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ORIGINAL REPORT

LONG-TERM EMPLOYMENT STATUS AND THE ASSOCIATION WITH FATIGUE IN PATIENTS WITH GRADE II GLIOMAS

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Objective: **To investigate employment status and return to work in relation to fatigue in patients with World Health Organization (WHO) grade II glioma.**
Design: **Exploratory cross-sectional study.**
Subjects: **Patients with grade II glioma, who underwent surgery between 2005 and 2016.**
Methods: **A postal survey was sent in 2019, which included the Short Form-Health and Labour Questionnaire and the Multi-dimensional Fatigue Index. Outcomes of fatigue in subgroups of (not-) return to work were compared using independent *t*-tests and χ^2 tests. The association between fatigue and return to work was analysed using multivariable logistic regression.**
Results: **In total, 73 patients were included in the study (age at diagnosis 41.0 years (standard deviation (SD) 9.2 years), time post-diagnosis 8.0 years (interquartile range (IQR) 6–11 years). At diagnosis, 61 patients were employed and 32 returned to work during follow-up. The return to work group was significantly younger than the not-return to work group ($p = 0.007$). The proportion of patients who indicated that the consequences of glioma had affected return to work, in terms of demotion or reduced working hours, was 68.7%. The not-return to work group reported significantly more fatigue in all domains than the return to work group ($p < 0.05$). Mental fatigue ($p = 0.023$) and physical fatigue ($p = 0.065$) were independently associated with return to work, adjusted for age, sex and the use of anti-epileptic drugs.**
Conclusion: **Long-term fatigue is associated with return to work in patients with grade II glioma. Patients who were able to work in the long term were less fatigued, younger, more often male, and used less anti-epileptic drugs than the patients who did not return to work.**

Key words: employment; glioma; return to work; fatigue.

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LAY ABSTRACT

Patients with glioma have adult brain cancer. These patients are relatively young and are of working age when they develop this disease. Treatment options for glioma have improved over recent years, and patients will survive approximately 5–15 years. Almost all patients are of working age. Because of the increased survival time, patients find it important to continue to participate in society, especially in work. This study examined working patterns in patients with glioma several years after the start of their disease. Fifty-two percent of patients were working 8 years after the diagnosis of glioma. Many patients with brain tumours felt tired (fatigued), both mentally and physically. Patients who were able to work in the long term were less fatigued, younger, more often male, and used less anti-epileptic drugs than the patients who did not return to work.

Engagement in work is very important from a societal perspective and from an individual perspective, in preventing financial stress, social isolation and loss of self-esteem (1–3).

In the general cancer population, improvements in diagnosis and treatment have increased the prognosis of patients, and an increasing number of patients return to work (RTW) following treatment or continue to work during therapy (4). A focus on RTW is part of the societal reintegration of cancer survivors (5).

Rates of RTW in the overall cancer population range widely, from 30% to 93% (5–7). A meta-analysis reported that cancer survivors overall were 1.37 times more likely to be unemployed than healthy control participants, but patients with a central nervous system cancer were 1.78 times more likely to be unemployed (7).

Patients diagnosed with grade II glioma are usually early in their working age and have a favourable mid-term prognosis, with a survival time between 5 and 15 years (8, 9). RTW has long been an understudied aspect. Recently, Yoshida et al. (10) and Senft et al. (11) studied rates of RTW for patients with grade II and III glioma. They reported a RTW rate of 54.0% one year after surgery and after a median follow-up of 43.8 months (range 11–82 months) 70.7% of patients were able to resume a working life.

Fatigue is a highly prevalent and debilitating symptom in cancer survivors, including patients with glioma

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(12). Cancer-related fatigue is defined as a "persistent, subjective sense of tiredness related to cancer and cancer treatment that interferes with usual functioning". It is described as a multidimensional phenomenon. In all types of cancer, fatigue is common during treatment and follow-up (13, 14).

Fatigue is a negative predictor of RTW in patients who survive cancer (1, 15, 16). Fatigue and treatment-related symptoms are important reasons for not returning to work in diffuse glioma of all grades (11, 17). Since many patients with low-grade glioma have a relatively favourable prognosis, RTW is an important element of survival. The present study therefore investigated employment status and RTW in patients who underwent surgery for a grade II glioma after diagnosis, and the association between fatigue and employment status.

METHODS

Study design

The Assessment of Work in Glioma study is an exploratory cross-sectional study. The study included patients aged 18 years and over who underwent surgery or biopsy between 1 Jan 2003 and 3 Jan 2016, and were still being followed at the Erasmus MC Cancer Institute in Rotterdam for a histologically confirmed grade II glioma in January 2019 (18, 19). The Erasmus MC has a supra-regional function for brain tumour patients in the Netherlands. This cohort was previously involved in a molecular tumour classification study (19). Exclusion criteria were: (*i*) neurological comorbidity or a psychiatric disorder according to the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM IV); and (*ii*) older than 65 years at the start of the study. Patients who required treatment (chemotherapy, radiotherapy or surgery) at time of enrolment were excluded. In January 2019, patients were sent a postal invitation to complete questionnaires, to be returned in a pre-paid envelope. The study (MEC-2019-0052) was approved by the Medical Ethics Committee of Erasmus MC, University Medical Center Rotterdam, the Netherlands. All patients provided written informed consent.

Measurements

Employment status was measured with the Short Form-Health and Labour Questionnaire (SF-HLQ), a generic instrument to collect data on work and productivity loss due to health problems (20). The SF-HLQ aims to measure absence from work and reduced efficiency of paid and unpaid work. In addition, a number of general questions were added to collect data on respondents' demographic characteristics and co-morbidity. Fatigue was measured with the Multi-dimensional Fatigue Index (MFI), which is a self-report questionnaire (21). The MFI is a 20-item scale designed to evaluate 5 dimensions of fatigue: general fatigue, physical fatigue, reduced motivation, reduced activity, and mental fatigue (21). Each subscale contains 4 items, with scores on a 1–5-point Likert scale. The subdomain score ranges from 4 to 20, with higher scores indicating more fatigue.

Statistical analysis

Data were analysed using SPSS version 23. Descriptive statistics and frequency distributions were generated for the sociodemographic and disease-related characteristics of the sample. Subgroups of employed and unemployed participants were compared with respect to fatigue, and to sociodemographic, histopathological, disease-related, and treatment-related characteristics and comorbidity using independent *t*-tests and χ^2 tests. A *p*-value of 0.05 was considered statistically significant. Given the exploratory nature of this study we did not correct for multiple testing.

To study associations of the level of fatigue and employment status (unemployed vs employed) univariable and multivariable logistic regression analyses were performed. Because of multiplicity, only the domains of physical and mental fatigue were considered in relation to employment status. Potential confounding variables, such as age and sex, were also taken into account. The variables that were associated with employment status in univariable analyses at a significance level of $p<0.10$ were entered in the multivariable model and retained in the model if $p<0.10$.

RESULTS

Total group (n=73)

Of the 129 questionnaires sent, 74 (57%) were returned, of which one was not completed. Thus, the study sample included a total of 73 patients of working age with a mean age of 41.0 years (SD 9.2 years) at diagnosis. Of the 73 patients, 61 (83.6%) were employed at the time of the glioma diagnosis. Almost half of the patients were in contact with a rehabilitation specialist at least one time. Patients who were unemployed at time of diagnosis ($n=12$) included significantly more women ($p=0.01$) than those who were employed ($n=61$; Table I). No other sociodemographic or clinical differences between the 2 groups were present.

Patients employed at diagnosis (n = 61)

The mean age at diagnosis for the working group was 40.9 years (SD 9.19 years) with a median time post-diagnosis of 8.0 years (interquartile range (IQR) 6–11 years).

Oligodendroglioma (52.5%) was the most frequent type of brain tumour, followed by astrocytoma II isocitrate dehydrogenase (IDH) mutant (36.1%). Gliomas were located mainly in the frontal cerebral lobe (52.5%). Almost all patients (91.8%) had undergone a surgical resection, and 27.9% had a re-resection with a mean time of 5 years after the initial resection. The proportion of patients treated with radiotherapy was 73.8%. The mean time between surgery and radiotherapy was almost 3 years. The proportion of patients

Table I. Baseline and clinical characteristics ($n=73$)

	Total group ($n=73$)	Employed at diagnosis ($n=61$)	Unemployed at diagnosis ($n=12$)
Socio-demographic			
Sex, male, *n* (%)	37 (50.7)	35 (57.4)	2 (16.7)
Age at diagnosis, years, mean (SD) [IQR]	41.0 (9.2) [21–58]	40.9 (9.2) [21–58]	41.6 (9.7) [29–54]
Mean age, years, mean (SD) [IQR]	49.2 (9.4) [31–65]	48.7 (9.1) [31–65]	51.8 (10.7) [34–64]
Education, years, mean (SD)	14.20 (3.8)	14.4 (3.2)	13.3 (6.1)
Education level			
Elementary school	4 (5.5)	2 (3.3)	2 (16.7)
High school	41 (56.2)	34 (55.7)	7 (58.3)
College/university	28 (38.4)	25 (41)	3 (25)
Living with partner, yes, *n* (%)	55 (75.4)	49 (80.3)	6 (50)
Histopathology, *n* (%)			
Diffuse astrocytoma II IDH wild-type	2 (2.7)	2 (3.3)	–
Diffuse astrocytoma II IDH mutant	27 (37.0)	22 (36.1)	5 (41.7)
Diffuse astrocytoma II NOS	7 (9.6)	5 (8.2)	2 (16.7)
Oligodendroglioma II IDH mutant/1p19q co-deletion	37 (50.7)	32 (52.5)	5 (41.7)
Disease characteristics			
Time post-diagnosis, years, mean (SD) [IQR]	8.2 (3.3) [3–19]	7.84 (3.0) [3 –14]	10.16 (3.9) [5–19]
Laterality, left, *n* (%)	38 (52.1)	31 (50.8)	7 (58.3)
Location, *n* (%)			
Frontal, *n* (%)	36 (49.3)	32 (52.5)	4 (33.3)
Parietal, *n* (%)	5 (6.8)	5 (8.2)	–
Temporal, *n* (%)	10 (13.7)	6 (9.8)	4 (33.3)
Occipital, *n* (%)	1 (1.4)	1 (1.6)	–
Diffuse, *n* (%)	21 (28.8)	17 (27.9)	4 (33.3)
Treatment characteristics			
Biopsy only, *n* (%)	8 (11.0)	5 (8.2)	3 (25.0)
Resection, *n* (%)	65 (89.0)	56 (91.8)	9 (75.0)
Re-resection, *n* (%)	19 (26.0)	17 (27.9)	2 (16.7)
Chemotherapy, *n* (%)	42 (57.5)	35 (57.4)	7 (58.3)
Time between surgery and chemotherapy, mean (SD), months	40.7 (35.3)	39.6 (33.3)	46.0 (46.5)
Radiotherapy, *n* (%)	54 (74.0)	45 (73.8)	9 (75.0)
Time between surgery and radiotherapy, mean (SD), months	33.3 (33.6)	34.8 (32.0)	25.7 (42.0)
Time between surgery and re-resection, mean (SD), months	62.1 (23.7)	60 (24.3)	79.5 (2.1)
Combination treatment (SR, RT, CT), *n* (%)	37 (50.7)	32 (52.5)	5 (41.7)
Contact rehabilitation specialist, *n* (%)	36 (49.3)	28 (45.9)	8 (66.7)
Co-morbidity			
Epilepsy, *n* (%)	47 (64.4)	38 (62.3)	9 (75.0)
AED treatment	42 (57.5)	34 (55.7)	8 (66.7)
Multi AED (≥2)	14 (19.2)	13 (21.3)	1 (8.3)

IDH: isocitrate dehydrogenase; NOS: not otherwise specified; SR: surgery treatment; RT: radiotherapy treatment; CT: chemotherapy treatment; AED: anti-epileptic drugs; SD: standard deviation; IQR: interquartile range.

who underwent chemotherapy, after a mean interval of slightly more than 3 years after surgery, was 57.4%. Half of all patients (52.5%) received all treatments (surgery, radiotherapy and chemotherapy). The majority (62.3%) of patients experienced epilepsy, and 55.7% of patients used anti-epileptic drugs. Patient and clinical characteristics are shown in Table I.

Return to work

RTW was studied in the subgroup of patients who were employed at the time of initial histological diagnosis ($n=61$) (Table II). At the time of investigation, 32 of these patients had returned to work and 29 had not. The RTW group was more frequently male than the not-RTW group and was significantly younger at the time of diagnosis ($p<0.007$). The level of education was not significantly different, but there was a trend ($p=0.125$) towards a higher level of education in the RTW group. With regard to the disease and treatment characteristics, there were no significant differences between the RTW and not-RTW patients. In the not-RTW group, the use of multiple (2 or more) anti-epileptic drugs was significantly more ($p=0.027$). The characteristics of both groups are shown in Table II.

Twenty-two patients (68.7%) indicated that their work changed after the diagnosis due to their brain tumour; 7 (31.8%) indicated a change in employment positions, 6 (27.3%) changed from employer, 4 (18.2%) reduced working hours, 4 (18.2%) were partially unable to work as a result of the brain tumour, and 1 (4.5%) patient reported a new diagnosis. In addition, 10 out of 32 (31.3%) patients reported that they experienced difficulties during their job due to their illness. Most frequent were self-reported cognitive difficulties, such as concentration problems (25%) and slower task performance (22%).

Table II. Analyses of patient characteristics between return to work (RTW) and not-RTW group at time of questionnaire

	RTW ($n=32$)	Not-RTW ($n=29$)	p-value
Socio-demographics			
Sex, male, *n* (%)	22 (68.8)	13 (44.8)	0.074
Age at diagnosis, years, mean (SD) [IQR]	37.9 (8.2) [21–51]	44.2 (9.2) [22–58]	0.007
Mean age, years, mean (SD) [IQR]	45.7 (7.8) [32–58]	52.0 (9.4) [31–65]	0.006
Education, years, mean (SD)	15.0 (3.3)	13.7 (2.9)	0.134
Education level			0.125
Elementary school, *n* (%)	1 (3.1)	1 (3.4)	
High school, *n* (%)	14 (43.8)	20 (69.0)	
College/university, *n* (%)	17 (53.1)	8 (27.6)	
Living with partner, yes, *n* (%)	28 (87.5)	21 (72.4)	0.200
Histopathology, *n* (%)			
Diffuse astrocytoma II IDH wild-type[a]	1 (3.1)	1 (3.4)	–
Diffuse astrocytoma II IDH mutant[b]	17 (53.1)	5 (17.2)	–
Diffuse astrocytoma II NOS[c]	1 (3.1)	4 (13.8)	–
Oligodendroglioma II IDH mutant/1p19Q co-deletion	13 (40.6)	19 (65.6)	–
Oligodendroglioma II vs astrocytoma II[a,b,c]			0.730
Disease characteristics			
Time post-diagnosis, years, mean (SD) [IQR]	7.81 (3.08) [3–14]	7.86 (3.02) [3–14]	0.950
Laterality, left, *n* (%)	18 (56.3)	13 (44.8)	0.446
Location of tumour, *n* (%)			0.753
Frontal	17 (53.1)	15 (51.7)	
Parietal	2 (6.3)	3 (10.3)	
Temporal	4 (12.5)	2 (6.9)	
Occipital	0	1 (3.4)	
Diffuse	9 (28.1)	8 (27.6)	
Treatment characteristics			
Biopsy only, *n* (%)	1 (3.1)	4 (13.8)	
Surgery resection, *n* (%)	31 (96.9)	25 (86.2)	0.182
Re-resection, *n* (%)	10 (31.3)	7 (24.1)	0.580
Chemotherapy (SR + CT), *n* (%)	19 (59.4)	16 (55.2)	0.799
Time between surgery and chemotherapy, mean (SD), months	43.4 (36.8)	34.7 (28.6)	0.460
Radiotherapy (SR + RT), *n* (%)	22 (68.8)	23 (79.3)	0.395
Time between surgery and radiotherapy, mean (SD), months	39.0 (34.9)	30.7 (29.1)	0.390
Time between surgery and re-resection, mean (SD), months	56.1 (29.2)	65.6 (15.2)	0.450
Combination treatment (SR + RT + CT), *n* (%)	17 (53.1)	15 (51.7)	1.000
Contact rehabilitation specialist, *n* (%)	11 (34.4)	17(58.6)	0.153
Co-morbidity, *n* (%)			
Epilepsy	18 (56.3)	20 (69.0)	0.428
AED treatment	14 (43.8)	20 (69.0)	0.071
Multi AED (≥2)	3 (9.4)	10 (34.5)	0.027

[a,b,c]This variable means the tumor types a,b,c versus oligodendroglioma. IDH: isocitrate dehydrogenase; NOS: not otherwise specified; SR: surgery treatment; RT: radiotherapy treatment; CT: chemotherapy treatment; AED: anti-epileptic drugs; SD: standard deviation; IQR: interquartile range.

Fatigue and work status

From the 61 patients who were employed at diagnosis, the MFI was completed by 58 patients, 31 RTW and 27 not-RTW. The not-RTW patients reported significantly more fatigue on all fatigue domains than the employed patients. The results are shown in Table III.

Table III. Fatigue and employment

	Total $n=58$ Mean (SD)	RTW $n=31$ Mean (SD)	Not-RTW $n=27$ Mean (SD)	p-value
Fatigue (MFI)				
General Fatigue	12.07 (4.21)	10.94 (4.70)	13.37 (3.19)	0.023
Physical Fatigue	10.52 (4.59)	8.45 (4.55)	12.89 (3.36)	0.000
Reduced Activity	10.52 (4.28)	8.58 (4.12)	12.74 (3.31)	0.000
Reduced Motivation	9.16 (3.75)	8.03 (3.51)	10.44 (3.66)	0.013
Mental Fatigue	11.55 (4.49)	9.71 (4.41)	13.67 (4.41)	0.000

RTW: return to work; MFI: Multi-dimensional Fatigue Index; SD: standard deviation.

Association between fatigue and RTW

A multivariable logistic regression analysis was performed to study the association between mental and physical fatigue and RTW adjusted for all factors that showed an association in the univariable analyses. Age ($p=0.027$), sex ($p=0.008$), physical fatigue ($p=0.065$), mental fatigue ($p=0.023$) and the use of multiple anti-epileptic drugs (AED) ($p=0.009$) were independently associated with the ability to RTW (Table IV).

Table IV. Results of the logistic regression analyses for the prediction of return to work

	Multivariate odds ratio	p-value
Risk factors for unemployment		
Age at diagnosis, years	1.134	0.027
Sex, male	0.062	0.008
Physical fatigue	1.215	0.065
Mental fatigue	1.325	0.023
Multiple AED (≥2), no	0.024	0.009

AED: anti-epileptic drugs.

DISCUSSION

This exploratory cross-sectional study showed that 52% of patients with grade II glioma who were employed at the time of diagnosis returned to work within 8 years post-diagnosis. Of the RTW group, 69% reported that the brain tumour had affected their work in terms of demotion or reduced working hours, and 31.8% reported cognitive problems during their work due to their illness. The multivariate logistic regression model shows that 5 factors, including younger age, male sex, little physical fatigue, little mental fatigue, and no use of multiple AED, were significantly associated with the ability to RTW.

In the current study 88% of the included patients were diagnosed with IDH-mutated glioma. Recent studies indicated that IDH-mutated gliomas were associated with relatively good performance status in the long term (22, 23). Surprisingly, no statistical difference was found in the RTW and not-RTW in relation to the IDH mutation status or treatment status.

With the increased survival rate of the, usually young, adults diagnosed with low-grade glioma, employment status is a highly relevant topic. Earlier studies reported RTW rates between 54% and 70.7% in a variety of patients with glioma with a mean follow-up time of 1–4 years after diagnosis (10, 24, 25). A possible explanation as to why the RTW rate in the current study is at the low end of this range is the longer time post-diagnosis, with patients often developing progressive cognitive deficits over time, and the fact that patients were at risk of tumour progression for longer and needed re-treatment (re-resection, chemotherapy of radiotherapy) or neuro-deterioration (26).

Cancer and its treatment have been associated with cognitive problems and RTW (27, 28) due to a reduced efficiency and slower speed at work (29). A substantial proportion of patients with glioma have objective or subjective cognitive impairments (30). Patients with glioma may have neurocognitive problems before surgery and these may subsequently increase (31). The current study assessed only subjective cognitive symptoms. As expected, the patients in the current study reported subjective cognitive symptoms, such as concentration problems (25%), and slower task performance (22%). It would be interesting to gain deeper insight into the difference between objective and subjective cognitive symptoms and deficits in relation to RTW.

AED may also contribute to cognitive impairment (32). In the current study the multivariable logistic regression analysis shows that patients who do use multiple AED have a higher risk of not returning to work, which could be due to persistent seizures, but also to side-effects of AEDs.

Fatigue is a problem of high prevalence and impact in patients with brain tumours. Quality of life studies in patients with brain tumours show that having symptoms in the fatigue cluster was associated with poorer functioning, and that fatigue was an independent factor for RTW (33, 34). More awareness of the high prevalence of fatigue, the underlying mechanisms and the correlation with RTW issues may help to develop treatments with the intention to prevent fatigue, and subsequently unemployment. Unfortunately, no interventions that target fatigue are known to be effective to date (35, 36).

This study has several limitations. The data are retrospective, the response rate is slightly more than 50% and may be influenced by unrecognized bias. Employment status was assessed on the date of diagnosis and approximately 8 years later in a cross-sectional study. A consequence is that we do not know the employment status of the patients within this period or how it changed during this period. This assessment of RTW does not allow quantification of the stability of employment, which may be a relevant factor if patients with glioma are unable to maintain previous levels of functioning. Patient selection may have played a role, because there is an over-representation of IDH mutated (IDHmt) tumour patients in the study population. Because of the long time post-diagnosis, the tumour patients with an unfavourable prognosis will have passed away, and most of them will be patients with a IDH wild type (IDHwt) tumour.

This study, nonetheless, has several potential implications. Patients with low-grade glioma are relatively young and a substantial number of them remain employed despite being hindered by fatigue and cognitive complaints. These patients might benefit from targeted vocational rehabilitation programmes. This requires involvement of the rehabilitation team early after diagnosis and long-term support programmes in order to enable patients to return to and maintain paid, as well as unpaid, employment.

The authors have no conflicts of interest to declare.

REFERENCES

1. Spelten ER, Verbeek JH, Uitterhoeve AL, Ansink AC, van der Lelie J, de Reijke TM, et al. Cancer, fatigue and the return of patients to work-a prospective cohort study. Eur J Cancer 2003; 39: 1562–1567.
2. Steiner JF, Cavender TA, Main DS, Bradley CJ. Assessing the impact of cancer on work outcomes: what are the research needs? Cancer 2004; 101: 1703–1711.
3. Peteet JR. Cancer and the meaning of work. Gen Hosp Psychiatry 2000; 22: 200–205.
4. Hoffman B. Cancer survivors at work: a generation of progress. CA Cancer J Clin 2005; 55: 271–280.
5. Spelten ER, Sprangers MA, Verbeek JH. Factors reported to influence the return to work of cancer survivors: a literature review. Psychooncology 2002; 11: 124–131.
6. Short PF, Vasey JJ, Tunceli K. Employment pathways in

a large cohort of adult cancer survivors. Cancer 2005; 103: 1292–1301.
7. de Boer AG, Taskila T, Ojajarvi A, van Dijk FJ, Verbeek JH. Cancer survivors and unemployment: a meta-analysis and meta-regression. JAMA 2009; 301: 753–762.
8. van den Bent MJ. Practice changing mature results of RTOG study 9802: another positive PCV trial makes adjuvant chemotherapy part of standard of care in low-grade glioma. Neuro Oncol 2014; 16: 1570–1574.
9. Soffietti R, Baumert BG, Bello L, von Deimling A, Duffau H, Frenay M, et al. Guidelines on management of low-grade gliomas: report of an EFNS-EANO Task Force. Eur J Neurol 2010; 17: 1124–1133.
10. Yoshida A, Motomura K, Natsume A, Chalise L, Iijima K, Hara D, et al. Preoperative predictive factors affecting return to work in patients with gliomas undergoing awake brain mapping. J Neurooncol 2020; 146: 195–205.
11. Senft C, Behrens M, Lortz I, Wenger K, Filipski K, Seifert V, et al. The ability to return to work: a patient-centered outcome parameter following glioma surgery. J Neurooncol 2020; 149: 403–411.
12. Asher A, Fu JB, Bailey C, Hughes JK. Fatigue among patients with brain tumors. CNS Oncol 2016; 5: 91–100.
13. Mock V, Atkinson A, Barsevick A, Cella D, Cimprich B, Cleeland C, et al. NCCN practice guidelines for cancer-related fatigue. Oncology (Williston Park) 2000; 14: 151–161.
14. Mock V, Atkinson A, Barsevick AM, Berger AM, Cimprich B, Eisenberger MA, et al. Cancer-related fatigue. Clinical practice guidelines in oncology. J Natl Compr Canc Netw 2007; 5: 1054–1078.
15. Pryce J, Munir F, Haslam C. Cancer survivorship and work: symptoms, supervisor response, co-worker disclosure and work adjustment. J Occup Rehabil 2007; 17: 83–92.
16. Curt G, Johnston PG. Cancer fatigue: the way forward. Oncologist 2003; 8 Suppl 1: 27–30.
17. Grier JT, Batchelor T. Low-grade gliomas in adults. Oncologist 2006; 11: 681–693.
18. Louis DN, Perry A, Reifenberger G, von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary. Acta Neuropathol 2016; 131: 803–820.
19. Wijnenga MMJ, French PJ, Dubbink HJ, Dinjens WNM, Atmodimedjo PN, Kros JM, et al. The impact of surgery in molecularly defined low-grade glioma: an integrated clinical, radiological, and molecular analysis. Neuro Oncol 2018; 20: 103–112.
20. van Roijen L, Essink-Bot ML, Koopmanschap MA, Bonsel G, Rutten FF. Labor and health status in economic evaluation of health care. The Health and Labor Questionnaire. Int J Technol Assess Health Care 1996; 12: 405–415.
21. Smets EM, Garssen B, Bonke B, De Haes JC. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. J Psychosom Res 1995; 39: 315–325.
22. van Kessel E, Emons MAC, Wajer IH, van Baarsen KM, Broekman ML, Robe PA, et al. Tumor-related neurocognitive dysfunction in patients with diffuse glioma: a retrospective cohort study prior to antitumor treatment. Neurooncol Pract 2019; 6: 463–472.
23. van den Bent MJ, Brandes AA, Taphoorn MJ, Kros JM, Kouwenhoven MC, Delattre JY, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC brain tumor group study 26951. J Clin Oncol 2013; 31: 344–350.
24. Kleinberg L, Wallner K, Malkin MG. Good performance status of long-term disease-free survivors of intracranial gliomas. Int J Radiat Oncol Biol Phys 1993; 26: 129–133.
25. Ryden I, Carstam L, Gulati S, Smits A, Sunnerhagen KS, Hellstrom P, et al. Return to work following diagnosis of low-grade glioma: a nationwide matched cohort study. Neurology 2020; 95: e856–e866.
26. Douw L, Klein M, Fagel SS, van den Heuvel J, Taphoorn MJ, Aaronson NK, et al. Cognitive and radiological effects of radiotherapy in patients with low-grade glioma: long-term follow-up. Lancet Neurol 2009; 8: 810–818.
27. Lycke M, Lefebvre T, Pottel L, Pottel H, Ketelaars L, Stellamans K, et al. Subjective, but not objective, cognitive complaints impact long-term quality of life in cancer patients. J Psychosoc Oncol 2019; 37: 427–440.
28. Wefel JS, Kesler SR, Noll KR, Schagen SB. Clinical characteristics, pathophysiology, and management of noncentral nervous system cancer-related cognitive impairment in adults. CA Cancer J Clin 2015; 65: 123–138.
29. Duijts SF, van der Beek AJ, Boelhouwer IG, Schagen SB. Cancer-related cognitive impairment and patients' ability to work: a current perspective. Curr Opin Support Palliat Care 2017; 11: 19–23.
30. van Loon EM, Heijenbrok-Kal MH, van Loon WS, van den Bent MJ, Vincent AJ, de Koning I, et al. Assessment methods and prevalence of cognitive dysfunction in patients with low-grade glioma: a systematic review. J Rehabil Med 2015; 47: 481–488.
31. Hoffermann M, Bruckmann L, Mahdy Ali K, Zaar K, Avian A, von Campe G. Pre- and postoperative neurocognitive deficits in brain tumor patients assessed by a computer based screening test. J Clin Neurosci 2017; 36: 31–36.
32. Klein M, Engelberts NH, van der Ploeg HM, Kasteleijn-Nolst Trenite DG, Aaronson NK, Taphoorn MJ, et al. Epilepsy in low-grade gliomas: the impact on cognitive function and quality of life. Ann Neurol 2003; 54 514–520.
33. Coomans MB, Dirven L, Aaronson NK, Baumert BG, Van Den Bent M, Bottomley A, et al. Symptom clusters in newly diagnosed glioma patients: which symptom clusters are independently associated with functioning and global health status? Neuro Oncol 2019; 21: 1447–1457.
34. Boele FW, Meads D, Jansen F, Verdonck-de Leeuw IM, Heimans JJ, Reijneveld JC, et al. Healthcare utilization and productivity loss in glioma patients and family caregivers: the impact of treatable psychological symptoms. J Neurooncol 2020; 147: 485–494.
35. Vargo M, Henriksson R, Salander P. Rehabilitation of patients with glioma. Handb Clin Neurol 2016; 134: 287–304.
36. Day J, Yust-Katz S, Cachia D, Wefel J, Katz LH, Tremont I, et al. Interventions for the management of fatigue in adults with a primary brain tumour. Cochrane Database Syst Rev 2016; 4: CD011376.