A validation study of a new prognostic index for patients with brain metastases: the Graded Prognostic Assessment

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Objective. The purpose of this study was to validate a new prognostic index for patients with brain metastases. This index, the Graded Prognostic Assessment (GPA), is based on an analysis of 1960 patients whose data were extracted from the Radiation Therapy Oncology Group (RTOG) database. The GPA is based on 4 criteria: age, Karnofsky Performance Scale score, number of brain metastases, and the presence/absence of extracranial metastases. Each of the 4 criteria is given a score of 0, 0.5, or 1.0, so the patient with best prognosis would have a GPA score of 4.0.

Methods. Between April 2005 and December 2006, 140 eligible patients with brain metastases were treated at the Gamma Knife Center at the University of Minnesota. The GPA score was calculated for each patient, and the score was then correlated with survival. Survival duration was calculated from the date treatment began for the brain metastases. Eligibility criteria included patients treated with whole-brain radiation therapy, stereotactic radiosurgery, or both.

Results. The median survival time in months observed in the RTOG and Minnesota data by GPA score was as follows: GPA 3.5–4.0, 11.0 and 21.7; GPA 3.0, 8.9 and 17.5; GPA 1.5–2.5, 3.8 and 5.9; and GPA 0–1.0, 2.6 and 3.0, respectively.

Conclusions. The University of Minnesota data correlate well with the RTOG data and validate the use of the GPA as an effective prognostic index for patients with brain metastases. Clearly, not all patients with brain metastases have the same prognosis, and treatment decisions should be individualized accordingly. The GPA score does appear to be as prognostic as the RPA and is less subjective (because the RPA requires assessment of whether the primary disease is controlled), more quantitative, and easier to use and remember. A multiinstitutional validation study of the GPA is ongoing. (DOI: 10.3171/JNS/2008/109/12/S14)

Key Words • brain metastasis • prognosis • radiation therapy • stereotactic radiosurgery

Brain metastases are a common problem. Estimates of incidence vary from 170,000 to 300,000 in the US. The incidence continues to rise, most likely due to advances in systemic therapy and the wide availability of MR imaging. Compared with primary brain tumors, brain metastases are 10 times more common. If compared with the incidence of primary malignancies, brain metastases would rank third behind only prostate and breast cancer. Historically, the prognosis has been uniformly poor, with MST without treatment of just 2–4 months. In recent years, it has become clear that not all patients with brain metastases have the same prognosis. Further complicating the issue are the numerous available treatment options and the resulting controversy regarding which treatment(s) is most appropriate for which patients. Treatment options include surgery, WBRT, and SRS or some combination thereof. There are current clinical trials exploring the role of chemotherapy as well. Cli-
nicians are often faced with difficult decisions regarding which patients should be referred to hospice and which patients warrant aggressive treatment. For these reasons, there is great need for an accurate prognostic index to guide clinical decision making.

A new prognostic index for patients with brain metastases, based on an analysis of data collected in 1960 patients from 5 prior randomized trials performed by the RTOG (Protocols 7916, 8528, 8905, 9104, and 9508), was recently published. These 1960 patients represent the largest collection of randomly assigned cases of brain metastases in the literature. In this index, the GPA, each of 4 clinical criteria (age, Karnofsky Performance Scale score, number of brain metastases, and presence of extracranial metastases) is given a score of 0, 0.5, or 1.0 (Table 1). A patient with the best prognosis would have a GPA score of 4.0.

The rationale for this index was data from a landmark prospective randomized clinical trial (RTOG 9508), which showed that the number of metastases was prognostic of survival. This study randomized patients to receive WBRT alone or WBRT plus SRS. There was a statistically significant survival advantage (p = 0.04) for patients with solitary brain metastases when treated with WBRT plus SRS, but no such benefit for the study overall (p = 0.13), which included patients with 1–3 metastases. Furthermore, there was no statistically significant difference in survival based on method of SRS (Gamma Knife vs linear accelerator). Heretofore, the most commonly used prognostic index for patients with brain metastases, the RPA published by Gaspar et al. prior to the publication of RTOG 9508, did not include the number of brain metastases as a criteria. Another limitation of the RPA was the need to estimate the control of systemic disease, which was fraught with inconsistency due to the variation in type and timing of imaging studies. In the original article describing the new index, the GPA was found to be as prognostic as the RPA, less subjective, more quantitative, and easier to use.

The purpose of the present study was to assess the validity of the GPA by comparing the RTOG data used for the original description of the index to clinical data obtained at the University of Minnesota Gamma Knife Center.

### Methods

Between April 2005 and December 2006, 140 consecutive patients with brain metastases were treated at the University of Minnesota Gamma Knife Center. The GPA score was calculated for each patient, and it was then correlated with survival. Survival time was calculated from the date treatment began for the brain metastases. Eligibility criteria included patients treated with WBRT (3 patients), SRS (26 patients), or both (111 patients).

### Results

The MSTs calculated from the RTOG and Minnesota data are shown in Table 2. The MSTs for the RTOG and the University of Minnesota patients with a GPA score of 3.5–4.0 were 11.0 and 21.7 months, respectively. The MSTs for the RTOG and the University of Minnesota patients with a GPA score of 3.0 were 8.9 and 17.5 months, respectively. The MSTs for the RTOG and the University of Minnesota patients with a GPA score of 1.5–2.5 were 3.8 and 5.9 months, respectively. The MSTs for the RTOG and the University of Minnesota patients with a GPA score of 0.0–1.0 were 2.6 and 3.0 months, respectively. The log-rank test showed a statistically significant difference in MSTs between each GPA grouping (p < 0.0001) in both groups.

### Discussion and Conclusions

The University of Minnesota data correlate well with the RTOG data and validate the use of the GPA as an effective prognostic index for patients with brain metastases. Clearly, not all patients with brain metastases have the same prognosis, and treatment decisions should be individualized accordingly. The GPA was designed to incorporate the most recent randomized data and is thus an updated, new, and improved version of the RPA. The GPA is a useful tool for clinical decision making regarding which patients should be referred to hospice and which patients warrant aggressive treatment. The GPA does appear to be as prognostic as the RPA and is less subjective, more quantitative, and easier to use.

The purpose of the present study was to assess the validity of the GPA by comparing the RTOG data used for the original description of the index to clinical data obtained at the University of Minnesota Gamma Knife Center.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>GPA Score</th>
</tr>
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<tbody>
<tr>
<td>Age (yrs)</td>
<td>0 0.5 1.0</td>
</tr>
<tr>
<td>Karnofsky Performance Scale score</td>
<td>0 0.5 1.0</td>
</tr>
<tr>
<td>Number of CNS metastases</td>
<td>0 0.5 1.0</td>
</tr>
<tr>
<td>Extracranial metastases</td>
<td>0 0.5 1.0</td>
</tr>
</tbody>
</table>

* CNS = central nervous system; NA = not applicable.

### Table 2

<table>
<thead>
<tr>
<th>GPA</th>
<th>RTOG No. of Cases</th>
<th>MST (mos)</th>
<th>Minnesota No. of Cases</th>
<th>MST (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.5–4.0</td>
<td>102</td>
<td>11.0</td>
<td>9</td>
<td>21.7</td>
</tr>
<tr>
<td>3.0</td>
<td>168</td>
<td>8.9</td>
<td>20</td>
<td>17.5</td>
</tr>
<tr>
<td>1.5–2.5</td>
<td>666</td>
<td>3.8</td>
<td>90</td>
<td>5.9</td>
</tr>
<tr>
<td>0–1.0</td>
<td>143</td>
<td>2.6</td>
<td>21</td>
<td>3.0</td>
</tr>
</tbody>
</table>

* CNS = central nervous system; NA = not applicable.
The Graded Prognostic Assessment score

of this series. These limitations preclude any assessment of the association between survival, GPA, and treatment, but this association will be evaluated in the larger ongoing multiinstitutional validation study of the GPA index.

References


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