Residual Enhancing Tumor Volume Predicts Overall Survival in Recurrent Glioblastoma

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Introduction

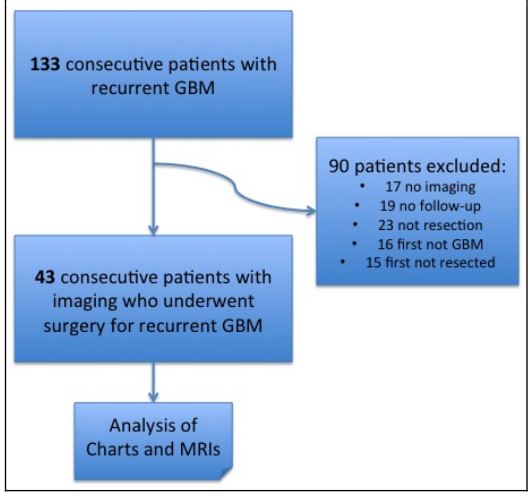
Glioblastoma (GBM) is a highly lethal brain tumor with a median survival of less than two years and a median time to recurrence of about 7 months (Stupp 2005). Residual enhancing tumor volume (RETV) after surgery has been shown to be a better predictor of overall survival (OS), compared to extent of resection (EOR) for newly-diagnosed GBM (Grabowski 2014), but the role of RETV versus EOR in predicting OS has yet to be elucidated in recurrent GBM.

Is RETV a better predictor of OS in glioblastoma patients with first recurrence, compared to EOR?

Methods

This is an IRB-approved retrospective chart review that included volumetric analysis of peri-operative MRIs to evaluate predictors of OS in recurrent GBM. A REDCap database was used to collect and store data. Volumetric analysis of preoperative enhancing tumor volume (PETV) and RETV was completed using BrainLab. Statistical analysis consisted of descriptive statistics as well as the Wilcoxon Rank Sum Test, Fisher's Exact Test, and Cox Proportional Hazards.

Schematic of Case Selection with Exclusion Criteria



Results

43 consecutive patients who underwent surgery for recurrent GBM were identified. Median age at diagnosis was 59 years. Median Karnofsky Performance Score at diagnosis was 90, and it was found to be a significant predictor of survival (p = 0.0214). Median preoperative tumor volume at recurrence was 26.9cm3 while median RETV was 0.9cm3. Median EOR was 94.5%. 48% of patients had intraoperative MRI (iMRI) used for their recurrent resection. Median RETV in patients with iMRI was 0.451cm3 (IQR: 0, 1.095), while median RETV in patients without iMRI was 3.5cm3 (IQR: 0, 5.7); these were significantly different (p = 0.039). Median OS from the date of recurrent resection was 11.9 months. Using the Cox proportional hazards model, RETV and EOR were not found to be significant predictors of OS in the full population; however RETV was associated with OS in patients who did not have iMRIs (p = 0.008), while EOR was not.

Patient Characteristics

	N	Median [Interquartile Range]
Age at Diagnosis (Years)	43	59 [48,64]
Sex (% Female)	43	30
Race (% White)	41	88
Karnofsky Performance Score (KPS) at Original Diagnosis	18	90 [80, 90]
KPS at First Recurrence	36	80 [80,90]

Case Characteristics

	N	Median [Interquartile Range]
IDH Mutation Status (% Wildtype)	20	90
MGMT Methylation (% Methylated)	20	35
Ki-67 (%)	34	24 [10,50]
Intraoperative MRI (% Yes)	42	48

Imaging and Outcomes

	N	Median [Interquartile Range]
Preoperative Enhancing Tumor Volume (cm^3)	43	26.9 [17.4, 41.8]
Residual Enhancing Tumor Volume (cm^3)	43	0.9 [0, 4.8]
Extent of Resection (%)	43	94.5 [87.3, 100]
Overall Survival from Date of Recurrent Surgery (Months)	36	11.9 [6.7, 14.3]

Effects of iMRI

	Yes iMRI (N=20)	No iMRI (N=22)	P-Value
Age at Diagnosis	60 [48.5, 64]	58.5 [49.5, 61]	0.211
Sex (% Female)	20	36	0.314
Race (% White)	85	90	0.605
KPS at Diagnosis	90 [75, 90]	90 [85, 90]	0.429
KPS at First Recurrence	80 [80, 90]	80 [70, 90]	0.336
IDH Mutation Status (% Wildtype)	91	89	1
MGMT Methylation (% Methylated)	30	40	1
Ki-67 (%)	23 [10, 50]	25 [9, 50]	0.848
Preoperative Tumor Volume (cm^3)	21.7 [8.4, 28.3]	35.3 [21.9, 47.0]	0.021
Residual Enhancing Tumor Volume (cm^3)	0.451 [0, 1.095]	3.5 [0, 5.7]	0.039
Extent of Resection (%)	97.1 [92.3, 100]	90.7 [74.4, 100]	0.075
Overall Survival from Date of Recurrent Resection (months)*	10.87 [5.77, 17.50]	8.30 [6.34, 15.21]	0.974

*of patients who reached endpoint

Predictors of Overall Survival

	P-Value
Yes iMRI (N=20)	
RETV	0.185
EOR	0.462
No iMRI (N=22)	
RETV	0.008
EOR	0.082

Conclusions

After adjusting for use of iMRI, RETV was a better predictor of OS than EOR. Remarkably, the use of iMRI consistently produced minimal RETVs to the point where other variables became drivers of OS. Unless functional considerations are present, complete or near complete removal of enhancing tumor should be considered standard of care in recurrent GBM.

Learning Objectives

By the conclusion of this session, participants should be able to:

1) Describe the role of residual enhancing tumor volume in predicting overall survival after resection of recurrent glioblastoma in comparison to extent of resection
2) Discuss the role of intraoperative MRI in complete or near complete removal of recurrent glioblastoma

References

Stupp R, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med. 2005; 352(10): 987-96.
Grabowski M, et al. Residual tumor volume versus extent of resection: predictors of survival after surgery for glioblastoma. J Neurosurg. 2014; 121: 1115-1123.