



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

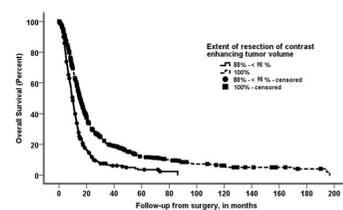


Fig. 2: Overall Survival by Extent of Resection of T2 FLAIR Abnormality

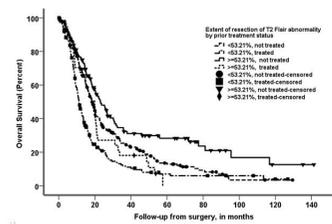


Table 1: Patient and Tumor Characteristics

Variables	All Patients (N=1175)	100% Extent of resection of contrast-enhancing tumor (N=875)	80-99% Extent of resection of contrast-enhancing tumor (N=300)	P value					
Age at surgery, years (mean)	55.8	46.8(0.5)	55.5	4.6(0.02)	0.0784				
Gender (N, %)	725 (61.7)	529 (60.4)	196 (65.0)	0.02	0.04				
Tumor functional grade (N, %)	450 (38.3)	337 (38.5)	113 (37.7)	0.10	<0.001				
Performance status (KPS) (mean)	90	100	80	10.1(0)	<0.001				
Preoperative KPS, (No. %)	1038	89	819	63	289	90	0.0	0.04	
Tumor functional grade (N, %)	1	155	14	151	17	14	6	0	0.04
Symptoms before surgery	No	102	6	80	0	17	0	0	0.02
Yes	1073	91	701	30	282	24	103	0.02	
Disseminated (N, %)	707	60	528	62	168	58	58	0.10	
Newly Diagnosed (N, %)	468	66	337	38	131	44	44	0.10	
Necrosis on imaging (N, %)	No	261	23	225	28	38	12	0.01	
Yes	811	79	645	74	263	30	30	0.01	
Cyst on imaging (N, %)	No	1000	80	750	59	200	94	0.03	
Yes	175	16	153	11	16	6	6	0.001	
Pre-operative contrast-enhancing tumor volume, cm ³ , (mean)	30.0	0.3	180.3	25.9	0.3, 175.1	45.4	3.6, 185.3	<0.001	
Pre-operative T2 FLAIR abnormality volume, cm ³ , (mean)	47.3	<0.01	333.1	45.9	<0.03, 333.1	49.0	0.7, 229.7	0.36	
Extent of resection of contrast-enhancing tumor volume, % (N)	100	876	75	876	100	299	100	0.001	
98-99%	259	25	237	38	131	44	44	0.001	
Extent of resection of T2 FLAIR abnormality, % (N)	187	22	160	25	27	13	13	0.001	
$\leq 53.21\%$	681	78	488	75	175	87	87	0.001	

Table 2: Patient Outcomes

Variables	All Patients (N=1175)	100% Extent of resection of contrast-enhancing tumor (N=875)	80-99% Extent of resection of contrast-enhancing tumor (N=300)	P value			
Extent of resection of contrast-enhancing tumor volume (N, %)	876	75	299	28	0.001		
0-99%	299	28	271	28	0.001		
100%	577	47	228	0	0.001		
Median overall survival (months), (95% CI)	15.2	14.2	16.2	14.6, 16.3	9.7	9.8, 10.7	<0.001
Postoperative 30 day complications, % (N)	913	79	669	79	220	74	0.05
Neurological complications	202	22	183	21	79	20	0.05
Preoperative (N, %)	803	63	728	63	200	79	0.08
Motor deficit	272	19	248	17	64	21	0.08
Speech impairment	105	8	95	6	33	11	0.08
Visual impairment	69	5	61	5	19	5	0.08
Seizure	28	2	24	2	11	4	0.08
Intracranial hemorrhage	16	1	12	1	4	1	0.02
CSF leak	12	1	10	1	2	0.7	0.74
Hydrocephalus	11	1	7	1	4	1	0.08
Seizure	7	1	5	1	4	1	0.08
Central nerve deficit	6	1	5	0	1	0.3	0.03
Stroke	4	1	3	0	1	0.3	0.03
Other	35	3	28	3	9	3	0.07

Table 3: Kaplan-Meier Analysis of Overall Survival

Variables	Total number of patients	Events	Median Survival (months)	95% Confidence Interval	
Gender (N, %)	725	609	13.0	12.5-13.8	
Tumor functional grade (N, %)	450	377	14.6	14.1-15.1	
1	165	125	17.1	16.2-20.3	
2	155	125	12.9	11.7-14.1	
3	130	127	12.3	11.1-14.5	
Symptoms before surgery	No	102	80	13.2	12.5-13.9
Yes	1073	900	13.5	12.5-14.2	
Disseminated (N, %)	707	572	11.6	11.6	
Newly Diagnosed (N, %)	468	414	12.9	12.5-13.7	
Necrosis on imaging (N, %)	No	261	192	18.3	16.3-20.8
Yes	811	709	12.8	12.5-13.6	
Cyst on imaging (N, %)	No	1000	807	13.0	12.5-13.8
Yes	175	161	21.6	19.7-23.5	
Extent of resection of contrast-enhancing tumor volume (N, %)	100%	876	722	15.2	14.1-16.3
98-99%	259	246	9.7	8.9-10.7	
Extent of resection of T2 FLAIR abnormality (N, %)	$\leq 53.21\%$	187	185	18.8	17.7-19.9
>53.21%	681	545	13.4	12.5-14.5	

Table 4: Overall Survival N=1175

Variables	Univariate Analysis			Multivariate Analysis			
	HR	95% CI	P value	HR	95% CI	P value	
Age at surgery, years (mean)	1.03	1.00, 1.05	<0.001	1.00	1.00, 1.01	<0.001	
Gender (N, %)	1.03	0.97, 1.00	0.05	1.00	1.00, 1.01	<0.001	
Tumor functional grade (N, %)	1.00	0.99, 1.00	0.001	1.00	0.99, 1.00	<0.001	
1	1.00	1.00, 1.00	0.001	1.00	1.00, 1.00	<0.001	
2	1.34	1.10, 1.65	0.001	1.00	1.00, 1.00	<0.001	
3	1.28	1.02, 1.64	0.001	1.00	1.00, 1.00	<0.001	
Symptoms before surgery	No	1.00	0.93, 1.24	0.98	1.00	1.00, 1.00	
Yes	1.00	0.93, 1.24	0.98	1.00	1.00, 1.00	<0.001	
Disseminated (N, %)	1.00	1.29, 0.95	<0.001	1.00	1.40, 0.89	<0.001	
Newly Diagnosed (N, %)	1.00	1.29, 0.95	<0.001	1.00	1.40, 0.89	<0.001	
Necrosis on imaging (N, %)	No	1.00	1.30, 1.80	<0.001	1.00	1.40, 0.78	<0.001
Yes	1.00	1.30, 1.80	<0.001	1.00	1.40, 0.78	<0.001	
Cyst on imaging (N, %)	No	1.00	0.47, 0.73	<0.001	1.00	0.40, 0.78	<0.001
Yes	1.00	0.47, 0.73	<0.001	1.00	0.40, 0.78	<0.001	
Pre-operative contrast-enhancing tumor volume, cm ³ (mean)	1.004	1.001, 1.003	0.001	1.005	1.003, 1.006	<0.001	
Pre-operative T2 FLAIR abnormality volume, cm ³ (mean)	1.001	1.001, 1.001	0.001	1.001	1.001, 1.001	<0.001	
Extent of resection of contrast-enhancing tumor volume	1.00	1.00	0.001	1.00	1.00	<0.001	
100%	1.91	1.65, 2.20	<0.001	1.00	1.34, 0.82	<0.001	
98-99%	1.91	1.65, 2.20	<0.001	1.00	1.34, 0.82	<0.001	

Table 5: Overall Survival N=645

Variables	Univariate Analysis			Multivariate Analysis			
	HR	95% CI	P value	HR	95% CI	P value	
Age at surgery, years (mean)	1.03	1.00, 1.04	<0.001	1.00	1.00, 1.01	<0.001	
Gender (N, %)	1.03	0.94, 0.92	0.004	1.00	1.00, 1.01	<0.001	
Tumor functional grade (N, %)	1.00	0.99, 0.99	<0.001	1.00	0.99, 0.99	<0.001	
1	1.00	0.99, 0.99	<0.001	1.00	0.99, 0.99	<0.001	
2	1.29	1.01, 1.65	0.04	1.00	1.00, 1.00	<0.001	
3	1.34	0.93, 1.93	0.17	1.00	1.00, 1.00	<0.001	
Symptoms before surgery	No	1.00	0.78, 1.28	0.98	1.00	1.00, 1.00	
Yes	1.00	0.78, 1.28	0.98	1.00	1.00, 1.00	<0.001	
Disseminated (N, %)	1.00	1.00, 1.00	0.10	1.00	1.00, 1.00	<0.001	
Newly Diagnosed (N, %)	1.00	1.41, 2.02	<0.001	1.00	1.41, 2.02	<0.001	
Necrosis on imaging (N, %)	No	1.00	1.30, 1.80	<0.001	1.00	1.40, 0.82	<0.001
Yes	1.00	1.30, 1.80	<0.001	1.00	1.40, 0.82	<0.001	
Pre-operative contrast-enhancing tumor volume, cm ³ (mean)	1.004	1.001, 1.003	0.001	1.005	1.003, 1.006	<0.001	
Pre-operative T2 FLAIR abnormality volume, cm ³ (mean)	1.001	1.001, 1.001	0.001	1.001	1.001, 1.001	<0.001	
Extent of resection of contrast-enhancing tumor volume	1.00	1.00	0.001	1.00	1.00	<0.001	
100%	1.91	1.65, 2.20	<0.001	1.00	1.34, 0.82	<0.001	
98-99%	1.91	1.65, 2.20	<0.001	1.00	1.34, 0.82	<0.001	