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Advances in palliative care in neuro-oncology come in many forms

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If we consider the entire care trajectory of a patient with a malignant brain tumor—the compilation of phone calls, dilemmas, in-person evaluations, discussions, and decisions—a modest proportion of activities and interventions are oncologic in nature, that is, oriented towards tumor control. The majority of our efforts, rather, are focused upon management of symptoms, mitigation of toxicities, explaining disease and treatment to patients and their caregivers, and ultimately supporting them in facing what the future holds for this dread disease. Palliative care is critical, even inherent, to the practice of neuro-oncology; advances in its investigation and implementation are therefore at the center of our discipline, not its periphery. Innovations in this area can take the form of pharmacologic or behavioral interventions evaluated in randomized trials. They can also take the form of studies that characterize symptoms or problems that we have yet to manage, and they can even take the form of studies that reveal our shortcomings and define opportunities for improvement.

The systematic review executed by Koekkoek and colleagues[1] is a comprehensive and informative accounting of published literature from 2016 to 2021 across domains of palliative care in neuro-oncology. A collaborative international group of topic experts recapitulated the literature search performed for the European Association for Neuro-Oncology (EANO) guidelines on this topic from 2016 and they synthesize the finding of 140 articles pertaining to preservation of cognition, seizures, fatigue, headaches and pain, psychiatric symptoms, caregiver needs, early palliative care, and end-of-life care. The identified literature is presented thoroughly and with granular and egalitarian detail.

A portion of the review presents published trial data with ready implications for practice. Several trials in the area of cognition highlight the potential for alternatives to conventional whole-brain radiation therapy (WBRT) to be associated with less deleterious effects upon cognition, namely stereotactic radiosurgery in some clinical instances and hippocampal avoidance during WBRT in others. In the domain of seizure management, the predominant practice of levetiracetam monotherapy for secondary seizure prophylaxis is buttressed by large-scale retrospective data and by a systematic review. Administration of brivaracetam, lacosamide, and perampanel have accumulated additional evidence, also in alignment with evolution in current practice.

A unifying theme that emerged from the multiple spheres of literature reviewed is that of the uninspiring efficacy of pharmacologic interventions for neuro-oncologic symptomatology on the one hand, and the data supporting non-pharmacologic interventions on the other. Negative randomized controlled trials were conducted for donepezil, dexamphetamine, and armodafinil for cognition, fatigue, and mood in patients with glioma. By contrast, a randomized trial (albeit pilot) suggested benefit from home-based and remotely coached aerobic exercise (20–45 min of moderate to vigorous activity, three times weekly) for cognition and fatigue. Additionally, a 150-patient randomized trial of a reminiscience-therapy based intervention performed twice per month for 1 year demonstrated reduction in depression and anxiety in glioma. These findings resonate with what has been observed in systematic reviews and meta-analysis in non-neurologic cancers, that is, that fatigue is an intrusive and pervasively common symptom[2] that is generally not amenable to pharmacological therapies.[3] There is ample collective data, by contrast, that exercise-based interventions can confer benefit for cancer-related fatigue[4] and that cognitive therapies such as mindfulness can reduce symptoms of fatigue, depression, and anxiety in patients with cancer.[5] The above data in neuro-oncologic patients, viewed in context of similar data in cancer generally, serve as a reminder for us to be consider interventions that may normally inhabit our blind spots and to advocate for non-pharmacologic measures for our patients in efforts to palliate symptoms.

A second theme from the recent literature is the opportunity for improved practice in support of caregivers and the patient-caregiver dyad, specifically with respect to addressing gaps in prognostic communication and advanced care planning (ACP). Several studies documented difficulties coping experienced by those providing care for patients with malignant brain tumors and that these psychological morbidities do not diminish over the disease trajectory. One review that was not encompassed by the authors' search specifically explored spiritual and existential distress endured by brain tumor caregivers that emanates from anxiety about patients' death compounded by the cognitive and behavioral changes manifest in patients.[6] Other studies, moreover, have brought into focus a concerning constellation of phenomena in patients with malignant brain tumors: patients' frequent lack of awareness of disease prognosis, discordance between patients' and caregivers' prognostic understanding, and prevalence of late acute hospitalization and hospice referral.[7] A very recent study suggested dramatic discordance in patients', caregivers, and oncologists' accounts of prognostic discussions in the setting of glioblastoma recurrence.[8] Recent years have also seen the emergence, however, of promising new supportive initiatives, including innovative modalities for social support, delivery of early palliative care, and even two glioma-specific ACP programs (one more recent than the search output of this review[9]). It may be of benefit to explore and leverage interventions specifically tailored to augment prognostic understanding in the context of other cancers and life-limiting illnesses[10]; the reality of cognitive impairment in brain tumor patients, however, likely poses obstacles unique to this clinical population. Taken together, the advances in this area in recent years may be most salient in their rigorous characterization of challenges yet to be addressed, although with encouraging ideas on the horizon.

The very fact of a robust systematic review of 6 years of palliative care literature in neuro-oncology, presenting rich data from observational and retrospective studies, meta-analyses, and even randomized trials, bespeaks the robust commitment to this work in our international community. Improvements in this area will, we hope, be accompanied by tangible advances in therapeutics and survival.

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