Low Karnofsky Performance Scale score and glioblastoma multiforme

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Glioblastomas multiforme (GBMs) have a dismal prognosis. The Stupp protocol has improved survival in patients with GBM; however, as in many prospective studies, only nonelderly patients with a favorable performance status were enrolled in that study. Other published clinical trials and retrospective chart reviews often exclude both elderly patients (maximum age is typically 70–75 years) and those with low Karnofsky Performance Scale (KPS) scores (minimum is usually 60 or 70). Studies that evaluate a broader range of ages and performance statuses often find poor presenting KPS scores or advanced age to be predictors of shorter overall survival. Patients who are elderly may be offered aggressive treatment such as surgery less frequently, may represent poorer surgical candidates, may have tumors less responsive to standard GBM treatments, and may exhibit a more rapid neurological decline compared with younger patients. Other work suggests that patients with poor functional status and those who are elderly may be poor candidates for aggressive therapy and may be better served with palliative measures such as a short course of radiation. Overall, patients who present with a poor performance status, of whom the elderly are a significant percentage, represent a subset of patients with GBM and a poor performance status at presentation.

In the present study, Marina et al. reviewed 74 patients with GBM who presented with low KPS scores. The greatest survival benefit for this population was achieved with radiation therapy and concomitant chemotherapy. Overall survival in these patients approached 10 months as compared with < 2 months’ survival in those who received radiation alone, and 70% of patients who received radiation had an improved KPS score at their follow-up clinic visit. In addition to radiation therapy, resection also predicted a decreased mortality rate. These findings demonstrate a potential benefit of radiation and concomitant chemotherapy following resection for GBM in patients with a poor performance status. This study has limitations inherent to a retrospective review. Of significant concern is the fact that the study patients were identified through reviews of radiation oncology and pathology databases. Thus, all patients had been referred for treatment and were presumably deemed healthy enough by their physician to merit this referral. This selection bias weakens the conclusions of the study but also underscores the need for prospective data. Current prospective data in these patients are limited but suggest a survival benefit following a short course of radiation and temozolomide. The authors present an excellent analysis of the data available to them, and their important findings warrant further studies. Future prospective trials may help to optimize treatment paradigms for this subgroup of patients with GBM.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

References

Editorial

Response

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We thank Drs. Elder and Chiocca for taking the time to highlight important issues pertaining to our article. As they point out, there are no large prospective trials evaluating outcomes in elderly or low-performance-status patients treated with the modern therapy typically delivered to younger patients with good performance status, including resection, temozolomide, and radiation. 2 As a result, a significant number of patients with GBM may not undergo optimal treatment.

Our retrospective review of the treatment of 74 patients with KPS scores ≤ 50 at a single institution suggests that these patients, whose median age was 69 years, may benefit from subtotal or gross-total resection as well as radiation therapy. The fact that the KPS score improved at the first follow-up visit after radiation therapy suggests that this treatment provides not only a survival benefit, but also a quality-of-life benefit. Determining to what extent temozolomide, modern chemotherapy for GBM, further improves outcomes is limited by the small sample that received this treatment and by the higher prevalence of a lower Radiation Therapy Oncology Group recursive partitioning analysis (RPA) class 1 in those receiving this treatment (Table 1). The finding of a significantly increased median survival for concurrent chemoradiation as compared to radiation alone is, however, suggestive of benefit.

As Drs. Elder and Chiocca point out, our retrospective review does have multiple biases, such as a highly selected group of patients who were evaluated at a tertiary care center and referred for radiation therapy. In addition, the rationale for selecting interventions is rarely available. However, we identified patients who did not receive radiation or chemotherapy and were not offered these interventions (Table 2). We therefore excluded patients not offered treatment in part of our analyses. At the same time, we compared patients who were not offered, were offered but declined, or were offered and accepted radiation therapy, and found these groups to be similar in age and KPS score (Table 3). However, further details, such as the reasons for the differing extent of surgical treatment, could not be identified and accounted for in our analyses.

Our retrospective review provides evidence supporting an overall survival and quality-of-life benefit for treatment in a subset of patients with GBM who have low KPS scores at presentation, including a significant number of elderly patients. Like Drs. Elder and Chiocca, we believe that our findings support the inclusion of patients who are elderly and who have low KPS scores in prospective trials for GBM. These studies would provide clearer evidence for the optimal management of this group of patients.

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Table 1: Chemotherapy during and after radiation therapy by RTOG RPA class and surgical intervention

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<th>RTOG RPA Class &amp; Surgery</th>
<th>Chemotherapy</th>
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