Neuro-Oncology Practice
9(6), 459–460, 2022 | https://doi.org/10.1093/nop/npac072 | Advance Access date 13 September 2022

# Screening for long-term complications in brain tumor care, thinking one step ahead

**Annette Compter and Joost J.C. Verhoeff**

*Department of Neuro Oncology, Netherlands Cancer Institute—Antoni van Leeuwenhoek, Amsterdam, The Netherlands(A.C.); Department of Radiation Oncology, University Medical Center Utrecht, Utrecht, The Netherlands(J.J.C.V.)*

**Corresponding Author**: Annette Compter, Department of Neuro Oncology, Netherlands Cancer Institute—Antoni van Leeuwenhoek, Amsterdam, Plesmanlaan 121, 1066 CX, The Netherlands. (a.compter@nki.nl).

Advances in diagnostics and treatment lead to prolonged survival in brain tumor patients, in particular in patients with brain metastases, due to new systemic treatment options with targeted molecular therapy and immune checkpoint inhibitors.[1] This results in an increasing group of brain tumor survivors facing potential long-term complications from the brain tumor itself, and from local or systemic treatment.

Long-term complications caused by the tumor itself and tumor resection, include physical disability, cognitive dysfunction, mood and sleep disorders, and the subsequent negative effects on all aspects of daily life, including the capacity to work and participate in other roles.[2] The main long-term complication of radiotherapy in brain tumor patients is cognitive dysfunction. With new imaging, planning, and delivery technologies, advances aim at optimizing local tumor control and minimizing neurotoxicity, thereby reducing the risk of cognitive decline.[3,4] Possible additional long-term complications from radiotherapy include vasculopathy and secondary malignancies.[5] Systemic treatment includes both antitumor treatment, and symptomatic treatment with steroids and antiepileptic drugs. Systemic treatment can significantly add to cognitive dysfunction, ocular toxicity (mainly in patients with immune checkpoint inhibitors), and endocrinopathy.[6] The abovementioned complications form a potential burden in brain tumor survivors, and have a potentially negative effect on daily functioning and the quality of life.

Currently, guideline recommendations for screening long-term complications are lacking for adult-onset brain tumor patients. This is in contrast to pediatric brain tumor patients for whom extensive guidelines and recommendations from the Children's Oncology Group are available.[7] Screening for long-term complications could be the next step in care for adult brain tumor survivors and might help to identify and treat complications at an early stage.

In this issue of *Neuro-Oncology Practice*, Figuracion and colleagues[8] provide a relevant literature review of the long-term complications in adult-onset brain tumor survivors by a multidisciplinary team of health care professionals. In addition, the team formulates recommendations for screening long-term complications. Recommendations involve both monitoring and treatment of cognitive dysfunction, vasculopathy, endocrinopathy, ophthalmic sequelae, ototoxicity, physical disability, sleep disturbance, mood disorder, unemployment, financial toxicity, and secondary malignancy. Screening involves subjective assessment of symptoms, laboratory testing, and objective evaluations. Close collaboration with primary care providers and other specialties (eg, ophthalmologists, otolaryngology, and support services) is advocated.

Cognitive dysfunction is a relevant complication in the majority of brain tumor patients and is multifactorial determined by the location and type of tumor, patients factors (eg, age and cognitive reserve), and the tumor treatment (eg, radiotherapy and antiepileptic drugs).[9] Patient reports potentially suffer from underreporting due to symptom unawareness and over-reporting due to psychosocial factors including mood and sleeping disorders.[10] The provided screening program recommends performing routine screening of subjective and objective cognitive functioning to evaluate changes over time and guide further interventions. It suggests performing cognitive screening every 6–12 months in brain tumor patients by a triad of a cognitive screening tool (eg, Montreal Cognitive Assessment [MoCA]), patient-reported symptoms, and care partner's observations.

With increasing survival in brain tumor patients, prevention and screening for long-term treatment complications will further gain importance. The literature review provided reveals the paucity of data on the incidence and time course of long-term complications in adult-onset brain tumor patients. Available data are mainly from pediatric brain tumor survivors. Data on late complications in pediatric brain tumor patients should not be applied directly to adult-onset brain tumor patients. Tumor biology, treatment strategies, and pretreatment risk profiles for complications (eg, cognitive dysfunction and vasculopathy)

differ in pediatric and adult patients. High-quality data on the optimal screening method and method are lacking in this review, and data on the validity and reliability of the screening instruments are scarce. Inherently, screening recommendations proposed in this review are rarely evidence-based and should rather be seen as a multidisciplinary expert opinion. Therefore, it is a great stimulus to the adult neuro-oncology community to improve evidence on this topic.

During further development of the proposed screening program, an evaluation of the optimal screening interval, the burden of screening for both health care professionals and patients, the risks and side effects of screening, and costs should take place. At this stage, a panel of patient advocates has not been involved in the development of the screening program. Their views on the pros and cons of this screening program, and an evaluation of their willingness to undergo screening, will be valuable for further development of the screening program.

In conclusion, this review and the recommendations form a first and very important step in the rapidly developing field of survivorship care in adult brain tumor patients. The work conducted by Figuracion and colleagues[8] raises awareness of the long-term treatment complications. The limited evidence for screening and treatment of these complications underpins the need for prospective studies on the incidence and risk factors of long-term complications in adult brain tumor patients. Screening for long-term complications has the potential to improve daily functioning and impact quality of life. Nonetheless, critical assessment of the efficacy, benefits, and harms of the proposed screening program is essential before implementation in clinical practice. Then we stay one step ahead in optimizing the lives of our patients.

## Conflict of Interest Statement

None declared.

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