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Quantifying the benefit of chemotherapy and radiation in low-grade glioma: A systematic review and meta-analysis of numbers needed to treat.

Timothy J Brown, Daniela Annenelle Bota, Elizabeth A. Maher, Dawit Gebremichael Aregawi, Linda M. Liau, Paul D. Brown, ...

Abstract

Background: The optimal role of chemotherapy and radiation (RT) in adult low-grade glioma (LGG, WHO grade 1 & 2) is unclear. We conducted a systematic review and study-level meta-analysis of the literature on overall survival (OS) and progression free survival (PFS) in patients with LGG. Methods: Pubmed was queried with MeSH terms. All comparative studies of adults with newly diagnosed, supratentorial LGG were included. Comparisons of interest were OS and PFS at 2, 5, and 10 years in chemotherapy versus no chemotherapy and early RT versus delayed or no RT. Data were extracted from studies and synthesized with a random effects model. Quality of evidence was determined by American Academy of Neurology criteria and further analysis was performed, separating high quality (class I and II) from low quality (class III and IV) evidence. Numbers needed to treat (NNT) were determined from the risk difference. Results: 1531 articles were screened; 18 studies were included. Chemotherapy was not associated with a significant survival advantage compared to control. However, an analysis of high quality data revealed a survival advantage at 10 years associated with chemotherapy compared to control with NNT 5 (relative risk death chemo vs control 0.69 [0.56-0.86] p = 0.0006). Furthermore, NNT to prevent one progression with chemotherapy at 5 and 10 years was 6 and 3, respectively. Early RT was not associated with an OS advantage compared to control. However, early RT had progression benefit at all time points, with NNT of 10, 6, and 5 at 2, 5, and 10 years. Conclusions: Further study will be needed to confirm the optimal role of chemotherapy and RT. Caution must be used in interpretation as much of the literature consists of low-quality studies.

<table>
<thead>
<tr>
<th>Event</th>
<th>N (studies)</th>
<th>N (participants)</th>
<th>RR progression (intervention vs control)</th>
<th>Lower 95% CI</th>
<th>Upper 95% CI</th>
<th>P</th>
<th>NNT (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 Year Progression, Chemo vs Control</td>
<td>3</td>
<td>431</td>
<td>0.69</td>
<td>0.55</td>
<td>0.87</td>
<td>0.001</td>
<td>6 (4-12)</td>
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<tr>
<td>10 Year Progression, Chemo vs Control</td>
<td>3</td>
<td>431</td>
<td>0.58</td>
<td>0.39</td>
<td>0.87</td>
<td>0.008</td>
<td>3 (2-10)</td>
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<td>2 Year Progression Early RT vs Control</td>
<td>6</td>
<td>1473</td>
<td>0.66</td>
<td>0.51</td>
<td>0.86</td>
<td>0.002</td>
<td>10 (5-50)</td>
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<tr>
<td>5 Year Progression Early RT vs Control</td>
<td>6</td>
<td>1473</td>
<td>0.73</td>
<td>0.61</td>
<td>0.88</td>
<td>0.0008</td>
<td>6 (4-15)</td>
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<tr>
<td>10 Year Progression Early RT vs Control</td>
<td>4</td>
<td>1114</td>
<td>0.74</td>
<td>0.60</td>
<td>0.91</td>
<td>0.005</td>
<td>5 (3-17)</td>
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</tbody>
</table>