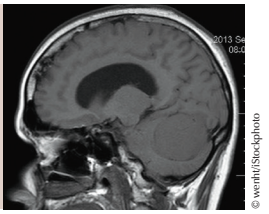
Update on . . . Patients With Primary Brain Tumors

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The focus of this column is to present topics of interest from a variety of journals to Oncology Nursing Forum *readers. The topic of this issue is the clinical management of patients with primary brain tumors.*



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Effect of Chemotherapy on Cognitive Function in Patients With Low-Grade Glioma

The purpose of this prospective phase II/III trial was to study the effect of therapy intensification when combining procarbazine, lomustine, and vincristine (PCV) chemotherapy with a standard course of radiation therapy (RT) on cognitive functioning for patients with World Health Organization grade 2 low-grade gliomas (LGGs). Initial results of the trial demonstrated a progression-free survival benefit with adjuvant PCV, but no overall survival benefit in the intention-to-treat analysis. Because patients with LGGs have favorable prognostic indicators, the five-year overall survival rates range from 60%–70%. The effect of cancer treatment on neurocognitive function is a topic of increasing interest to healthcare providers and patients. The negative effect is commonly called "chemobrain" and refers to diminished concentration and compromised short-term memory following treatment. Chemobrain has been studied in other populations of patients with cancer (e.g., breast cancer) with associated statistically significant chemotherapy-associated compromised cognitive function when chemotherapy was added to RT.

This trial prospectively captured cognitive function evaluations for 362 patients with LGGs. Cognitive function was measured using the Folstein Mini-Mental State Examination (MMSE), which is a validated screening test for dementia and cognitive impairment. Scores on the MMSE range from 1–30, and higher scores indicate greater cognitive impairment. The purpose of the secondary analysis was to assess patterns of cognitive function changes post-treatment and to determine the potential for an untoward effect on cognitive function when chemotherapy is added to RT, when compared to RT alone. Of the 362 patients, 251 had World Health Organization grade 2 glioma and were either aged 40 years or older with any resection or younger than age 40 years with subtotal resection or biopsy. Those patients were randomly assigned to RT or RT plus PCV. The remaining 111 patients were younger than age 40 years with gross total resections, and those patients were observed. All participants were assessed by MMSE at baseline and at years 1, 2, 3, and 5 prospectively.

The results indicated that, with a gain or decline in the MMSE score, the majority of patients maintained their baseline cognitive function. Significant decline of MMSE score was rare, and those with a baseline MMSE score of less than 27 were more likely to experience significant gains in their MMSE score, which may have been caused by baseline deficits in cognitive function from the tumor that were reversed with therapy.

The authors cautioned that MMSE is an insensitive tool and has not been validated in patients receiving cranial RT. Therefore, the tool may not have identified changes in cognitive function in the study population. The authors concluded that the addition of PCV to RT for LGGs did not result in significant MMSE score decline when compared to RT alone during five years of follow-up. Additional findings demonstrated that patients in both study arms experienced a statistically significant increase in average MMSE score over time, with no difference in cognitive function. The authors suggested that enhanced neurocognitive assessments may detect subtle changes and should be used to supplement MMSE in future studies.

This study pointed to the importance of validating a more intensive treatment regimen for this patient population with high overall survival rates. Future studies also should assess the potential for serious compromised cognitive function outweighing the benefit of progression-free survival. By studying the association of the addition of PCV to RT with the effect on cognitive function, an enhanced decision-making process was facilitated for clinicians and patients.

Prabhu, R.S., Won, M., Shaw, E.G., Hu, C., Brachman, D.G., Buckner, J.C., . . . Mehta, M.P. (2014). Effect of the addition of chemotherapy to radiotherapy on cognitive function in patients with low-grade glioma: Secondary analysis of RTOG 98-02. *Journal of Clinical Oncology, 32,* 535–541. doi:10.1200/JCO.2013.53.1830

Uncertainty, Mood States, and Symptom Distress in Patients With Brain Tumors

This study aimed to decrease symptom severity and enhance quality of life for patients with primary brain tumors (PBTs) by reducing uncertainty and encouraging positive mood states. PBTs are identified as a group of central nervous system tumors that do not have the propensity to metastasize distantly. Gliomas are the predominant class, and glioblastoma multiforme (GBM) is the predominant type of malignant glioma in adults. The treatment trajectory is lengthy and may involve a combination of surgery, radiation, and chemotherapy. This patient population is plagued with poor overall prognoses and intense treatment-related toxicities, and they must face fear of the unknown and the inability to be in charge of health-related events. The researchers of the study methodically identified the uncertainties faced by patients with PBTs, and they sought to document the direct and indirect relationships between uncertainty, mood states, and symptoms.

A total of 186 patients with PBTs were enrolled in the study. The participants were primarily Caucasian (n = 149, 80%) and men (n = 99, 53%). GBM was the most common pathologic diagnosis, and the participants ranged in age from

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19–80 years ($\bar{X}$ = 44.2 years). Thirty-two patients (17%) were newly diagnosed, 85 (46%) were on current treatment, and 69 (37%) had completed treatment and were being observed. The authors examined the influences of treatment stage and functional status on uncertainty. In addition, the authors tested the direct impact of uncertainty on negative mood states and patient-perceived symptom severity, as well as mediation effects of negative mood states between uncertainty and symptom severity.

The mood states in this study were considered mediators, and a conceptual model was produced using five negative mood states (i.e., tension, depression, anger, fatigue, and confusion). All mood states were tested individually. The authors proposed that, by decreasing mood disturbance caused by uncertainty, symptom distress in patients with PBTs may be reduced and ultimately facilitate patient adaptation to the illness. The study used five data collection instruments, including the Mishel Uncertainty in Illness Scale–Brain Tumor Form, a 33-item scale used to measure uncertainty; the MD Anderson Symptom Inventory Brain Tumor Module, which rates 22 symptoms on an 11-point scale to indicate the presence and severity of the symptoms; and the Profile of Mood States–Short Form (POMS-SF), a 37-item short form used to measure negative moods. The study used only five of six subscales from the POMS-SF. A demographic information sheet also was completed to determine potential variables that may affect uncertainty, mood, and symptom distress. The final instrument was a clinical assessment tool documenting disease type, stage, clinical and diagnostic information, Karnofsky performance status, and type of clinical encounter.

Findings included confirmation that all working models were significant according to structural equation modeling (SEM), which was conducted to indicate the strength of influence among all considered variables. Because the authors wanted to test the hypothesis that uncertainty is directly and indirectly correlated to symptom severity, SEM was used to test the significance of direct and indirect relations among uncertainty, mood states, and symptom severity. The study revealed that lower functional status and being lower in the illness trajectory were associated with greater uncertainty ($p < 0.01$ for both). Uncertainty ($p < 0.05$) was directly associated with symptom severity perceived by patients ($p < 0.01$ for all), with the exception of the confusion model. The effect of perceived symptom severity also was significantly mediated by mood states.

The study results showed distinct correlations between uncertainty, mood states, and symptom severity. Patients with PBTs experience uncertainty throughout the trajectory of care. These research findings support the conceptual framework suggesting the development of effective, prompt clinical interventions to modify negative mood states, relieve symptom distress, lessen the degree of uncertainty, and enhance quality of life.

Lin, L., Chiang, H.H., Acquaye, A.A., Vera-Bolanos, E., Gilbert, M.R., & Armstrong, T.S. (2013). Uncertainty, mood states, and symptom distress in patients with primary brain tumors: Analysis of a conceptual model using structural equation modeling. *Cancer, 119,* 2796–2806. doi:10.1002/cncr.28121

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