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ORIGINAL ARTICLE

Do elderly patients (≥ 75 years old) with glioblastoma benefit from more radical surgeries in the era of temozolomide?

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Abstract

This study assesses the effect of extent of resection (EOR) on the longer-term survival and early mortality of elderly patients (≥ 75 years old) with glioblastoma. We used the Surveillance, Epidemiology, and End Results (SEER) database and data from our center to evaluate the effect of EOR on the long-term survival and early mortality of patients with glioblastoma. We included 50 elderly patients (≥ 75 years old) with glioblastoma visiting our hospital. The median overall survival of the patients who underwent a gross total resection, a subtotal resection, and a partial resection were 278, 200, and 83 days, respectively. The multivariate analysis showed that gross total resection (HR: 0.100; 95% CI: 0.015–0.671, $p < 0.001$) and subtotal reresection (HR: 0.134, 95% CI: 0.022–0.831, $p < 0.001$) were independent predictors of favorable prognosis when compared with partial resection. The data extracted from the SEER database also indicated that EOR was an independent predictor of OS, CCS, and early mortality. The stratification analysis revealed that gross total resection was the best protective factor of OS, early mortality, and CCS. Radical resection may improve the OS and CCS of glioblastoma patients aged ≥ 75 years and decrease early mortality.

Keywords Glioblastoma · Overall survival · Extent of resection · Early mortality

Introduction

Glioblastoma (GBM) is a malignant brain tumor found in adult patients, which primarily occurred in patients aged 65 years or older [20]. The clinical outcome of GBM patients remained poor even after the gross total resection of the tumor followed by adjuvant radio- and chemotherapy [1]. The prognosis of GBM patients also worsens as age increases [9, 19]. Elderly patients have a median overall survival of 6 months when compared with younger patients with GBM patients [2, 14]. This may be due to concomitant disorders and the use of less aggressive treatments [5]. A previous study indicated that a safe maximal resection may confer a modest survival benefit for GBM patients (> 65 years old). On the other hand, the use of standard treatments and additional chemotherapeutics may increase their overall survival [4]. Another study also showed that the elderly patients with GBM who underwent a gross total resection experienced enhanced survival [3]. This suggests that aggressive treatments could be appropriate for elderly patients with GBM. However, some studies revealed that the patients aged 75 or older experienced significantly worse survival compared with elderly patients aged < 75 years [4]. This suggests that the survival and early mortality of elderly patients (≥ 75 years old) deserve more attention. As a result, this study aims to assess the effect of extent of resection (EOR) on the longer-term survival and early mortality of elderly patients (≥ 75 years old) with GBM.

Materials and methods

Patients

We enrolled elderly patients (≥ 75 years old) with GBM who underwent their tumor resection in the West China Hospital from 2014 to 2018 in the present study. Furthermore, we used the Surveillance, Epidemiology, and End Results (SEER) database to evaluate the effect of EOR on the long-term survival and early mortality of patients with GBM. We enrolled GBM patients aged 75 years or older with a

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diagnosed confirmation in the era of TMZ (2005–2016). This study was approved by the Institutional Review Board of the West China Hospital.

Treatments

Patients included in this study received gross total, subtotal, and partial resection. A total radiotherapy dose of 50–54 Gy was given in 25–30 fractions (1.8–2.0 Gy once daily, 5 days per week). During radiotherapy, temozolomide (75 mg/m^2 per day) was taken orally for concurrent chemoradiotherapy. Adjuvant chemotherapy with temozolomide started on the 28th day after radiotherapy, which mainly consisted of 6 cycles of temozolomide, 150 to 200 mg/m^2 per day for five consecutive days, repeated every 4 weeks. Radiotherapy alone, temozolomide alone, and radiotherapy plus temozolomide were identified as salvage treatments.

Parameters

We collected variables including age at diagnosis, gender, preoperative KPS, tumor location, MGMT promoter methylation (yes or no), TERT mutation (yes or no), IDH1 mutation (yes or no), EOR (partial, subtotal, gross total), radiation, and chemotherapy. For the SEER data, we extracted the information regarding age at diagnosis (< 80 and ≥ 80 years old), gender (male vs. female), marital status (married, divorced/separated, widowed, and single), tumor location (frontal, temporal, parietal lobe, and other sites), tumor size (0–3, 3–5, and > 5 cm), EOR (no surgery, biopsy, subtotal resection, and gross total resection), adjuvant treatments(radiotherapy alone, chemotherapy alone, Stupp regimen, radiotherapy plus chemotherapy, and none).

Definition of EOR

All patients underwent intraoperative electrophysiological monitoring. Surgical tools such as intraoperative ultrasound, navigation, and 5-ALA were used to ensure safe removal of tumors for some patients. The evaluation of EOR was mainly based on volumetric measurements by postoperative MRI within 72 h. Ninety percent tumor volume removal was defined as gross total resection, 80–90% removal was identified as subtotal resection, less than 80% removal was defined as partial resection.

Statistical analysis

In this study, we primarily focused on the overall survival (OS), cancer-specific survival (CCS), and early mortality of elderly patients with GBM. We defined the OS as the duration from diagnosis to death or last follow-up and the CCS as the duration from diagnosis to death resulting from the GBM. We calculated the early mortality from the proportion of patients who were deceased within 3 months after the initial diagnosis. We used the SPSS version 25 (IBM Corporation, Armonk, NY) to perform all the statistical analyses in the present study. We used univariate analysis and

Table 1 The ≥ 75 years old from the author hospital

Characteristics	Frequency (%)
Gender	
Male	39 (78%)
Female	11 (22%)
Age (year)	77.22 ± 2.93
Preoperative KPS (IQR)	80 (70,80)
Preop symptoms	
Motor deficit	23 (46%)
Sensory deficit	2 (4%)
Seizure	3 (6%)
Headaches/nausea/vomiting	13 (26%)
Language deficit	5 (10%)
Confusion/memory loss	8 (16%)
Tumor location	
Frontal	25 (50%)
Temporal	17 (34%)
Parietal	10 (20%)
Occipital	7 (14%)
Other	7 (14%)
Eloquent area	
Yes	6 (12%)
No	44 (88%)
MGMT methylation	22 (44%)
TERT mutation	21 (42%)
IDH1 mutation	0 (0%)
Extent of resection	
Partial	4 (8%)
Subtotal	7 (14%)
Gross total	39 (78%)
Adjuvant treatments	
Radiation	26 (52%)
Chemotherapy	26 (52%)

Table 2 The basic characteristics of chemotherapy and radiotherapy in patients with different degrees of tumor resection

Parameter	Gross total	Subtotal	Partial
Stupp	13	1	1
RT + Chemo	3	0	0
RT alone	3	2	0
Chemo alone	3	0	0
None	16	4	4

RT, radiotherapy; *Chemo*, chemotherapy

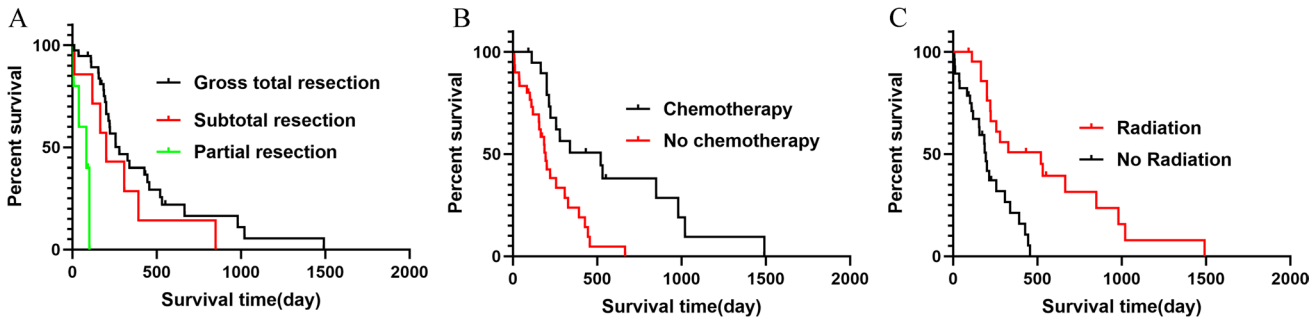

Fig. 1 The prognostic role extent of resection (**A**), chemotherapy (**B**), and radiation (**C**) in elderly GBM patients from the author center

multivariate analysis with Cox proportional hazards regression to evaluate the role of EOR in predicting the survival of patients with GBM. We defined a p-value < 0.05 with two sides as statistically significant.

Results

We included 50 elderly patients (≥ 75 years old) with GBM visiting our hospital. The mean age at diagnosis was 77.22 ± 2.93 years (Table 1). Among the patients, 39 (78%) were male and 11 (22%) female. The most common tumor site was located in the frontal lobe (50%); it was followed by the temporal lobe (34%), the parietal lobe (20%), and the occipital lobe (14%). We also identified 6 (12%) patients involved with eloquent areas. We found that 44% of the patients harbored methylation of the MGMT promoter and 42% a TERT mutation. We did not identify any IDH1 mutant GBM or GBM with co-deletion of 1p19q. Thirty-eight (78%) patients underwent gross total resection, 14% subtotal resection, and 8% partial resection. We calculated that 52% of the patients received radiation and chemotherapy. Among those patients, 15 (30%) patients experienced Stupp regimen, and 6%, 10%, and 6% patients received radiotherapy plus TMZ, radiotherapy alone, and TMZ alone, respectively. Table 2 shows the distribution of patients who received radiotherapy and chemotherapy in each group of the gross total, subtotal, and partial resection. A total of 14 (36.8%) patients with MGMT promoter methylation received gross total resection and 5 (71.4%) and 3 (60%) of patients underwent subtotal and partial resection, respectively. The median OS for the patients who underwent gross total resection, subtotal resection, and partial resection were 278 days (95% CI: 144.342–411.658), 200 days (95% CI: 110.182–289.818), and 83 days (95% CI: 0–179.618), respectively (Fig. 1). The multivariate analysis showed that gross total resection (HR:

Table 3 The multivariate analysis of OS in elderly patients with glioblastoma from author hospital

Characteristics	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Gender	1.229 (0.557–2.617)	0.593	0.920 (0.374–2.262)	0.856
KPS < 80	2.099 (1.044–4.220)	0.037	2.299 (0.825–6.407)	0.111
Tumor location				
Frontal	Ref	1	Ref	1
Temporal	1.045 (0.515–2.123)	0.903	0.761 (0.311–1.862)	0.549
Parietal	0.903 (0.267–3.060)	0.87	0.742 (0.170–3.234)	0.692
Occipital	0.536 (0.120–2.385)	0.413	0.385 (0.061–2.411)	0.308
Other	1.086 (0.342–3.450)	0.889	1.570 (0.389–6.326)	0.526
MGMT methylation	0.660 (0.343–1.272)	0.215	0.706 (0.264–1.893)	0.490
TERT mutation	1.160 (0.614–2.193)	0.648	3.257 (1.384–7.664)	0.007
Extent of resection				
Partial	Ref	1	Ref	1
Subtotal	0.084 (0.016–0.448)	0.004	0.134 (0.022–0.831)	0.031
Gross total	0.052 (0.011–0.243)	< 0.001	0.100 (0.015–0.671)	0.018
Adjuvant treatments				
Radiation	0.295 (0.150–0.581)	< 0.001	0.562 (0.200–1.584)	0.276
Chemotherapy	0.237 (0.115–0.488)	< 0.001	0.258 (0.096–0.699)	0.008

Table 4 The basic characteristics for glioblastoma patients ≥ 75 years old from the SEER database

Characteristics	All cohort (%)	Death within 3 months (%)
Gender		
Male	3291 (54.14%)	1370 (22.54%)
Female	2788 (45.86%)	1174 (19.31%)
Age (year)		
75–79	3204 (52.71%)	1130 (18.59%)
80–84	2019 (33.21%)	962 (15.82%)
≥ 85	856 (14.08%)	452 (7.44%)
Year of diagnosis		
2005–2010	2819 (46.37%)	1193 (19.62%)
2011–2016	3260 (53.63%)	1351 (22.22%)
Tumor location		
Frontal	1622 (26.68%)	681 (11.20%)
Temporal	1575 (25.91%)	585 (9.62%)
Parietal	1032 (16.98%)	427 (7.02%)
Occipital	323 (5.31%)	105 (1.72%)
Others	1527 (25.12%)	746 (12.27%)
Tumor size (cm)		
0–3	1195 (19.66%)	430 (7.07%)
3–5	2248 (36.98%)	895 (14.72%)
> 5	1660 (27.31%)	741 (12.20%)
Unknown	976 (16.06%)	478 (7.86%)
Surgery		
Non-surgery	1735 (28.54%)	1014 (16.68%)
Biopsy	1176 (19.35%)	507 (8.34%)
Subtotal/partial	1570 (25.83%)	573 (9.43%)
Gross total	1598 (26.29%)	450 (7.40%)
Radiotherapy		
Yes	2606 (42.87%)	476 (7.83%)
No	3473 (57.13%)	2068 (34.02%)
Chemotherapy		
Yes	2762 (45.44%)	546 (8.98%)
No	3317 (54.56%)	1998 (32.87%)
Marital status		
Married	3575 (58.81%)	1411 (23.21%)
Divorced/separated	326 (5.36%)	141 (2.32%)
Single	355 (5.84%)	160 (2.63%)
Widowed	1594 (26.22%)	735 (12.09%)
Unknown	229 (3.77%)	97 (1.59%)
Vital status		
Alive	399 (6.56%)	
Dead	5680 (93.44%)	

0.100; 95% CI: 0.015–0.671) and subtotal reresection (HR: 0.134, 95% CI: 0.022–0.831) were independent predictors of favorable prognosis when compared with partial resection (Table 3). The 3-month mortality was 14% for our elderly patients. In these patients, two patients died of heart failure, 2 died of tumor progression, the remaining 2 patients died of pneumonia and septicemia, respectively. We could not perform further analysis to identify the risk factors associated with early mortality and CCS because of the small sample size. We identified 3 (6%) patients who underwent postoperative complications including hydrocephalus, surgical hematoma, and septicemia. One patient with a tumor located in the third ventricle developed hydrocephalus on the third day after the operation and then ventricular drainage was performed. One patient with left frontal diffuse astrocytoma experienced surgical hematoma on the second day following resection, and reoperation was conducted to remove the hematoma for this patient. The remaining patient was initially infected in the surgical area and eventually developed bacteremia and died 1 month after surgery. The EOR did not affect the development of postoperative complications (relative risk: 1.017, p: 0.985). Following tumor resection, 2 (4%) and 3 (6%) patients developed new language impairments and motor deficits, respectively. Motor impairment arose in 1 (2%) patient while both language and motor deficit experienced complete recovery in 2 (4%) and 2 (4%) patients, respectively, on long-term follow-up. However, no association was observed between EOR and the development of new neurological deficit following operation (relative risk: 1.018, p: 0.979).

Furthermore, we used the SEER database to verify our results. We also explored the role of EOR on CCS and early mortality. We enrolled a total of 6079 elderly patients (≥ 75 years old) with GBM from the SEER database. We found that 1598 patients underwent gross total resection and 1570 patients subtotal/partial resection. Additionally, 1176 patients had biopsies and 1735 patients did not experience any surgery. Unfortunately, 2544 patients died within 3 months following the initial diagnosis and the 3-month mortality was 41.85% (Table 4). The median OS for patients who underwent gross total resection, subtotal/partial resection, biopsy, and no surgery were 6 months (95% CI: 5.54–6.46), 4 months (95% CI: 3.72–4.28), 3 months (95% CI: 2.72–3.27), and 2 months (95% CI: 1.87–2.12), respectively. The median CCS of patients who received gross total resection, subtotal/partial resection, biopsy, and no surgery were 9 months (95% CI: 8.24–9.76), 6 months (95% CI: 5.51–6.49), 5 months (95% CI: 4.50–5.49), and 3 months (95% CI: 2.74–3.26), respectively. Table 5 presents the survival range, mean, and median for each of the gross total resection, subtotal/partial resection, biopsy, and no surgery groups subdivided into radiotherapy alone, chemotherapy alone, both, and none. The median and mean overall survival of patients receiving chemotherapy plus radiotherapy following tumor gross total resection was longer than patients experiencing other therapeutic regimes (Table 5). The 3-month mortality following gross total resection, subtotal/partial resection, biopsy, and no surgery was 28.16%, 36.50%, 43.11%, and 58.44%, respectively.

Table 5 The survival information based on the therapeutic schedule

Variables	OS(months)			CCS(months)		
	Median	Mean	Range	Median	Mean	Range
No surgery + none	1	2.294	0–45	1	2.132	0–51
Biopsy + none	1	2.521	0–81	1	2.322	0–87
Subtotal + none	2	2.668	0–48	2	2.668	0–46
Gross + none	5	6.49	0–112	6	7.18	1–112
No surgery + RT	1	7	1–13	1	4	0–15
Biopsy + RT	3	4.401	0–33	3	4.931	1–31
Subtotal + RT	3	6.447	0–62	4	7.481	0–69
Gross + RT	5	7.08	0–81	7	7.31	0–89
No surgery + Chemo	2	6.19	0–21	2	6.88	0–20
Biopsy + Chemo	3	8.44	0–62	3	5.56	0–51
Subtotal + Chemo	4	5.714	0–35	4	5.324	0–33
Gross + Chemo	5	7.193	0–86	7	8.003	0–87
No surgery + RT + Chemo	4	5.648	2–16	4	6.344	1–17
Biopsy + RT + Chemo	4	6.234	0–118	4	5.004	0–115
Subtotal + RT + Chemo	7	10.352	0–88	8	9.657	0–89
Gross + RT + Chemo	10	14.241	0–122	11	15.31	1–122

RT, radiotherapy; *Chemo*, chemotherapy

The multivariate analysis indicated that EOR was an independent predictor of OS, CCS, and early mortality (Tables 6 and 7) for elderly patients with GBM. The patients who underwent gross total resection (HR: 0.566; 95% CI: 0.472–0.680, $p < 0.001$) and subtotal/partial resection (HR: 0.796; 95% CI: 0.665–0.791, $p < 0.001$) had a longer OS than the patients who had biopsies. We did not detect any difference between the survival of the patients who had a biopsy or no surgery. The patients who underwent gross total resection (HR: 0.776; 95% CI: 0.721–0.836, $p < 0.001$) also showed longer OS compared with the patients who experienced subtotal/partial resection. We also observed the same results regarding the CCS (Table 6). As for early mortality, we found that gross total resection (HR: 0.561; 95% CI: 0.467–0.673, $p < 0.001$) and subtotal/partial resection (HR: 0.790; 95% CI: 0.661–0.994, $p < 0.001$) may decrease the 3-month mortality following diagnosis when the biopsy was taken as a reference (Table 7). Furthermore, gross total resection is more effective in reducing early mortality than subtotal/partial resection (OR: 0.710; 95% CI: 0.598–0.843, $p < 0.001$).

We next performed a stratification analysis to evaluate the clinical role of EOR in elderly patients with GBM (Tables 8, 9, and 10). The stratification results based on gender, age, marital status, tumor location, tumor size, radiation, and chemotherapy indicated that gross total resection was the best protective factor of longer OS and CCS (Tables 8 and 9). For example, gross total resection may improve the OS and CCS in patients aged 75 to 79 and 80 to 84 years ($p < 0.05$). Although gross total resection did not affect the OS of patients aged 85 + years, their CCS was prolonged after gross total resection when we used biopsy as a reference (Tables 8 and 10). Furthermore, gross total resection reduced the early mortality of different subgroups when compared with other EOR as revealed by the stratification results based on gender, age, marital status, tumor location, tumor size, radiation, and chemotherapy (Table 10). For instance, gross total resection was an independent predictor of low early mortality in cohorts consisting of patients aged 75 to 79, 80 to 84, and 85 + years ($p < 0.05$).

Discussion

GBM patients constitute a large proportion of patients with brain tumors each year because of the increasing population of elderly people worldwide. In the face of an aging population, strong evidence and surgical decision-making guidelines are necessary when patients are admitted to the hospital. However, only a few studies focused on the optimization of surgical treatments for patients aged over 75 years. As a result, we used a public database and data from our center to evaluate the clinical role of EOR in elderly patients with GBM. Our results indicate that gross total resection may improve the OS and CCS of elderly patients with GBM. Furthermore, gross total resection was associated with decreased early mortality following diagnosis. Our stratification analysis also revealed that gross total resection was the best protective factor for prognosis and early mortality in different subgroups.

Due to the higher mortality rate in the elderly population, reducing the loss of neurological function after tumor

Table 6 The multivariate analysis of OS and CCS in elderly patients with glioblastoma

Characteristics	OS				CCS			
			95% CI				95% CI	
	p	HR	Low CI	High CI	p	HR	Low CI	High CI
Sex								
Male	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Female	0.137	0.908	0.800	1.031	0.037	0.929	0.867	0.995
Age (year)								
75–79	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
80–84	0.000	1.158	1.092	1.228	0.001	1.130	1.052	1.215
≥ 85	0.000	1.197	1.105	1.298	0.009	1.141	1.033	1.260
Year								
2005–2010	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
2011–2016	0.077	1.112	0.989	1.252	0.337	1.032	0.968	1.100
Tumor location								
Frontal	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Temporal	0.238	0.906	0.768	1.067	0.019	0.899	0.822	0.982
Parietal	0.866	1.016	0.847	1.219	0.205	0.938	0.849	1.036
Occipital	0.021	0.712	0.534	0.951	0.457	0.944	0.811	1.099
Other location	0.100	1.146	0.974	1.348	0.270	1.051	0.962	1.149
Tumor size (cm)								
0–3	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
3–5	0.007	1.256	1.065	1.482	0.003	1.144	1.046	1.253
> 5	0.000	1.600	1.341	1.909	0.000	1.301	1.182	1.433
Unknown	0.895	0.979	0.714	1.342	0.644	0.959	0.805	1.144
Marital status								
Married	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Divorced/Separated	0.301	0.871	0.669	1.132	0.652	0.967	0.836	1.118
Single	0.780	1.037	0.804	1.338	0.928	1.006	0.876	1.156
Widowed	0.406	1.065	0.918	1.236	0.031	1.093	1.008	1.184
Extent of resection								
Biopsy	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Subtotal	0.012	0.796	0.665	0.951	0.225	0.942	0.856	1.037
Gross total	0.000	0.566	0.472	0.680	0.000	0.717	0.651	0.790
No surgery	0.745	0.970	0.805	1.168	0.358	1.050	0.946	1.166
Radiotherapy								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.000	0.308	0.263	0.361	0.000	0.597	0.546	0.652
Chemotherapy								
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.000	0.283	0.247	0.325	0.000	0.519	0.481	0.560

resection may be an important factor to be considered in the surgical treatment of gliomas. Maintaining the balance between maximum resection and surgical risk has always been a paramount theme in elderly patients with GBM [6]. The maximum and safe tumor resection is a cornerstone concept for GBM surgery that is also valid for older patients [6]. Roh et al. performed a retrospective study including 40 patients to evaluate the survival benefit of lobectomy over gross total resection without lobectomy for GBM patients in the non-eloquent area [17]. Their results suggest that supratotal resection promotes a higher progression-free survival and overall survival in patients with completely resectable and non-eloquent area GBMs [17]. A previous study also indicated that radical resection conferred a favorable prognosis in elderly patients (≥ 65 years) with GBM [3–5, 7, 10, 14, 18]. A retrospective study including 273 older patients with GBM revealed that the median overall survival of the patients

Table 7 The multivariate analysis of early mortality in elderly patients with glioblastoma

Characteristics	Early mortality			
			95% CI	
	p	HR	Low CI	High CI
Sex				
Male	Ref	Ref	Ref	Ref
Female	0.109	1.109	0.977	1.259
Age (year)				
75–79	Ref	Ref	Ref	Ref
80–84	0.000	1.295	1.136	1.475
≥ 85	0.027	1.221	1.024	1.456
Year				
2005–2010	Ref	Ref	Ref	Ref
2011–2016	0.068	0.896	0.796	1.008
Tumor location				
Frontal	Ref	Ref	Ref	Ref
Temporal	0.239	0.906	0.769	1.068
Parietal	0.825	1.021	0.851	1.225
Occipital	0.023	0.717	0.537	0.956
Other location	0.125	1.135	0.965	1.335
Tumor size(cm)				
0–3	Ref	Ref	Ref	Ref
3–5	0.006	1.260	1.068	1.486
> 5	0.000	1.583	1.327	1.888
Unknown	0.961	0.992	0.724	1.359
Marital status				
Married	Ref	Ref	Ref	Ref
Divorced/separated	0.293	0.868	0.668	1.129
Single	0.715	1.049	0.813	1.352
Widowed	0.169	1.108	0.957	1.284
Extent of resection				
Biopsy	Ref	Ref	Ref	Ref
Subtotal	0.009	0.790	0.661	0.944
Gross total	0.000	0.561	0.467	0.673
No surgery	0.775	0.973	0.808	1.172
Radiotherapy				
No	Ref	Ref	Ref	Ref
Yes	0.000	0.304	0.259	0.356
Chemotherapy				
No	Ref	Ref	Ref	Ref
Yes	0.000	0.276	0.241	0.316

who underwent gross total resection was 12 months. On the other hand, the median overall survival of the patients who underwent subtotal resection and biopsy was 9 and 4 months, respectively. Multivariate analysis showed that EOR was an independent predictor of overall survival [3]. Besides, Heiland et al. [11] showed an increased median OS (10.8 months) for GBM patients with gross total resection. Babu et al. [4] reported that the OS after GTR was 14.1 months compared to only 9.1 months after subtotal resection. Zhang et al. [21] recently also showed that GTR was significantly correlated with longer OS when compared to subtotal resection. However, only few studies have evaluated the predictive effect of surgical resection on the survival of elderly patients (≥ 75 years) with GBM. The elderly patients with GBM (≥ 75 years) who underwent gross total resection had a mean overall survival of 12.1 ± 3.0 months, while the mean overall survival for the patients who underwent subtotal resection and biopsy was 5.0 ± 1.4 months and 3.7 ± 1.1 months, respectively. This indicates that a greater resection volume is significantly correlated with longer survival [13]. The sample size in this study was small and about 50 patients underwent tumor resection. In our study, we enrolled 6078 GBM patients aged more than 75 years to assess the effect of EOR on OS, CCS, and early mortality. The median OS for the patients who underwent gross total resection, subtotal/partial resection, biopsy, and no surgery were 6, 4, 3, and 2 months, respectively. The median CCS of the patients subjected to gross total resection, subtotal/partial resection, biopsy, and no surgery were 9, 5, 4, and 3 months, respectively. Additionally, the data collected from our center also supported that gross total resection was associated with a favorable prognosis. This is in accordance with previous studies involving a younger subset of elderly patients (median age of 61 to 75 years) [3, 4, 16, 18, 21]. Our previous study showed that the rate of early mortality was higher in patients with GBM than with lower-grade glioma. Older patients also had greater odds of early death compared with younger patients [22]. In our study, we found that gross total resection may provide superior 3-month mortality compared to subtotal/partial resection or biopsy. This is the first study to assess the effect of EOR on the early mortality of elderly patients with GBM aged over 75 years. Furthermore, our stratification results revealed that gross total resection was the best protective factor for OS, CCS, and early mortality in our different subgroups when compared with other EOR. This indicates that the maximum safety resection is also suitable for elderly patients with GBM aged over 75 years, even in different subgroups. However, the early mortality of elderly GBM calculated from the SEER dataset was higher than the death rate extracted from our hospital. There are two possible reasons for this phenomenon. On the one hand, the rate of gross total resection was 78% in elderly patients from our hospital, which was higher than 26.29% calculated from the SEER dataset. On the other hand, data extracted from SEER did not exclude patients who underwent biopsy or no surgery, which may contribute to the high early mortality.

Table 8 Stratification analysis for OS

Parameters	No surgery (HR (95% CI), p)	Biopsy	Subtotal/partial (HR (95% CI), p)	Gross total (HR (95% CI), p)
Sex				
Male	1.013 (0.900–1.140), 0.876	1	0.943 (0.847–1.049), 0.466	0.742 (0.666–0.826), < 0.001
Female	0.999 (0.883–1.131), 0.971	1	0.893 (0.794–1.004), 0.231	0.682 (0.607–0.766), < 0.001
Age				
75–79	0.942 (0.828–1.072), 0.291	1	0.916 (0.822–1.020), 0.431	0.700 (0.629–0.779), < 0.001
80–84	0.987 (0.857–1.138), 0.367	1	0.858 (0.747–0.986), < 0.001	0.709 (0.617–0.815), < 0.001
≥ 85	1.185 (0.967–1.452), 0.467	1	1.175 (0.945–1.460), 0.267	0.830 (0.661–1.042), 0.489
Marital status				
Married	0.971 (0.863–1.091), 0.612	1	0.880 (0.794–0.976), < 0.001	0.707 (0.638–0.784), < 0.001
Single	1.026 (0.773–1.436), 0.578	1	1.091 (0.786–1.514), 0.498	0.775 (0.549–1.093), 0.371
Widowed	1.069 (0.910–1.256), 0.387	1	1.016 (0.870–1.188), 0.176	0.690 (0.590–0.807), < 0.001
Divorced/separated	1.625 (1.110–2.379), < 0.001	1	0.618 (0.435–0.878), < 0.001	0.605 (0.427–0.858), < 0.001
Tumor location				
Frontal	1.034 (0.876–1.220), 0.650	1	0.918 (0.785–1.074), 0.281	0.667 (0.572–0.776), < 0.001
Temporal	1.036 (0.861–1.247), 0.698	1	0.972 (0.836–1.131), 0.697	0.825 (0.710–0.959), 0.012
Parietal	0.895 (0.724–1.016), 0.301	1	0.957 (0.786–1.166), 0.670	0.723 (0.598–0.874), < 0.001
Occipital	0.733 (0.478–1.126), 0.188	1	0.763 (0.541–1.076), 0.142	0.688 (0.493–0.960), 0.028
Tumor size (cm)				
1–3	0.910 (0.751–1.103), 0.341	1	1.008 (0.835–1.216), 0.891	0.718 (0.604–0.853), < 0.001
3–5	1.055 (0.912–1.219), 0.478	1	0.981 (0.860–1.119), 0.690	0.791 (0.694–0.901), < 0.001
> 5	1.076 (0.910–1.272), 0.378	1	0.823 (0.710–0.952), 0.011	0.610 (0.524–0.713), < 0.001
Chemotherapy	1.023(0.923–1.132),0.695	1	0.915 (0.823–1.017), 0.096	0.729 (0.653–0.812), < 0.001
Radiotherapy	1.025 (0.935–1.135), 0.602	1	0.955 (0.848–1.075), 0.451	0.727 (0.644–0.821), < 0.001

Table 9 Stratification analysis for CCS

Parameters	No surgery (HR (95% CI), p)	Biopsy	Subtotal/partial (HR (95% CI), p)	Gross total (HR (95% CI), p)
Sex				
Male	1.028 (0.885–1.193), 0.722	1	0.953 (0.833–1.090), 0.480	0.727 (0.634–0.833), < 0.001
Female	1.057 (0.912–1.224), 0.473	1	0.908 (0.790–1.044), 0.144	0.686 (0.598–0.788), < 0.001
Age				
75–79	0.999 (0.853–1.170), 0.691	1	0.940 (0.824–1.073), 0.187	0.724 (0.636–0.825), < 0.001
80–84	1.011 (0.829–1.204), 0.709	1	0.900 (0.759–1.067), 0.086	0.708 (0.595–0.841), < 0.001
≥ 85	1.152 (0.901–1.473), 0.801	1	1.036 (0.795–1.351), 0.759	0.674 (0.507–0.898), < 0.001
Marital status				
Married	1.032 (0.892–1.194), 0.641	1	0.932 (0.819–1.059), 0.248	0.735 (0.646–0.835), < 0.001
Single	1.013 (0.678–1.513), 0.968	1	1.064 (0.719–1.575), 0.758	0.732 (0.484–1.107), 0.142
Widowed	1.063 (0.876–1.290), 0.159	1	0.966 (0.801–1.164), 0.713	0.656 (0.543–0.791), < 0.001
Divorced/separated	1.109 (0.828–1.486), 0.692	1	0.529 (0.346–0.829), < 0.001	0.487 (0.317–0.748), < 0.001
Tumor location				
Frontal	1.006 (0.822–1.231), 0.883	1	0.867 (0.717–1.049), 0.198	0.642 (0.534–0.772), < 0.001
Temporal	1.240 (0.988–1.555), 0.976	1	0.987 (0.818–1.191), 0.985	0.854 (0.708–1.030), 0.672
Parietal	0.923 (0.711–1.199), 0.550	1	0.980 (0.770–1.247), 0.873	0.718 (0.568–0.906), < 0.001
Occipital	0.944 (0.549–1.625), 0.872	1	0.910 (0.591–1.402), 0.661	0.790 (0.517–1.208), 0.284
Tumor size (cm)				
1–3	1.028 (0.807–1.309), 0.807	1	1.125 (0.893–1.417), 0.245	0.707 (0.569–0.879), < 0.001
3–5	1.061 (0.888–1.268), 0.530	1	0.950 (0.809–1.115), 0.568	0.745 (0.634–0.874), < 0.001
> 5	1.094 (0.894–1.342), 380	1	0.825 (0.689–0.986), 0.039	0.662 (0.550–0.797), < 0.001
Chemotherapy	1.035 (0.914–1.171), 0.591	1	0.908 (0.799–1.033), 0.143	0.655 (0.572–0.750), < 0.001
Radiotherapy	1.031 (0.910–1.167), 0.528	1	0.955 (0.826–1.102), 0.693	0.612 (0.520–0.737), < 0.001

Table 10 Stratification analysis for early mortality

Parameters	No surgery (OR (95% CI), p)	Biopsy	Subtotal/partial (OR (95% CI), p)	Gross total (OR (95% CI), p)
Sex				
Male	0.925 (0.712–1.021), 0.569	1	0.802 (0.627–1.025), 0.192	0.592 (0.460–0.762), < 0.001
Female	1.015 (0.778–1.325), 0.865	1	0.763 (0.587–0.991), 0.019	0.551 (0.392–0.667), < 0.001
Age				
75–79	0.861 (0.656–1.130), 0.601	1	0.785 (0.612–1.008), 0.079	0.555 (0.430–0.716), < 0.001
80–84	0.989 (0.721–1.355), 0.387	1	0.720 (0.530–0.980), 0.006	0.638 (0.468–0.870), < 0.001
≥ 85	1.111 (0.702–1.758), 0.376	1	1.015 (0.625–1.650), 0.792	0.385 (0.229–0.647), < 0.001
Marital status				
Married	0.950 (0.735–1.228), 0.671	1	0.717 (0.564–0.911), 0.006	0.531 (0.416–0.679), < 0.001
Single	0.719 (0.343–1.508), 0.421	1	0.592 (0.287–1.219), 0.172	0.506 (0.238–1.075), 0.088
Widowed	1.144 (0.805–1.625), 0.200	1	1.074 (0.761–1.516), 0.342	0.565 (0.398–0.803), < 0.001
Divorced/separated	0.950 (0.466–1.934), 0.903	1	0.767 (0.358–1.645), 0.480	0.801 (0.367–1.750), 0.607
Tumor location				
Frontal	1.110 (0.777–1.587), 0.527	1	0.776 (0.545–1.103), 0.216	0.587 (0.416–0.829), 0.005
Temporal	0.967 (0.649–1.441), 0.859	1	0.788 (0.558–1.112), 0.141	0.645 (0.455–0.914), 0.014
Parietal	0.775 (0.494–1.217), 0.274	1	0.898 (0.578–1.395), 0.628	0.566 (0.366–-0.874), 0.013
Occipital	0.432 (0.171–1.093), 0.076	1	0.344 (0.144–0.823), 0.034	0.337 (0.144–0.787), 0.010
Tumor size (cm)				
1–3	0.795 (0.523–1.208), 0.254	1	0.700 (0.454–1.078), 0.148	0.488 (0.325–0.734), 0.001
3–5	1.070 (0.783–1.464), 0.686	1	0.955 (0.706–1.293), 0.750	0.800 (0.590–1.084), 0.178
> 5	1.154 (0.795–1.676), 0.413	1	0.775 (0.557–1.077), 0.172	0.424 (0.297–0.604), < 0.001
Chemotherapy	1.104 (0.885–1.377), 0.378	1	0.786 (0.629–0.983), 0.044	0.551 (0.439–0.692), < 0.001
Radiotherapy	1.142 (0.912–1.423), 0.243	1	0.877 (0.682–1.127), 0.344	0.593 (0.461–0.763), < 0.001

Although GBM patients older than 75 years could benefit from radical resection, we should consider the limitations in this study. First, the SEER dataset did not provide the genetic information of GBMs, such as the presence of IDH1 mutations, MGMT promoter methylation, TERT mutations, and 1p19q co-deletion. As a result, this information was not included in the analysis. We should further assess the impact of EOR in different subgroups based on genetic information. Second, the SEER database did not provide the type, dose, and course of chemotherapy drugs, nor the dose and course of radiotherapy. Third, data from our hospital showed that there were (24) 48% of patients who did not receive chemotherapy or radiotherapy following tumor resection. Of these patients, 14 (58.33%) refused further chemoradiotherapy due to poor financial ability. In addition, 8 (33.33%) and 2 (8.34%) patients did not undergo chemoradiotherapy because of poor physical condition and medical comorbidities. We should consider these factors in subsequent studies.

Conclusion

The effect of EOR on elderly patients with GBM remains unknown, especially for patients older than 75 years. Elderly patients aged more than 75 years generally receive less-extensive surgeries or no surgery when compared to younger patients [15]. This may be due to their historically dismal prognosis [12]. Furthermore, older GBM patients generally harbor more gene mutations, which may contribute to malignant cell behaviors and diffuse infiltrations [8]. As a result, older patients may suffer from more medical comorbidities than younger ones. It is also more difficult for them to bear longer surgical procedures and hospital stays. However, we found that radical resection may improve OS and CCS and decrease early mortality in GBM patients aged more than 75 years. Our stratification results also revealed that gross total resection was the best protective factor of OS, CCS, and early mortality in different subgroups when compared with other EO. This indicates that maximum safe resection of GBM is also suitable for the elderly aged more than 75 years, even in different subgroups.

Author contribution Yongzhong Cheng designed the study and supervised the research work. Tengfei Li and Yanhui Liu collected data. Xingwang Zhou, Tengfei Li, and Wanchun Yang did the statistical analysis. Tengfei Li wrote the article and Yongzhong Cheng revised it.

Data availability The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Code availability Not applicable.

Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Ethics committee of West China Hospital) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Consent to participate Informed consent was obtained from all individual participants included in the study and their parents/legally authorized representatives.

Consent for publication All the authors agreed to publish this manuscript in Neurosurgical review.

Conflict of interest The authors declare no competing interests.

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