Assessing the Efficacy of Repeat Resections in Recurrent GBM

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Introduction

- Glioblastomas (GBM), comprising 15% of all primary brain tumors, are among the most aggressive central nervous system (CNS) tumors in adults.
- Increased adoption of Stupp protocol has improved prognoses to a current median survival of 14 months. The inevitable recurrence of GBMs has resulted in patients undergoing up to 4 resections with little-to-no benefit to overall survival.
- Careful examination of the added benefit of resection at recurrence allows for future consideration of quality of life metrics in clinical decision-making.

Objectives

1) Describe the current state of Recurrent GBM treatment
2) Discuss the role of repeated resections (RR) in Recurrent GBM
3) Discuss the future of recurrent GBM treatment

Methods

- 191 adult patients with histologically-confirmed GBM treated at Johns Hopkins Hospital
- Covariates investigated included age, Stupp protocol completion, IDH-1 status, MGMT Methylation Status, Karnofsky performance status (KPS), 30-day Readmittance, Length of Stay (LOS), and Gross total vs Subtotal Resection (GTR/STR) at first and RR.
- Primary Outcomes: Overall Survival (OS) and Progression-Free Survival (PFS)
- Bivariate Analyses: \( \chi^2 \)-testing and student t-tests, where appropriate.
- Multivariate Analyses: Cox Proportional Hazards model for OS, adjusting for all investigated covariates except for IDH and Sex. (SAS 9.4)

Results

Table 1 - Demographics and Characteristics

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Single Surgery, n (%)</th>
<th>Repeat Surgery, n (%)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>79 (66)</td>
<td>30 (24)</td>
<td>0.847</td>
</tr>
<tr>
<td>Mean Age</td>
<td>58.85 yrs</td>
<td>56.62 yrs</td>
<td>0.2938</td>
</tr>
<tr>
<td>Mean KPS at Initial Surgery</td>
<td>77.24</td>
<td>84.69 yrs</td>
<td>0.0023</td>
</tr>
<tr>
<td>Patients with GTR at Initial Surgery</td>
<td>85 (67)</td>
<td>74 (57)</td>
<td>0.3581</td>
</tr>
<tr>
<td>Mean Length of Stay at Initial Surgery</td>
<td>6.09 days</td>
<td>3.54 days</td>
<td>0.0020</td>
</tr>
<tr>
<td>Stupp Protocol Completion</td>
<td>79 (63)</td>
<td>42 (31)</td>
<td>0.1917</td>
</tr>
</tbody>
</table>

Table 2 - Analyses of Covariate Effects on Overall Survival

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Univariate p</th>
<th>Multivariate p</th>
</tr>
</thead>
<tbody>
<tr>
<td>STR vs GTR at Initial Surgery</td>
<td>1.737</td>
<td>1.303</td>
</tr>
<tr>
<td>Sex (male v F)</td>
<td>0.077</td>
<td>1.462</td>
</tr>
<tr>
<td>Age</td>
<td>1.023</td>
<td>1.021</td>
</tr>
<tr>
<td>KPS at Initial Surgery</td>
<td>0.984</td>
<td>0.998</td>
</tr>
<tr>
<td>Cognitive Deficit at Presentation</td>
<td>1.691</td>
<td>1.282</td>
</tr>
<tr>
<td>Repeat Resection</td>
<td>0.514</td>
<td>0.620</td>
</tr>
<tr>
<td>IDH Mutation (IDH1 v IDH2)</td>
<td>0.779</td>
<td>0.4720</td>
</tr>
<tr>
<td>MGMT Methylation</td>
<td>0.685</td>
<td>0.562</td>
</tr>
<tr>
<td>30 Day Readmit</td>
<td>1.455</td>
<td>1.519</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>1.044</td>
<td>1.023</td>
</tr>
<tr>
<td>Stupp Completion</td>
<td>0.567</td>
<td>0.532</td>
</tr>
</tbody>
</table>

Discussion

- When comparing single vs RR groups, patients in the RR group had higher KPS and had a longer LOS at initial surgery. This may represent a decreased likelihood for neurosurgeons and neuro-oncologists to suggest a RR for patients with declining function.
- PFS was equivalent among each group which suggests no inherent difference in disease progression. Previously, unequal PFS has been proposed as the driver in OS. However we show that increased OS is more likely due to repeat resection and not inherent disease differences.
- Our results suggest a survival benefit with RR in properly selected patients, as well as collaboration to ensure completion of adjuvant therapy. Utilizing epigenetic data (such as MGMT) may help guide treatment and surgical planning.

Conclusion

Repeat resection for recurrent GBM remains controversial. In our series:
- Patients who received multiple resections demonstrated a remarkable increase in OS.
- Patients who failed to complete standard treatment demonstrated statistically significantly worse OS than counterparts who completed the Stupp Protocol.

Limitations

Our study was purely retrospective, creating the possibility of inherent selection biases for well patients to undergo more aggressive therapies.

Acknowledgements

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References

- Younger Age at Diagnosis (0.979, p = 0.0044)

Entire cohort: 191 Patients
- 119 Male, Median Age: 60.5 years
- 128 vs 63 underwent 1 vs 2+ surgeries, respectively
- Median OS: 12.4 months
- Median PFS: 9.4 months
- Groups were equivalent, except for:
  - Mean KPS at IS was higher in the RR cohort
  - Mean LOS at IS was lower in the RR cohort

Single Surgery vs Repeat Surgery Cohorts:
- Median OS: 8.3 vs 16.9 months, p = 0.0002
- Median PFS: 8.3 vs 10.4 months, p = 0.3100
- In multivariate analyses, the following significantly improved survival:
  - Completion of Stupp Protocol (HR: 0.532, p = 0.0137)
  - MGMT Methylation of GBM (0.562, p = 0.0096)
  - Repeat Resection (0.620, p = 0.0222)
  - Lack of a Readmittance w/in 30 days of discharge (0.658, p = 0.0436)
  - Younger Age at Diagnosis (0.979, p = 0.0044)