Towards improving health-related quality of life in glioma patients and their informal caregivers
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4.1 SUMMARY

The general aim of the studies described in this dissertation was to work towards an improvement in HRQOL for both glioma patients and their informal caregivers. Symptoms of fatigue, cognitive deficits, depression and changes in personality and behavior are frequently reported in glioma patients and all these symptoms can affect their HRQOL to a great extent. To improve the HRQOL of both glioma patients and their significant others, it is important to obtain a clearer view of the contribution of these tumor and treatment-related symptoms.

Therefore, in chapter 1.4, symptoms such as fatigue, cognitive deficits, depression and changes in personality and behavior, and the impact of these symptoms on the everyday lives of patients and their significant others were described in more detail. Unfortunately, the current practice guidelines that are available for managing these symptoms in a general (cancer) population are often not directly applicable to glioma patients, who have distinct problems and needs. Obtaining more evidence on the effectiveness of existing and new interventions targeting fatigue, cognitive deficits, depression, and changes in personality and behavior in this specific population is therefore advised.

Section 2: Towards improving health-related quality of life in glioma patients

Chapters 2.1 and 2.2 focused on identifying various aspects of functioning that affect HRQOL in low-grade glioma (LGG) patients. As LGG patients are not only confronted with the diagnosis and treatment of a brain tumor, but also with changes in cognitive and neurological functioning that can profoundly affect their daily functioning, it is often assumed that this diminished cognitive functioning is associated with poorer HRQOL. However, to our knowledge, this was never investigated as a primary research question. Therefore, the association between cognitive functioning and HRQOL in LGG patients (N=190) with stable disease at an average of six years after diagnosis was examined in chapter 2.1. In this cross-sectional study, poorer cognitive functioning appeared to be related to worse generic and disease-specific HRQOL.

LGG patients often experience long periods of stable disease. In the patient sample described in chapter 2.1, HRQOL was re-evaluated six years after the first evaluation (i.e., 12 years after diagnosis on average, also described as long-term follow-up) in those patients with ongoing stable disease (N=65). Compared with healthy matched controls, LGG patients had worse scores on the subscales ‘physical role functioning’ and ‘general health perceptions’ at long-term follow-up. Within LGG patients, physical aspects of HRQOL proved to be significantly worse at long-term follow-up in comparison to the first assessment. Although 48% of patients improved or remained stable on all HRQOL scales, 38.5% of patients experienced solely decline on one or more scales (chapter 2.2). Although this compromise in HRQOL remains mild, the results indicated that certain limitations in HRQOL in LGG patients can be present throughout years of stable disease.

In chapters 2.3 and 2.4 two interventions aiming at improving symptom management and HRQOL of glioma patients were presented.

To evaluate the effects of the psychostimulant modafinil on fatigue, depression, HRQOL, and cognitive functioning in primary brain tumor patients, a multicenter, double-blind placebo-
controlled crossover trial has been performed. Patients \((N=37)\) randomly received either six weeks of treatment with modafinil (up to 400 mg/day) or placebo. After a one-week washout period, the opposite treatment was provided for another six weeks. The results showed that modafinil does not exceed the effects of placebo with respect to symptom burden. In this study, patient accrual was slow, and relatively many patients dropped out during the trial, due mostly to experienced side effects. Therefore, other, preferably nonpharmacologic intervention studies should be considered to improve symptom management in these patients (chapter 2.3).

The second intervention study described is such a nonpharmacologic intervention (chapter 2.4). The standard treatment of depression (antidepressants and/or cognitive behavioral therapy) may encounter specific problems in glioma patients. Glioma patients often take many medications concurrently, which increases the risk of drug interactions. Psychotherapy usually requires adequate cognitive functioning in order for the patient to benefit most. However, many glioma patients experience cognitive deficits. At present, there are, to our knowledge, no reports of randomized controlled trials on the effectiveness of psychological treatment for depression in glioma patients. Therefore, a randomized controlled trial to evaluate the effects of an internet-based, guided self-help intervention for depressive symptoms in glioma patients has been initiated. This intervention, based on problem-solving therapy, consists of a five-week course adapted for use by adult glioma patients with depressive symptoms. Sample size calculations yield 126 glioma patients to be included, who will be randomly assigned to either the intervention group or a waiting list control group. Additionally, 63 patients with hematological cancer will be included in a non-central nervous system malignancy control group (chapter 2.4). This trial is currently in the recruitment phase, and the end of the inclusion process is scheduled in May 2015. If proven effective, this treatment will contribute to the mental health care of glioma patients in clinical practice.

Section 3: Towards improving health-related quality of life in informal caregivers of glioma patients

In chapter 3.1 the HRQOL of significant others of glioma patients was described. As neurological and cognitive symptoms of glioma patients are assumed to have a large impact on patient behavior, it is often assumed that partners of glioma patients may face greater stress than partners of patients with malignancies not involving the central nervous system (CNS). Although HRQOL has already been found to be worse in informal caregivers of glioma patients than in the normative population, it was still unknown if this is also the case in comparison to informal caregivers of other oncological populations. In a cross-sectional study, the HRQOL of significant others of high- and low-grade glioma patients \((N=55 \text{ and } N=213)\) was compared with the HRQOL of significant others of non-small cell lung cancer (NSCLC) patients \((N=29)\) and non-Hodgkin lymphoma or chronic lymphatic leukemia patients (NHL/CLL; \(N=99)\), respectively. The significant others of LGG and NHL/CLL patients, both assessed in a period of stable disease, had similar levels of HRQOL. Significant others of recently diagnosed HGG patients experienced worse mental health and worse social functioning compared with significant others of recently diagnosed NSCLC patients. The
mental health of the partners was associated with the mental health of the patients. Significant others of patients with high-grade CNS tumors in the acute phase are therefore at increased risk of compromised HRQOL compared to significant others of patients with systemic tumors without CNS involvement and with a comparable life expectancy (chapter 3.1).

In chapter 3.2 a randomized controlled trial was described in which the effects of a structured psychological intervention on the HRQOL and mastery of informal caregivers of HGG patients were investigated. Factors that may determine HRQOL and mastery of informal caregivers of HGG patients at baseline were also investigated. Patients’ HRQOL and neurological functioning were related to the HRQOL and feelings of mastery of informal caregivers (N=56) at baseline. Informal caregivers were randomly assigned to the intervention group or the care-as-usual group. The intervention, consisting of six one-hour sessions with a psychologist, was designed to empower informal caregivers through providing psycho-education and cognitive behavioral therapy. Results indicated that the intervention helps informal caregivers in maintaining a stable level of HRQOL and improves feelings of mastery over an eight month period compared to usual care.