric validation of a brain cancer quality-of-life questionnaire for use in combination with general cancer specific questionnaires. *Qual Life Res* 1996;5:139-50.
- Taphoorn MJ, Claassens L, Aaronson NK, Coens C, Mauer M, Osoba D, et al.; EORTC Quality of Life Group, and Brain Cancer, NCIC and Radiotherapy Groups. An international validation study of the EORTC brain cancer module (EORTC QLQ-BN20) for assessing health-related quality of life and symptoms in brain cancer patients. *Eur J Cancer* 2010;46(6):1033-40.
- Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst* 1993;85(5):365-76.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;30(6):473-83.
- Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67:361-70.
- Mahoney F, Barthel D. Functional evaluation: the Barthel Index. *Md State Med J* 1965;14:61-5.
- Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12(3):189-98.

18. Samėnienė J, Kriščiūnas A, Endzelytė E. The evaluation of the rehabilitation effects on cognitive dysfunction and changes in psychomotor reactions in stroke patients. *Medicina (Kaunas)* 2008;44(11):860-70.
19. Lendraitienė E, Kriščiūnas A. Physical therapy for persons with traumatic brain injury. *Medicina (Kaunas)* 2010;46(10):712-9.
20. Staniūtė M. Evaluation of health related quality of life using the SF-36 questionnaire. *Biol Psych Psychopharmacol* 2007;9(1):22-5.
21. Staniūtė M, Brozaitiene J, Bunevicius R. Effects of social support and stressful life events on health-related quality of life in coronary artery disease patients. *J Cardiovasc Nurs* 2013;28(1):83-9.
22. Bunevicius A, Staniūtė M, Brozaitiene J, Bunevicius R. Diagnostic accuracy of self-rating scales for screening of depression in coronary artery disease patients. *J Psychosom Res* 2012;72(1):22-5.
23. Bunevicius A, Peceliuniene J, Mickuviene N, Valius L, Bunevicius R. Screening for depression and anxiety disorders in primary care patients. *Depress Anxiety* 2007;24(7):455-60.
24. Bunevicius A, Brozaitiene J, Stankus A, Bunevicius R. Specific fatigue-related items in self-rating depression scales do not bias an association between depression and fatigue in patients with coronary artery disease. *Gen Hosp Psychiatry* 2011;33(5):527-9.
25. Leung A, Lien K, Zeng L, Nguyen J, Caissie A, Culleton S, et al. The EORTC QLQ-BN20 for assessment of quality of life in patients receiving treatment or prophylaxis for brain metastases: a literature review. *Expert Rev Pharmacoecon Outcomes Res* 2011;11(6):693-700.
26. Taphoorn MJ, Klein M. Cognitive deficits in adult patients with brain tumours. *Lancet Neurol* 2004;3(3):159-68.
27. Giovagnoli AR. Investigation of cognitive impairments in people with brain tumors. *J Neurooncol* 2012;108(2):277-83.
28. Mauer ME, Taphoorn MJ, Bottomley A, Coens C, Efficace F, Sanson M, et al. Prognostic value of health-related quality-of-life data in predicting survival in patients with anaplastic oligodendroglomas, from a phase III EORTC brain cancer group study. *J Clin Oncol* 2007;25(36):5731-7.
29. Harwood RH. Dementia for hospital physicians. *Clin Med* 2012;12(1):35-9.
30. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Text revision. Washington DC; 2000.
31. McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984;34(7):939-44.
32. Bunevicius A, Deltuva V, Tamasauskas S, Tamasauskas A, Bunevicius R. Screening for psychological distress in neurosurgical brain tumor patients using the Patient Health Questionnaire-2. *Psychooncology* 2012. In press.

Received 11 June 2012, accepted 28 December 2012