

Psychiatric histories and treatment in patients with brain tumors: association with psychological distress symptoms and health related quality of life

Psichikos sutrikimai ir jų gydymas pacientams, sergantiems galvos smegenų navikais: psichologinio distreso ir su liga susijusios gyvenimo kokybės sąsajos

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SUMMARY

Background. Anxiety and depression are common complications in brain tumor patient that often remain inadequately assessed and therefore undertreated. Untreated mental symptoms can impair health related quality of life (HRQoL) and increase risk for worse outcomes after brain tumor surgery.

Objective. In brain tumor patients admitted for surgery, to evaluate histories of psychiatric disorders and psychotropic medication treatment, and their relation to anxiety and depression symptom severity and HRQoL.

Methods. Within 3 days of admission for brain surgery patients were interviewed for past histories of psychiatric disorders, current use of psychotropic medication and were administered self-rating Hospital Anxiety and Depression Scale (or HADS) for evaluation of current depressive and anxiety symptom severity and SF-36 scale for evaluation of HRQoL.

Results. A total of 22 (8.1%) patients had past histories of psychiatric disorders and 12 (4%) patients were currently taking psychotropic medications. Means scores on the HADS-Depression (HADS-D) and HADS-Anxiety (HADS-A) subscales were 4.55±4.09 and 6.23±4.37, respectively. Twenty-three (11%) and 32 (15%) patients had moderate depressive and anxiety symptom severity (scores on respective HADS subscales range from 11 to 15). In a subgroup of patients with significant depressive symptom severity, only 17% of patients were receiving current treatment with psychotropic medication. Patients with past histories of psychiatric disorders scored significantly higher on the HADS-D (11.1±3.6 and 5.9±4.2, respectively, p<0.001) and HADS-A (7.3±4.3 and 4.3±4.0, respectively, p=0.02). Patients currently taking psychotropic medication scored significantly higher on the HADS-D (9.11±4.68 and 4.35±3.96, respectively, p=0.02) and HADS-A (10.33±4.72 and 6.05±4.27, respectively, p=0.03). Past histories of mental disorders and current use of psychotropic medication were associated with worse HRQoL, i.e., lower scores on the SF-36 subscales of energy/fatigue, emotional well-being, social functioning, pain and general health.

SANTRAUKA

Įvadas. Nerimas ir depresija yra smegenų navikų komplikacijos, kurios dažnai nepakankamai įvertinamos ir todėl nėra veiksmingai gydomos. Negydyti psichiatriniai simptomai gali pabloginti su sveikata susijusią gyvenimo kokybę (SSGK, angl. *HRQoL*) ir padidinti riziką smegenų navikų operacijų blogesnėms išėjimams.

Tikslas. Įvertinti pacientų, stacionarizuotų galvos smegenų naviko operacijai, psichikos sutrikimų ir gydymo psichotropiniais vaistais anamnezę, sąsajose su nerimo ir depresijos simptomų sunkumu ir SSGK.

Metodai. Per 3 dienas nuo stacionarizavimo galvos smegenų naviko operacijai pacientai buvo apklausti apie buvusius psichikos sutrikimus bei dabartinį psichotropinių vaistų vartojimą. Jie užpildė Hospitalinę Nerimo ir Depresijos Skalę (angl. *HADS*), kuria vertintas subjektyviai sau priskiriamų depresijos ir nerimo simptomų sunkumas ir SF-36 skalę, kuria vertinta SSGK.

Rezultatai. Dvidešimt du (8,1 proc.) pacientai praityje pažymėjo turėję psichikos sutrikimą ir 12 (4 proc.) pacientų apklaustos metu vartojo psichotropinius vaistus. HADS-Depresijos (HADS D) ir HADS-Nerimo (HADS-A) subskalių suminių balų vidurkiai buvo atitinkamai 4,55±4,09 ir 6,23±4,37. Dvidešimt trys (11proc.) pacientai sau priskyrė vidutiniškai išreikštus depresijos ir 32 (15 proc.) – vidutiniškai išreikštus nerimo simptomus (rezultatai atitinkamose HADS subskalėse – nuo 11 iki 15 balų). Tik 17 proc. pacientų, kurie sau subjektyviai priskyrė sunkios depresijos simptomus, dabartiniu metu buvo gydomi psichotropiniais vaistais. Pacientams su ankstesnių psichikos sutrikimų anamnezėje nustatytas reikšmingai didesnis ir HADS-D (11,1±3,6 ir 5,9±4,2, atitinkamai, p <0,001) ir HADS-A (7,3±4,3 ir 4,3±4,0, atitinkamai, p=0,02) subskalių suminis balas. Taip pat ir pacientų, dabartiniu metu vartojančių psichotropinius vaistus suminis balų skaičius buvo reikšmingai didesnis abiejų subskalių rodikliuose: HADS-D (9,11± 4,8 ir 4,35±3,96, atitinkamai, p=0,02) ir HADS-A (10,33±4,72 ir 6,05±4,27, atitinkamai, p=0,03). Psichikos sutrikimų anamnezė ir dabartinis psichotropinių vaistų vartojimas buvo susiję su blogesne SSGK, t. y. reikšmingai mažesniais SF-36 balais energijos/nuovargio, emocinės gerovės, socialinio funkcionavimo, skausmo ir bendros sveikatos būklės subskalėse.

Conclusions. Histories of mental disorders were common among patients with established brain tumor diagnosis. The rate of psychiatric medication use was low. Past histories of mental disorders and current use of psychotropic medication were associated with greater depressive and anxiety symptom severity and with worse HRQoL. Psychological distress often remained under-treated in brain tumor patients, since only every sixth of patients with significant symptom severity were receiving psychiatric treatment. Studies aiming to improve recognition and management of mental complication in brain tumor patients are strongly encouraged.

Keywords: brain tumor, anxiety, depression, health related quality of life

Išvados. Pacientai, kuriems diagnozuotas galvos smegenų navikas, dažnai anamnezėje turėjo psichikos sutrikimų, bet psichiatrinių vaistų vartojimo dažnis buvo mažas. Buvusių psichikos sutrikimų anamnezė ir dabartinis psichotropinių vaistų vartojimas siejosi su sunkesniais depresijos ir nerimo simptomais ir blogesne SSGK. Galvos smegenų naviką turinčių pacientų psichologinis distresas dažnai liko nepakankamai gydomas, nes tik šeštadalis pacientų su išreikštais simptomais gavo psichiatrinių gydymą. Reikia tolesnių tyrimų, kad pagerinti galvos smegenų navikų psichiatrinių komplikacijų atpažinimą ir gydymą.

Raktažodžiai: galvos smegenų navikas, nerimas, depresija, su sveikata susijusi gyvenimo kokybė

INTRODUCTION

Psychiatric complications are common in patients with brain tumor. Reported prevalence rates of brain tumor patients suffering from elevated depressive and anxiety symptoms varies across studies from 10% [1] to 40% [2, 3] and reaching nearly 90% in some reports [4]. Such different findings may be due to differences in study design, questionnaires used to identify psychiatric symptoms, and patient clinical characteristics, including histological type and location of brain tumor. Autopsy series by Furgal-Borzych et al. [5] have demonstrated pituitary microadenomas in 44.7% of suicidal patients, while in non-suicidal group pituitary microadenomas were present in only 18.3% of autopsies, concluding that pituitary adenomas may belong to suicide risk factors. Others have reported that left hemisphere tumors were associated with greater depressive symptoms and more memory problems than right hemisphere tumors, and patients with glioblastoma multiforme presented with slower psychomotor speed than patients with non-glioblastoma multiforme [6]. On the other hand, other studies have failed to demonstrate impact of tumor location on depression [4, 7]. Some argue that certain depressive symptoms, such as fatigue or apathy, can be attributed to other factors that are independent of depression, e. g. hormonal dysfunction [8]. Indeed, a recent study by Bunevicius et al. [9] found an association between low triiodothyronine (T3) levels and preoperative depression while no similar findings were observed in postoperative period.

Depression and anxiety symptoms are associated with significant decrease in quality of life [1, 6, 7, 10, 11]. A recent study conducted in Department of Neurosurgery of Lithuanian University of Health Sciences (LUHS) [12] showed that greater depressive symptom severity was the strongest and independent predictor of reduced HRQoL across different domains. Furthermore, it has been shown that depression is associated with shorter overall survival of brain tumor patients [4, 13]. This point to the urgency of adequate depression and anxiety treatment in neurosurgical patients, although one above mentioned study didn't find any survival benefits of antidepressant therapy [4].

Only few studies have examined prevalence and clinical significance of anxiety symptoms in neuro-oncology setting [2, 14]. Even though often expected and largely present in pre- and postoperative brain tumor patients [14], anxiety symptoms often remain undertreated [2]. It remains unclear if anxiety symptoms are misdiagnosed because they are attributed as reaction to life-

threatening diagnosis of brain tumor and are often perceived as “natural”; therefore, impact of anxiety symptoms on emotional and physical well-being is understudied.

It has been shown that psychiatric disorders often remain underdiagnosed and patients with psychiatric symptoms do not receive timely effective treatment. In a study of 598 patients with high-grade glioma, Litofsky with colleagues have found that 93% of patients reported depressive symptoms; however, physicians recognized depression in only 15% of patients [4]. The incidence of physician recognized depression increased to 22% at 3-month and 6-month of follow-up visits, while the rate of patient self-reported depressive symptoms remained largely the same. Furthermore, 60% of patients with physician-recognized depressive symptoms received antidepressant therapy against 15% of patients with self-reported depression symptoms, indicating that physician recognition of depression is low and is associated with under-treatment of depressed patients. Comorbidity anxiety and depressive symptoms in patients with brain tumors is recognized, but only 44% of those patients received psychiatric treatment [2]. These findings suggest that, while we understand the necessity of recognizing and treating depression and anxiety in brain tumor patients [15], data shows that depression and anxiety are often underdiagnosed [2, 4], which results in reduced access to antidepressant therapy. These findings also underscore the gap between physicians' attention to anxiety and/or depressive symptoms and actual needs of brain tumor patients. The data about evaluation and treatment of anxiety and depression in brain tumor patients in Lithuania remain largely unclear, although several studies have been published recently [9, 12, 14–16].

The aim of this study was to evaluate prevalence of histories of psychiatric disorders and psychotropic medication treatment, and their relation to anxiety and depressive symptom severity and HRQoL, in brain tumor patients admitted for surgery.

MATERIAL AND METHODS

Patients and study design

This cross-sectional, observational study took place in the Department of Neurosurgery of Hospital of LUHS, Kaunas Clinics, Lithuania in a period from May 2010 until December 2011. All consecutively admitted patients for elective brain tumor surgery were approached and invited to participate in the study. Patients who were unable to comprehend and complete the study assignments due to inability to speak Lithuanian or significant cognitive deterioration were excluded. The study and its consent procedure were approved by the Ethics

Committee for Biomedical Research of the LUHS, Kaunas, Lithuania. All patients gave written informed consent.

Within 3 days of admission patients were interviewed for history of psychiatric disorders and current use of psychotropic medication and were evaluated for current depressive and anxiety symptom severity using self-rating Hospital Anxiety and Depression Scale (HADS) (17) and health related quality of life using the SF-36 scale. The final histological diagnoses of brain tumor were recorded from the final pathology report.

Assessment

The HADS is a 14-item self-rating scale that was established for evaluation of depressive and anxiety symptom severity in somatic patients [17]. The HADS is comprised of two 7-item subscales of Depression (HADS-D) and Anxiety (HADS-A) that are designed for assessment of respective symptom severity. Each subscale consists of seven items scored from 0–3 to which patients respond based on their experience over the past week. Possible total scores on each subscale range from 0 to 21. Mild depressive and anxiety symptom severity corresponds to scores on the respective scale ranging from 8 to 10, moderate – from 11 to 15, and severe – equal to or greater than 16. Lithuanian translation of the HADS [18] is well-validated in somatic patient populations for assessment of depressive/anxiety symptom severity and for screening of depressive and anxiety [19–21].

Health related quality of life (HRQoL) was assessed by the SF-36 scale [22] which consist of 8 domains of physical function, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, energy/fatigue, pain, and general health perception. Total scores in each multi-item SF-36 subscale range from 0 to 100, and higher scores reflect better HRQoL. The SF-36 scale is widely used for HRQoL assessment in Lithuania and showed its usability in studies with Lithuanian patients [23, 24].

Statistical analyses

Data were analyzed using the PASW for Windows (IBM Corporation, Chicago, IL, USA) and are expressed as mean ± standard deviation for quantitative variables, and as number (percent) for qualitative variables. By using the independent-sample t-test we compared scores on depression and anxiety subscales on the HADS and SF-36 in patients with past histories of psychiatric disorders versus patients without past histories of psychiatric disorders, and in patients currently taking psychotropic medications versus patients not currently taking psychotropic medication.

RESULTS

Two-hundred seventy-one patients (mean age 56.8±14.8 years) were included in the study. Socio-demographic characteristics and histological diagnoses of brain tumor are presented in Table 1. A total of 22 (8.1%) patients had histories of psychiatric disorders. The most common diagnosis of psychiatric disorders was depressive disorder (n=18), followed by schizophrenia spectrum disorders (n=3) and anxiety disorder (n=1). Median timing from diagnosis of documented psychiatric disorders was 4 years (range from 6 months to 32 years). Twelve (4%) patients were currently taking different psychotropic medications.

Means scores on the HADS-D and HADS-A were

Table 1. Socio-demographic and clinical characteristics of study patients (n=271)

	N (%) or mean ± SD
Gender, n (%)	
Men	86 (32)
Women	185 (68)
Age (years) mean ± SD	56.8±14.8
Diagnosis of brain tumor, n (%)	
Meningioma	104 (38)
High grade glioma	47 (17)
Pituitary adenoma	33 (12)
Acoustic neuroma	24 (9)
Low-grade glioma	20 (7)
Metastatic tumor	6 (2)
Other brain tumors	37 (14)
Past histories of psychiatric disorders, n (%)	
Depression	18 (6)
Schizophrenia	3 (5)
Anxiety disorders	1 (0.4)
Current use of psychotropic medication, n (%)	
Antidepressants	5 (2)
Benzodiazepines	4 (2)
Mood stabilizers	2 (1)
Antipsychotics	1 (0.4)

4.55±4.09 and 6.23±4.37, respectively. Twenty-four (11%) patients had mild depressive symptom severity, 23 (11%) patients – moderate depressive symptom severity and 2 (1%) patients – severe depressive symptom severity. With regards anxiety symptoms, 40 (19%) patients were classified as having mild, 32 (15%) – as moderate and 8 (4%) – as severe anxiety symptoms (Figure 1). In a subgroup of patients with significant depressive or anxiety symptom severity – only 17% of patients were receiving current treatment with psychotropic medication.

Patients with past history of psychiatric disorders scored significantly higher scores on the HADS-D (11.1±3.6 and

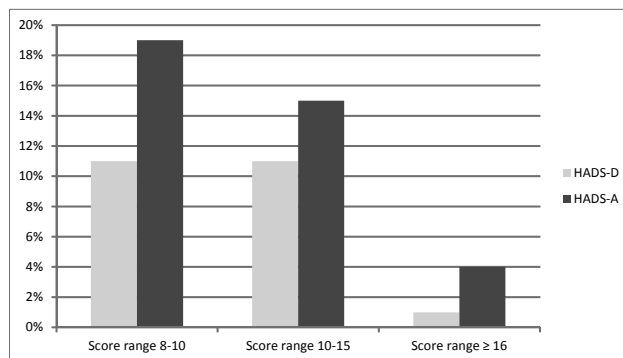


Figure 1. Scores on the Hospital anxiety and Depression scale (HADS) Depression and Anxiety subscales by symptom severity

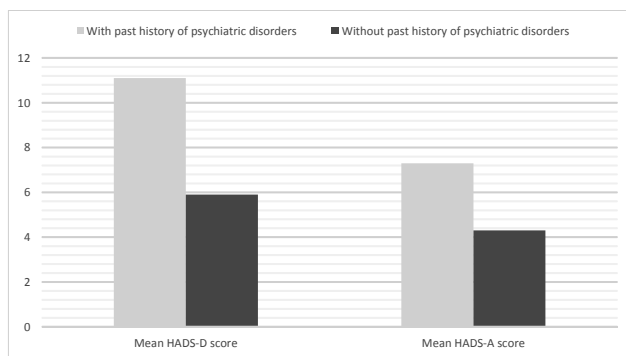


Figure 2. Scores on the Hospital anxiety and Depression scale (HADS) Depression ($p<0.001$) and Anxiety ($p=0.02$) subscales as a function of past histories of psychiatric disorders (Mean \pm SD)

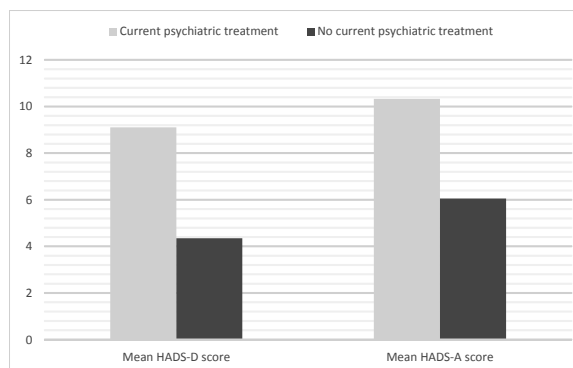


Figure 3. Scores on the Hospital anxiety and Depression scale (HADS) Depression ($p=0.02$) and Anxiety ($p=0.03$) subscales as a function of current psychiatric treatment (Mean \pm SD)

5.9 \pm 4.2, respectively, $p<0.001$) and HADS-A (7.3 \pm 4.3 and 4.3 \pm 4.0, respectively, $p=0.02$) subscales (Figure 2) and significantly lower scores on the SF-36 subscales of Physical functioning (52.5 \pm 27.3 and 69.7 \pm 27.6, respectively, $p=0.02$), Energy/fatigue (35.0 \pm 20.6 and 55.1 \pm 20.9, $p=0.002$), Emotional well-being (43.7 \pm 20.5 and 64.4 \pm 18.8, respectively, $p=0.002$), Social functioning (45.2 \pm 18.7 and 57.4 \pm 20.2, respectively, $p=0.03$), Pain (34.5 \pm 13.3 and 61.3 \pm 31.5, respectively, $p<0.001$) and General Health (33.8 \pm 16.9 and 49.0 \pm 20.1, respectively, $p=0.003$) relative to patients without past histories of psychiatric disorders (Table 2).

Patients currently taking psychotropic medication scored significantly higher on the HADS-D (9.11 \pm 4.68 and 4.35 \pm 3.96, respectively, $p=0.02$) and HADS-A (10.33 \pm 4.72 and 6.05 \pm 4.27, respectively, $p=0.03$) (Figure 3) and significantly lower on the SF-36 subscales of Energy/fatigue (28.3 \pm 16.2 and 54.8 \pm 21.0, respectively, $p=0.001$), Emotional Well-being (40.4 \pm 19.2 and 63.9 \pm 19.0, respectively, $p=0.006$), Social Functioning (36.4 \pm 15.6 and 57.4 \pm 20.1, respectively, $p=0.004$), Pain (44.4 \pm 18.8 and 60.0 \pm 31.6, respectively, $p=0.04$) and General Health (32.2 \pm 16.7 and 48.6 \pm 20.1, respectively, $p=0.02$) relative to patients not currently taking psychotropic medication (Table 2).

The evaluation of psychiatrist consultations frequency in the Department of Neurosurgery during a 12 month period (year of 2011) revealed that consulting psychiatrist had been

invited to consult 92 patients (6.1%) admitted in neurosurgery clinic. The most common reason for psychiatrist consultation was acute mental state deterioration after neurosurgery – 69 (73.9%) patients. Ten patients (10.9%) were diagnosed as having recurrent depressive disorder (F33), 4 patients (4.4%) – schizophrenia spectrum disorder (F20-29) and 1 patient (1.1%) – emotionally unstable personality disorder (F60.3). Nine patients (9.8%) were evaluated as mentally healthy and were not prescribed with psychiatric treatment. All 83 patients with diagnosed mental disorders received treatment with psychiatric medications and continued treatment in the Department of Neurosurgery. Two of these patients were referred for further treatment in Psychiatry clinic (1 patient with personality disorder due to suicidal ideation and 1 patient with organic delirium and severe psychomotor agitation) after repeated psychiatrist evaluation (Table 3).

DISCUSSION

The data of our study shows that histories of mental disorders are common among patients with established brain tumor diagnosis; however, the rate of psychiatric medication use is low. About quarter of observed patients reported depression symptoms of varying severity. Nearly half of study patients had varying severity anxiety symptoms. Only every sixth of patients with significant depressive or anxiety symptom severity were receiving any psychiatric treatment.

Table 2. Health related quality of life as a function of past histories of psychiatric disorders and current psychiatric medication use

	Past histories of psychiatric disorders		p-value	Current use psychiatric medication		p-value
	Yes	No		Yes	No	
SF-36 Physical functioning	52.5 \pm 27.3	69.7 \pm 27.6	0.02	58.9 \pm 33.5	68.8 \pm 27.6	0.41
SF-36 Role limitation due to physical problems	41.3 \pm 40.0	53.7 \pm 42.2	0.21	48.0 \pm 40.5	52.7 \pm 42.2	0.71
SF-36 Role limitation due to emotional problems	52.7 \pm 46.2	64.1 \pm 42.5	0.31	55.7 \pm 41.1	63.7 \pm 42.8	0.52
SF-36 Energy / fatigue	35.0 \pm 20.6	55.1 \pm 20.9	0.002	28.3 \pm 16.2	54.8 \pm 21.0	0.001
SF-36 Emotional well-being	43.7 \pm 20.5	64.4 \pm 18.8	0.002	40.4 \pm 19.2	63.9 \pm 19.0	0.006
SF-36 Social functioning	45.2 \pm 18.7	57.4 \pm 20.2	0.03	36.4 \pm 15.6	57.4 \pm 20.1	0.004
SF-36 Pain	34.5 \pm 13.3	61.3 \pm 31.5	<0.001	44.4 \pm 18.8	60.0 \pm 31.6	0.04
SF-36 General Health	33.8 \pm 16.9	49.0 \pm 20.1	0.003	32.2 \pm 16.7	48.6 \pm 20.1	0.02

Table 3. Psychiatrist consultations in the Department of Neurosurgery of Hospital of LUHS Kaunas Clinics in 2011 (12 month period) medication use

	N (%)
Patients admitted for neurosurgery	1500
Psychiatrist consultation	92 (6.1)
Of those due to acute mental state deterioration after neurosurgery	69 (73.9)
Diagnosed with psychiatric disorder/received psychiatric treatment	83 (90.2)
Specified mental disorders due to brain damage and dysfunction (F06, ICD-10 AM)	67 (71.7)
Mental and behavioural disorder due to use of alcohol (F10, ICD-10 AM)	2 (2.2)
Recurrent depressive disorder (F33, ICD-10 AM)	10 (10.9)
Schizophrenia spectrum disorder (F20-29, ICD-10 AM)	4 (4.4)
Emotionally unstable personality disorder (F60.3, ICD-10-AM)	1 (1.1)
Assessed as mentally healthy/no psychiatric treatment	9 (9.8)
Referred for further treatment in Psychiatry clinic	2 (2.2)
Due to suicidal ideation	1 (1.1)
Due to severe psychomotoric agitation	1 (1.1)

Patients with history of psychiatric disorder and patients currently taking psychotropic medication reported significantly higher depression/anxiety symptom severity and significantly poorer HRQoL related in Energy/fatigue, Emotional well-being, Social functioning, Pain and General Health domain; and patients with past history of psychiatric disorder – also reported lower physical functioning.

Regrettably, presented data and studies mentioned above clearly demonstrate that psychiatric symptoms are not properly evaluated and therefore often remain undertreated [2, 4]. Apparently the gap between clinical attention to anxiety and depression symptoms and perceived need of this attention is even greater in Lithuania. Out of 1500 neurosurgery inpatients, only 6.1% of patients were consulted by a mental health professional and depression was recognized in only 10% of consulted patients, when up to 60% of patients self-reported anxiety or depression symptoms. These findings lead to speculations whether depression and anxiety are properly recognized by mental health specialists. In this study only a minor portion (17%) of patients with high scorers on the HADS scale received any psychotropic medication. This rate is lower comparing to 44% [2] and 60% [4] of depressed patients receiving antidepressant treatment in other studies. Thus, we conclude that situation with treating probably clinically significant depression and anxiety symptoms in Lithuania is even worse. It is unclear whether it is due to inadequate evaluation of these symptoms or some depression symptoms are being perceived as tumor-associated symptoms, e. g. fatigue or apathy; although a controversy on the mentioned symptoms nature exists in the literature [8]. If left untreated, depressive/anxiety symptoms can negatively affect HRQoL and overall prognosis.

Evaluation of naturalistic data of psychiatric consultations

in the Department of Neurosurgery revealed that the physician focused on the treatment of the underlying disease and the patient's mental status remained underestimated. The consulting psychiatrist was only invited to treat acute mental state deterioration after brain surgery. So, in relation to this, we can conclude that successful management of important issue of improving HRQoL may be partially dependent on adequate evaluation and treatment of psychiatric symptoms. It may be advisable to include routine psychiatric evaluation of all brain tumor patients in future guidelines and treatment protocols or at least a consideration to include such evaluation in treatment plan.

We are aware that our data cannot explain a number of clinically important issues regarding treatment and diagnosis of mental disorders in neuro-oncology setting, e.g. organic vs. exogenous nature of mental symptoms and severity of depression and anxiety symptoms, whether they present as full syndromal disorder, their relation to clinical factors (tumor type, location and past treatments) and response to psychotropic medications in terms of HADS score and HRQoL. However, our major goal was to overview current situation with regards to identification and management of mental symptoms in brain tumor patients. This study and those mentioned above [1, 2, 4] suggest that a considerable portion of brain tumor patients report anxiety and depression symptoms, that may be clinically significant and when not properly managed can negatively affect course and outcome of brain tumor [1, 6, 7, 9–12, 13], decrease HRQoL and probably add additional risks, such as suicidality [5]. What is clearly seen from these results is that depression and anxiety symptoms are poorly evaluated by physician, which lowers demand for psychiatric consultation and available treatment options, while from patient's perspective this demand is considerably higher. Existing data still remains incomplete, so further controlled studies and metaanalyses are needed to improve understanding of psychiatric symptoms in brain tumor patients.

CONCLUSIONS

Histories of mental disorders were common among patients with established brain tumor diagnosis. The rate of psychiatric medication use was low. Past histories of mental disorders and current use of psychotropic medication were associated with greater depressive and anxiety symptom severity and with worse HRQoL. Psychological distress often remained under-treated in brain tumor patients, since only every sixth of patients with significant symptom severity were receiving psychiatric treatment. Studies aiming to improve recognition and management of mental complication in brain tumor patients are strongly encouraged.

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*Received 06 September 2014, accepted 29 November 2014
Straipsnis gautas 2014-09-06, priimtas 2014-11-29*