DISCUSSION OF THE MAIN FINDINGS

4.2 DISCUSSION OF THE MAIN FINDINGS

Discussion of the main findings of this dissertation is presented below, separately for the patient studies and for the informal caregiver studies.

Towards improving health-related quality of life in glioma patients

Cognitive functioning and HRQOL were found to be highly correlated in LGG patients (chapter 2.1), a notion that is supported by a recent publication in which global neuropsychological functioning was related to subjective well-being in a heterogeneous sample of brain tumor patients. Moreover, in preoperatively assessed brain tumor patients, a better score on a cognitive screening instrument (Mini Mental State Examination) was associated with better HRQOL, although other variables such as anxiety and depression explained a larger proportion of the variance. Through these studies, a causal relationship between cognitive functioning and HRQOL can neither be confirmed nor denied. However, given the associations found it seems worthwhile to explore the effect of successful cognitive rehabilitation on the HRQOL of glioma patients. To date, one cognitive rehabilitation program for brain tumor patients was tested in a RCT. Here, no significant effect on HRQOL or community integration was found at six months follow-up, despite the program’s beneficial effects on cognitive functioning. An explanation for this counterintuitive result could be, that cognitive functioning does not directly affect HRQOL, but is influenced by mediating factors such as the awareness of cognitive deficits, participation in society, or possibly disease phase or disease severity. To better understand the potentially complex relationship between cognitive functioning and HRQOL in this patient population, further longitudinal studies are necessary.

Longitudinal assessments of HRQOL and possible determinants can be worthwhile both in research and in a clinical context. This is illustrated in chapter 2.2, where mild compromise in HRQOL was found in LGG patients with stable disease, on average 12 years after diagnosis. Ever more frequently, efforts are directed towards monitoring HRQOL and supportive care needs throughout the patient’s disease trajectory, in order to provide referral to other health care specialists whenever necessary. In this context, the findings of chapter 2.2 may be particularly valuable. Statistically significant differences between LGG patients and healthy controls, statistically significant change within LGG patients specifically, and minimal detectable change per scale yielded different results. This emphasizes the complex nature of the concept of HRQOL and underlines the importance of combining different methods in determining what constitutes meaningful change in HRQOL. The combination of both anchor-based and distribution-based approaches has been investigated in different cancer patient populations, for various HRQOL questionnaires such as the Functional Assessment of Cancer Therapy, the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30, the Short Form-36, and others. However, these studies seldom focus on brain tumor patients. This is important as glioma patients may differ dramatically from other cancer patient populations in terms of their perception of meaningful change in HRQOL because of their unique symptom pattern and neurological or cognitive compromise. Before
implementing patient reported measures in clinical practice to monitor HRQOL issues and supportive care needs to provide referral to health care specialists as necessary, the concept of meaningful change in a brain tumor patient context should be clarified further.

Furthermore, to reduce symptom burden and improve HRQOL in glioma patients, efforts should be directed towards obtaining more evidence for the effectiveness of existing and new interventions targeting fatigue, cognitive deficits, depression, and changes in personality and behavior (chapter 1.4). In chapter 2.3, the effectiveness of prescribing modafinil for fatigue was investigated. The results were not as anticipated as modafinil proved no better than placebo at decreasing symptoms of fatigue. A recent publication on a large, placebo-controlled study in patients with NSCLC similarly concluded that the effects on fatigue did not exceed the effects of placebo. However, an interim-analysis of a study on armodafinil (a drug that is the R-enantiomer of modafinil) shows modest positive effects in brain tumor patients after cranial irradiation, in those patients who are most fatigued at baseline. These results mirror those of a large trial, in which it was found that only those cancer patients who were severely fatigued, benefited from modafinil. It seems that psychostimulants may help reduce fatigue in those who are very severely fatigued, and that patients with less severe symptoms may benefit more from other interventions.

Examples of other types of interventions aimed at decreasing symptom burden and/or increasing HRQOL in brain tumor patients have recently been reported on. An individualized, intensive multidisciplinary rehabilitation program improved physical activity levels (i.e. self-care, mobility, and continence) and psychosocial outcomes (i.e. psychosocial interactions, communication, and cognitive functioning) in brain tumor patients in the intervention group compared with a waitlist control group. However, participants were not allocated to the groups randomly but based on their clinical need, and HRQOL did not improve significantly. In addition, a non-controlled, retrospective study on inpatient rehabilitation showed that functional status, mobility in particular, improved from admission to discharge in newly diagnosed glioblastoma patients. Moreover, an Australian RCT on the ‘Making Sense of Brain Tumor Program’, a home-based therapy program for brain tumor patients and their family members, showed beneficial effects for patients’ well-being. After the intervention, patients had lower levels of depression, higher levels of existential and functional well-being, and better HRQOL than patients in the waitlist control group. In the Netherlands, Gehring et al. have recently initiated a RCT aimed at improving cognitive functioning through physical activity, and the first patients have been included. The results of this intervention, as well as of our own internet-based intervention aimed at reducing depressive symptoms in glioma patients (chapter 2.4) are eagerly anticipated.

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

From chapter 3.1, it becomes clear that informal caregivers of HGG patients, in particular, seem vulnerable for compromised HRQOL. However, the cross-sectional design of the study and the focus on two distinct groups of glioma patient caregivers make it difficult to determine
whether the vulnerability is mainly related to the patient’s disease phase (i.e., shortly after diagnosis versus months to years thereafter) or the patient’s disease severity (i.e., the diagnosis of HGG versus a lower-grade malignancy). This hinders identification of vulnerable (sub)groups of informal caregivers. Therefore, longitudinal assessments of caregiver burden and HRQOL in samples representative of the informal caregiver population in neuro-oncology are needed.

Findings from a large, longitudinal study of mind-body interactions in neuro-oncology caregivers performed in Pittsburgh are especially relevant in this respect. This study focused on examining the psycho-behavioral responses (i.e. depressive symptoms and sleep), biologic responses (i.e. blood pressure and interleukins) and overall physical health of family members of persons with a primary brain tumor at the time of diagnosis, and how the relationships between these variables vary over time in response to changes in the patient’s disease trajectory. As part of this large project, different psychological distress patterns in family caregivers were identified with group-based trajectory modeling, linking high depressive symptoms with more anxiety and burden, lower age, income, and social support, and worse functioning of the patient. This indicates that there are subgroups of caregivers who are more likely to benefit from interventions. Other factors that can be used to identify vulnerable subgroups of caregivers include spirituality, positive aspects of care, and marital adjustment. Furthermore, when patients experience more physical problems, family caregivers are more likely to report lost hours from work, which may cause financial burden. Experienced economic hardship in neuro-oncology was studied which showed its subsequent effect on emotional health. Studies into sleep characteristics showed that sleep deprivation was commonly found in family caregivers, and sleep quality was positively associated with quality of life.

In addition, in Denmark, a longitudinal study on the quality of life of informal caregivers of HGG patients has recently started. This study should shed additional light on informal caregivers’ HRQOL issues along the course of the patients’ disease trajectory. In addition to longitudinal research efforts, it would be valuable to monitor supportive care needs and HRQOL of informal caregivers throughout the patient’s disease trajectory in clinical practice, as tailored advice and referral to health care services can then be routinely provided as necessary. Alternatively, if the need for supportive care proves low despite the presence of HRQOL issues, self-management tools such as ‘Oncokompas’ could be useful.

In chapter 3.2, a first effort towards evidence-based psychological care for informal caregivers in neuro-oncology was made. In this trial, the attrition rate was high and the effects were modest, suggesting that perhaps other methods to improve psychological care should be employed in this unique group of informal caregivers. Therefore, attention should continue to be paid to testing the effectiveness of existing and new interventions in informal caregivers in neuro-oncology. At present, the possibilities of internet-based interventions for caregivers are under investigation. An Australian pilot study in cancer caregivers yielded promising results for those who completed the intervention, (a self-guided cognitive behavior therapy), as improvements in negative affect and emotional functioning were found, but the researchers experienced great difficulty with recruitment and retention. In addition to the study mentioned above, from personal communication we know of two ongoing randomized controlled trials focusing on...
Discussion of the main findings

4.2

Internet-based supportive care for cancer caregivers. Although results are not yet available, a study focusing on informal caregivers in neuro-oncology ('SmartCare') is presently conducted in the United States (principal investigators: Sherwood and Donovan) and a study targeted at cancer caregivers in general ('Houvast, voor elkaar') is conducted in the Netherlands.\(^{304}\)