



Maximal Safe Resection in Glioblastoma: Can We Do Better than Gross Total Resection? A Closer Look in 1175 Patients from a Single Center.

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Introduction

Glioblastoma multiforme (GBM) is the most common and deadliest primary brain tumor. The value of extent of resection (EOR) in improving survival in GBM patients has been repeatedly confirmed, with more extensive resections providing added advantages. We review the survival of patients with significant EORs and assess the relative benefit/risk of resecting 100% of the contrast-enhancing lesion. We also assess the relative benefit/risk of resecting additional surrounding FLAIR abnormality or what we define as super total resection.

Methods

The cohort included 1175 patients with histologically proven GBM in whom $\geq 80\%$ resection was achieved at MD Anderson Cancer Center 1993-2012. Excluded were patients with >1 tumor, those 80 years or older and those with 98 or 99% resection of contrast-enhancing tumor volumes. Patient data and data on tumor characteristics were collected prospectively.

Results

Complete resection of the T1 contrast-enhancing tumor volume was achieved in 76% of patients. The median survival in these patients (15.2 months) was significantly longer than the 9.7 months median in patients with lesser resections ($p<0.001$). This significant survival advantage was achieved without an increase in the risk of overall or neurological postoperative deficits, and after correcting for established prognostic factors including age, KPS, preoperative contrast-enhancing tumor volume, necrosis and cyst, and prior treatment

status. Additional analyses in 645 patients with available data showed that resection of $\geq 53.21\%$ of surrounding FLAIR abnormality beyond the 100% contrast-enhancing resection was associated with prolonged survival compared to less extensive resections (median 20.7 months vs. 15.2 months; $p<0.001$, respectively). This effect was statistically significant ($p<0.001$) among the previously untreated in multivariate analyses.

Conclusions

Based on what is, to our knowledge, the largest single-center series of GBM patients with extensive tumor resections, this study supports the established association between EOR and survival, but also presents additional data that pushing the boundary to 100% resection with removal of additional FLAIR abnormality can result in prolongation of survival without significant increases in postoperative neurological morbidity.

Fig. 1: Overall Survival by Extent of Resection of Contrast-Enhancing Lesion

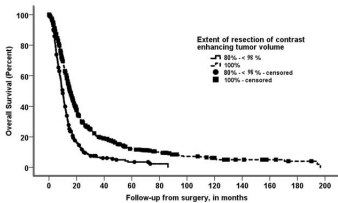


Fig. 2: Overall Survival by Extent of Resection of T2 FLAIR Abnormality

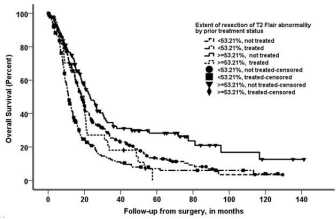


Table 1: Patient and Tumor Characteristics

Variables	All Patients (N=1175)	100% Extent of resection of contrast-enhancing tumor (N=725)	80-99% Extent of resection of contrast-enhancing tumor (N=450)	P value
Age at surgery, years (mean)	55.8	55.5	56.9	0.784
Gender (N, %)				0.93
Male	725	529	196	
Female	450	196	154	
Tumor functional grade (N, %)				
I	165	125	40	
II	155	125	30	
III	155	125	30	
IV	155	125	30	
Preoperative performance (KPS, mean)	80	80	80	10.100
Preoperative KPS, (No. %)				
<70	1058	819	239	
70-80	87	57	30	
Tumor functional grade (N, %)				0.104
I	165	125	40	
II	155	125	30	
III	155	125	30	
IV	155	125	30	
Symptoms before surgery	No	102	17	
Yes	1073	791	282	
Disease status (N, %)				0.103
Newly Diagnosed	707	529	178	
Not Newly Diagnosed	468	196	172	
Necrosis on imaging (N, %)				0.110
No	261	225	36	
Yes	811	599	212	
Cyst on imaging (N, %)				0.001
No	1000	720	280	
Yes	175	105	70	
Pre-operative contrast-enhancing tumor volume, cm ³ , (mean)	5.3	5.3	5.3	0.983
Pre-operative T2 FLAIR abnormality volume, cm ³ , (mean)	47.3	46.9	48.0	0.728
Extent of resection of contrast-enhancing tumor volume (N, %)				
<80%	876	725	151	
80-99%	299	196	103	
Extent of resection of T2 FLAIR abnormality (N, %)				
<53.21%	187	125	62	
53.21-100%	988	600	388	

Table 2: Patient Outcomes

Variables	All Patients (N=1175)	100% Extent of resection of contrast-enhancing tumor (N=725)	80-99% Extent of resection of contrast-enhancing tumor (N=450)	P value
Extent of resection of contrast-enhancing tumor volume (N, %)				
<80%	876	725	151	
80-99%	299	196	103	
Vital status at last follow-up (N, %)				0.02
Alive	876	725	151	
Dead	299	196	103	
Median overall survival (months, mean)	15.2	15.2	15.2	0.001
Postoperative 30 day complications (N, %)				0.05
No	913	725	188	
Yes	262	196	66	
Preoperative 30 day neurological complications (N, %)				0.08
No	963	725	238	
Yes	212	196	16	
Spastic hemiparesis	105	85	20	
Spastic paraparesis	85	65	20	
Visual impairment	85	65	20	
Speech impairment	85	65	20	
Seizures	85	65	20	
Incontinence/urinary retention	85	65	20	
COPD	85	65	20	
Hydrocephalus	85	65	20	
Memory deficit	85	65	20	
Cerebral hernia deficit	85	65	20	
Stroke	85	65	20	
Other	85	65	20	

Table 3: Kaplan-Meier Analysis of Overall Survival

Variables	Total number of patients	Events	Median Survival (months)	95% Confidence Interval
Gender (N, %)				
Male	725	600	13.0	12.5-13.8
Female	450	377	14.4	13.5-15.6
Tumor functional grade (N, %)				
I	165	125	17.7	16.2-20.3
II	155	125	12.9	11.7-14.1
III	155	125	12.9	11.7-14.1
IV	155	125	12.9	11.7-14.1
Symptoms before surgery	No	102	13.3	10.9-15.9
Yes	1073	900	13.5	12.5-14.2
Disease status (N, %)				
Newly Diagnosed	707	572	16.6	14.6-18.9
Not Newly Diagnosed	468	414	10.9	9.5-11.7
Necrosis on imaging (N, %)	No	261	18.3	16.1-20.8
Yes	811	791	12.8	11.8-13.6
Cyst on imaging (N, %)	No	1000	13.0	12.2-13.8
Yes	175	89	21.0	19.7-25.5
Extent of resection of contrast-enhancing tumor volume (N, %)				
<80%	876	722	16.2	14.3-18.3
80-99%	299	264	8.7	6.9-10.7
Extent of resection of T2 FLAIR abnormality (N, %)				
<53.21%	187	185	18.8	17.2-19.9
53.21-100%	988	845	13.4	12.5-14.5

Table 4: Overall Survival N=1175

Variables	HR	95% CI	P value	HR	95% CI	P value
Age at surgery, years (mean)	1.00	1.00	0.05	1.00	1.00	0.001
Gender (N, %)						
Male	1.00					
Female	0.89	0.77	0.005			
Tumor functional grade (N, %)						
I	1.00					
II	1.34	1.10	0.005			
III	1.38	1.08	0.008			
IV	1.00					
Symptoms before surgery	No	1.00				
Yes	1.00	0.90	0.24	0.98		
Disease status (N, %)						
Newly Diagnosed	1.00					
Not Newly Diagnosed	1.86	1.28	0.001	1.96	1.48	0.001
Necrosis on imaging (N, %)	No	1.00				
Yes	1.09	1.00	0.001	1.00		
Cyst on imaging (N, %)	No	1.00				
Yes	0.98	0.47	0.73	0.98	0.48	0.78
Pre-operative contrast-enhancing tumor volume, cm ³	1.004	1.001	0.008	1.005	1.003	0.008
Pre-operative T2 FLAIR abnormality volume, cm ³	1.004	1.001	0.008	1.005	1.003	0.008
Extent of resection of contrast-enhancing tumor volume	1.00			1.00		
<80%	1.91	1.65	0.001	1.96	1.94	0.001

Table 5: Overall Survival N=645

Variables	HR	95% CI	P value	HR	95% CI	P value
Age at surgery, years (mean)	1.00	1.00	0.001	1.00	1.00	0.001
Gender (N, %)						
Male	1.00					
Female	0.89	0.64	0.002			
Tumor functional grade (N, %)						
I	1.00					
II	1.34	1.01	0.04			
III	1.34	0.90	0.005			
IV	1.00					
Symptoms before surgery	No	1.00				
Yes	1.00	0.98	0.38	0.98		
Pre-operative contrast-enhancing tumor volume, cm ³	1.004	1.001	0.007	1.001		
Pre-operative T2 FLAIR abnormality volume, cm ³	1.004	1.000	0.10	1.000		
Disease status	Newly Diagnosed	1.00				
Not Newly Diagnosed	1.86	1.41	0.001			
Extent of resection of T2 FLAIR abnormality	<53.21%	1.00				
53.21-100%	0.88	0.66	0.001			
Disease status, EOR T2 FLAIR	No newly diagnosed	1.00				
Not newly diagnosed	0.88	0.52	0.77	0.88	0.41	0.001
Not newly diagnosed	0.88	0.52	0.77	0.88	0.41	0.001
Newly diagnosed	0.88	0.52	0.77	0.88	0.41	0.001