Clinical characteristics and survival outcomes of secondary glioblastoma

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Research

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Abstract

Background Secondary glioblastoma (sGBM) is a specific, and prognostic factors of sGBM are still unclear. This study retrospectively investigated clinical prognosis factors of survival outcomes of sGBM.

Methods All of 125 patients were recruited in this study. Clinical characteristics and survival outcomes were acquired from inpatient records and follow-ups. Kaplan-Meier survival analysis and Cox survival analysis were applied to identifying prognostic factors.

Results The median overall survival (OS) were 301 days. Gross total resection (GTR) (HR = 0.613, 95% confident interval (CI) = 0.408-0.923, p = 0.019), diagnosed sGBM without newly occurring symptoms when regular re-examination (DR) (HR= 0.481, 95% CI = 0.308-0.750, p = 0.001), higher postoperative Karnofsky Performance Status (KPS) score (HR = 0.977, 95% CI = 0.961-0.993, p = 0.006) were independently favorable prognosis factors for OS. GTR was the favorable factor for OS of sGBM patients of DR (HR = 0.238, 95% CI = 0.100-0.570, p = 0.001) and with new functional impairments (HR = 0.410, 95% CI = 0.205-0.821, p = 0.012). Additionally, postoperative KPS score not decreasing was the favorable factor for OS of sGBM patients with new functional impairments (HR = 0.401, 95% CI = 0.202-0.795, p = 0.009) and with new occurring epilepsy (HR = 0.295, 95% CI from 0.092 to 0.950, p = 0.041).

Conclusions For patients with sGBM, GTR, higher postoperative KPS score, and diagnosed without newly occurring symptoms were favorable factors for the OS. The GTR was recommended for sGBM patients to improve survival outcomes.

Background

Compared to primary glioblastoma (pGBM), secondary glioblastoma (sGBM) affects younger patients and progresses from diffuse low-grade (WHO grade II) or anaplastic glioma (WHO grade III).[1, 2] Although it is difficult to distinguish between sGBM and pGBM through histopathology, sGBM has different epidemiological characteristics and genetic profiles compared to pGBM.[3] In addition, the fact that sGBM has a better prognosis than pGBM[4, 5] indicates that sGBM is the less malignant of the two.[6] We can infer that these two types of GBM are distinct from one another; thus, it is important to investigate treatment strategies specific for sGBM.

Surgical resection remains the first-line therapy for recurrent GBM (rGBM).[7, 8] Numerous studies have shown that some clinical characteristics, such as gross total resection (GTR)[7, 9, 10] and preoperative and postoperative KPS scores, were favorable factors for prolonged overall survival (OS) and progression-free survival in patients with rGBM.[10, 11] However, there is limited information on prognostic factors for patients with sGBM. Our previous study on sGBM showed that subtotal resection (STR), poor postoperative Karnofsky Performance Status (KPS) score, and no adjuvant treatment were prognostic factors for poor survival.[12] However, due to the small sample size and the statistical method (univariate analysis) used in that study, [12]the reported finding was not conclusive.

Therefore, in the current study, we enrolled more patients and analyzed more clinical characteristics, including preoperative neurological status and preoperative epileptic status, recorded in the Chinese Glioma Genome Atlas Network. The present study aimed to retrospectively investigate the clinical prognostic factors for the OS of patients with sGBM.

Materials And Methods

Ethics statement

This investigation has been conducted in accordance with the ethical standards and according to the Declaration of Helsinki and according to national and international guidelines and has been approved by local institutional review board.

Patients

We enrolled patients with sGBM who underwent secondary tumor resection at the Glioma Treatment Center at ** Hospital between March 2006 and March 2017. To avoid the influence of different numbers of operations, only patients who underwent two tumor resections were enrolled in the present study, the first resection for a primary low-grade glioma and the second for sGBM. The inclusion criteria were as follows: (1) those aged from 18 to 65 years at the time of tumor resection; (2) diagnosed with sGBM as a secondary diagnosis (their primary pathological diagnosis was low-grade or anaplastic glioma); (3) who had available clinical, postoperative treatment, and follow-up information from the study period. The exclusion criteria were as follows: (1) those who underwent more than two surgeries for glioma resection; (2) those who could not be contacted or refused follow-up; (3) those who underwent biopsy before the second operation.

Data collection

We retrospectively collected patient characteristics from inpatient and follow-up records, including general information (age, sex, etc.), the first and second histopathological diagnoses, IDH status (mutation or wildtype), EOR of the second tumor resection, onset of symptoms, preoperative seizure status, preoperative neurological status, preoperative and postoperative KPS scores, and the difference between preoperative and postoperative KPS scores.

To investigate the different prognoses of patients with various newly occurring symptoms, all patients were divided into four sub-groups as follows: (1) patients with newly occurring epileptic seizures upon diagnosis with sGBM (group E); (2) patients with newly occurring functional impairments, including paralysis, aphasia, and cognitive functional impairments, upon diagnosis with sGBM (group F); (3) patients with other newly occurring symptoms, such as headache and/or vomiting, upon diagnosis with sGBM (group O); and (4) patients without any newly occurring symptoms upon diagnosis with sGBM, based on T1 contrast-enhanced magnetic resonance imaging (MRI) during follow-up (group R).

Evaluation of the EOR

The EOR was evaluated based on the preoperative and postoperative T1 contrast-enhanced MRI by a radiologist with over 25 years of glioma-diagnosis experience. The preoperative and postoperative MRI were scanned within one week prior to surgery and within 72 hours after surgery, respectively. GTR and STR were defined as EOR greater than 90% and between 50% and 90%, respectively.

Statistical analysis

Statistical analysis was performed with SPSS (19.0 version, IBM) and GraphPad Prism 7 (GraphPad Software Inc, San Diego, USA). The Mann-Whitney U-test was used for nonparametric comparisons between two groups. Categorical comparisons between two groups were made using the Chi-square test or Fisher's exact test according to the circumstances. The log-rank test was used to evaluate the survival differences between groups after Kaplan–Meier analysis. A two-tailed p-value < 0.05 was considered statistically significant.

Results

Patient clinical characteristics

One hundred twenty-five patients (mean age, 41.7 years; 79 men) were enrolled in this study (Table 1). Of these, 58 (46.4%) were younger than 40 years, and 67 (53.6%) were older than 40 years. The median follow-up time was 529 days (range, 142–1382). Up to the final follow-up date, 113 patients (90.4%) died and 12 patients (9.6%) were still alive. Additionally, 72 patients (57.6%) underwent GTR and 53 patients (42.4%) underwent STR. Moreover, there were 33 patients (26.4%) in group R, 39 patients (31.2%) in group F, 23 patients (18.4%) in group E, and 30 patients (24.0%) in group O (Fig. 1).

Table 1
Demographic and clinical characteristics of the study population

Characteristics	Number of patients
Gender	
Male	79
Female	46
Age	
Mean age ± SEM (years old)	41.7 ± 0.75
< 40 years old	58
≥ 40 years old	67
Extent of resection	
Total	72
Subtotal	53
Pathological Diagnosis (primary operation)	
Astrocytoma	43
Anaplastic Astrocytoma	11
Oligodendrocytoma	25
Anaplastic Oligodendrocytoma	15
Lower grade but unknown detailed pathology	31
Pathological Diagnosis (secondary operation)	
GBM-O (include oligodendrocyte)	16
GBM	109
Newly occurring functional impairments	
Health	86
Neurological impairments	39
Newly occurring epileptic seizure	
Epileptic seizure	23
Non-epileptic seizure	102
Diagnosis status	
※ KPS = Karnofsky Performance Status	

Characteristics	Number of patients
Without newly occurring symptoms	33
With newly occurring symptoms	92
Preoperative KPS score (secondary operation)	
100	15
90 ~ 100 (< 100)	27
80 ~ 90 (< 90)	34
70 ~ 80 (< 80)	49
Postoperative KPS score (secondary operation)	
90 ~ 100 (≦ 100)	14
80 ~ 90 (< 90)	26
70 ~ 80 (< 80)	41
60 ~ 70 (< 70)	24
50 ~ 60 (< 60)	20
※ KPS = Karnofsky Performance Status	

According to the WHO 2007 criteria, the patients' primary histopathology included astrocytoma (43/125, 34.4%), anaplastic astrocytoma (11/125, 8.8%), oligodendrocytoma (25/125, 20.0%), and anaplastic oligodendrocytoma (15/125, 12.0%). Thirty-one patients (31/125, 24.8%) had low-grade gliomas with unknown detailed pathology.

KPS scores were evaluated before and after the second tumor resection. The preoperative KPS scores were categorized as 70 ~ 80 (< 80), 80 ~ 90 (< 90), 90 ~ 100 (< 100), and 100, with 49, 34, 27, and 15 patients in each group, respectively. Similarly, the postoperative KPS scores were categorized as 50 ~ 60 (< 60), 60 ~ 70 (< 70), 70 ~ 80 (< 80), 80 ~ 90 (< 90), 90 ~ 100 (< 100), and 100, with 20, 24, 41, 26, and 14 patients in each group, respectively.

Prognostic factors for OS in all patients

OS data after the second tumor resection were available for all patients. The median OS of all patients was 301 days (10.0 months) and the mean OS was 400 days (13.3 months). Univariate Cox regression analysis showed that male sex (hazard ratio (HR), 0.678; 95% confidence interval (CI), 0.461–0.997; p = 0.048), GTR (HR, 0.464; 95% CI, 0.317–0.678; p < 0.0001), diagnosis without newly occurring symptoms on follow-up (HR, 0.474; 95% CI, 0.306–0.733; p = 0.0006), high preoperative KPS score (HR, 0.975; 95% CI, 0.958–0.993; p = 0.005), high postoperative KPS score (HR, 0.971; 95% CI, 0.956–0.987; p = 0.0004),

and isocitrate dehydrogenase (IDH) mutation (HR, 0.572; 95% CI, 0.385–0.851; $p = 0.006$) were favorable prognostic factors for OS (Table 2).

Table 2
Univariate and multivariate analysis of secondary OS in all sGBM patients

	Univariate analysis		Multivariate analysis	
	HR (95.0% CI)	p value	HR (95.0% CI)	p value
Gender (male)	0.678 (0.461 to 0.997)	0.048	0.748 (0.495 to 1.130)	0.168
Age	0.992 (0.971 to 1.014)	0.492	-	-
Extent of resection (gross total resection)	0.464 (0.317 to 0.678)	< 0.0001	0.613 (0.408 to 0.923)	0.019
Diagnosed sGBM without newly occurring symptoms	0.474 (0.306 to 0.733)	0.0006	0.481 (0.308 to 0.750)	0.001
Preoperative KPS score (higher KPS score)	0.975 (0.958 to 0.993)	0.005	0.987 (0.965 to 1.009)	0.231
Postoperative KPS score (higher KPS score)	0.971 (0.956 to 0.987)	0.0004	0.977 (0.961 to 0.993)	0.006
Un-decreased postoperative KPS score	0.759 (0.508 to 1.133)	0.177	-	-
IDH status of sGBM (mutation)	0.572 (0.385 to 0.851)	0.006	0.701 (0.465 to 1.055)	0.088
※ KPS = Karnofsky Performance Status				

In addition, multivariate Cox regression analysis revealed that GTR (HR, 0.613; 95% CI, 0.408–0.923; $p = 0.019$), diagnosis without newly occurring symptoms on follow-up (HR, 0.481; 95% CI, 0.308–0.750; $p = 0.001$), and high postoperative KPS score (HR, 0.977; 95% CI, 0.961–0.993; $p = 0.006$) were independent favorable prognostic factors for prolonged OS (Table 2).

Subgroup analysis for prognostic factors for OS

To investigate the factors that affected the OS of patients with various newly occurring symptoms, we divided all recruited patients into four sub-groups based on their new symptoms upon diagnosis with sGBM (Tables 3–6).

Table 3
Univariate and multivariate analysis of secondary OS in sGBM patients in group-R

	Univariate analysis		Multivariate analysis	
	HR (95.0% CI)	p value	HR (95.0% CI)	p value
Age	0.981 (0.935 to 1.030)	0.448	-	-
Extent of resection (gross total resection)	0.238 (0.100 to 0.570)	0.001	0.238 (0.100 to 0.570)	0.001
Preoperative KPS score (higher KPS score)	0.969 (0.937 to 1.003)	0.071	-	-
Postoperative KPS score (higher KPS score)	1.009 (0.967 to 1.053)	0.682	-	-
Un-decreased postoperative KPS score	1.472 (0.582 to 3.724)	0.415	-	-
IDH status of sGBM (mutation)	1.453 (0.634 to 3.331)	0.377	-	-

※ KPS = Karnofsky Performance Status, group-R = patients without any newly occurring symptoms when they were diagnosed as sGBM basing on T1 contrast enhancement MRI when they regularly re-examined.

Table 4
Univariate and multivariate analysis of secondary OS in sGBM patients in group-E

	Univariate analysis		Multivariate analysis	
	HR (95.0% CI)	p value	HR (95.0% CI)	p value
Age	0.980 (0.918 to 1.046)	0.541	-	-
Extent of resection (gross total resection)	0.875 (0.283 to 2.707)	0.816	-	-
Preoperative KPS score (higher KPS score)	1.013 (0.955 to 1.076)	0.664	-	-
Postoperative KPS score (higher KPS score)	0.964 (0.928 to 1.001)	0.056	-	-
Un-decreased postoperative KPS score	0.295 (0.092 to 0.950)	0.041	0.295 (0.092 to 0.950)	0.041
IDH status of sGBM (mutation)	0.391 (0.122 to 1.252)	0.114	-	-

※ KPS = Karnofsky Performance Status, group-E = patients with newly epilepsy when they were diagnosed as sGBM.

Table 5
Univariate and multivariate analysis of secondary OS in sGBM patients in group-F

	Univariate analysis		Multivariate analysis	
	HR (95.0% CI)	p value	HR (95.0% CI)	p value
Age	0.999 (0.960 to 1.041)	0.974	-	-
Extent of resection (gross total resection)	0.410 (0.204 to 0.822)	0.012	0.410 (0.205 to 0.821)	0.012
Preoperative KPS score (higher KPS score)	1.005 (0.941 to 1.074)	0.874	-	-
Postoperative KPS score (higher KPS score)	0.952 (0.924 to 0.982)	0.002	0.988 (0.935 to 1.044)	0.222
Un-decreased postoperative KPS score	0.400 (0.201 to 0.795)	0.009	0.401 (0.202 to 0.795)	0.009
IDH status of sGBM (mutation)	0.944 (0.487 to 1.831)	0.865	-	-

※ KPS = Karnofsky Performance Status, group-F = patients with newly functional impairments such as paralysis, aphasia, cognitive functional deficits when they were diagnosed as sGBM.

Table 6
Univariate and multivariate analysis of secondary OS in sGBM patients in group-O

	Univariate analysis		Multivariate analysis	
	HR (95.0% CI)	p value	HR (95.0% CI)	p value
Age	0.967 (0.929 to 1.007)	0.102	-	-
Extent of resection (gross total resection)	0.984 (0.464 to 2.083)	0.965	-	-
Preoperative KPS score (higher KPS score)	0.984 (0.938 to 1.033)	0.518	-	-
Postoperative KPS score (higher KPS score)	0.993 (0.965 to 1.021)	0.603	-	-
Un-decreased postoperative KPS score	0.943 (0.419 to 2.122)	0.887	-	-
IDH status of sGBM (mutation)	1.049 (0.492 to 2.240)	0.901	-	-

※ KPS = Karnofsky Performance Status, group-O = patients with newly other symptoms, such as headache and/or vomiting, when they were diagnosed as sGBM.

Using univariate Cox regression analysis, we found that GTR was the only favorable prognostic factor for patients in group R (HR, 0.238; 95% CI, 0.100–0.570; $p = 0.001$). Moreover, a consistent or increased postoperative KPS score was the only favorable prognostic factor for patients in group E (HR, 0.295; 95% CI, 0.092–0.950; $p = 0.041$). In addition, for patients in group F, GTR (HR, 0.410; 95% CI, 0.204–0.822; $p = 0.012$), high postoperative KPS score (HR, 0.952; 95% CI, 0.924–0.982; $p = 0.002$), and a consistent or increased postoperative KPS score (HR, 0.400; 95% CI, 0.201–0.795; $p = 0.009$) were favorable prognostic factors. After multivariate Cox regression analysis, GTR (HR, 0.410; 95% CI, 0.204–0.822; $p = 0.012$) and a consistent or increased postoperative KPS score (HR, 0.401; 95% CI, 0.202–0.795; $p = 0.009$) were favorable independent factors for patients in group F. Furthermore, no clinical characteristics were found to affect the OS of patients in group O.

OS outcomes for patients with various newly occurring symptoms

After using the Kaplan–Meier method, our results showed that the independent factors GTR and diagnosis without newly occurring symptoms on follow-up could discriminate the OS of patients with sGBM (Fig. 2, the Kaplan–Meier results of other factors are shown in supplemental Fig. 1). We further subdivided the patients into four sub-groups based on their various newly occurring symptoms upon diagnosis with sGBM. Using Kaplan–Meier analysis, the different OS in these four sub-groups were shown. The OS of patients in group E was significantly longer than that of patients in groups F and O

(Fig. 3). Groups R, F, and O had similar results. However, there was no significant difference in OS between groups E and R. Additionally, there was no significant difference in OS between groups F and O.

Discussion

In the current study, we found that GTR, diagnosis without newly occurring symptoms on follow-up, and high postoperative KPS scores were independent favorable prognostic factors for OS in all patients with sGBM. In addition, other specific clinical characteristics were found to have value for guiding tumor resection in patients with sGBM and various newly occurring symptoms.

The value of the extent of resection in sGBM

GTR is essential for improving OS in patients with GBM.[13] A previous study has verified that reoperation was beneficial for the prognosis of patients with rGBM. [8] Several studies have supported that GTR, especially for the second operation, was an independent favorable prognostic factor for OS in patients with rGBM.[7, 10, 14] However, there are limited studies that focus on the relationship between extent of resection (EOR) and OS in patients with sGBM. Our results showed that GTR was also an independent factor for improved OS in patients with sGBM. This finding helped to confirm the conclusion of our previous study, [12] because the present results were generated with multivariate Cox regression analysis, which allowed us to evaluate the independency of the prognostic factors.

The value of KPS scores in patients with sGBM

Our results were consistent with those of our previous study on sGBM, [12] which reported that a high postoperative KPS score was an independent prognostic factor for the OS of patients with sGBM, whereas preoperative KPS score was not. Undoubtedly, a worsened quality of life leads to extremely poor survival outcomes. As most studies have shown, preoperative KPS score ≥ 70 was a beneficial factor for the OS of patients with rGBM.[7, 15–18] However, this result was not similar to that in the rGBM study.[7, 17] We believe this is because the preoperative KPS scores of all patients in the current study were ≥ 70. Hence, preoperative KPS had no influence on the survival outcomes in this study.

The value of regular follow-up in patients with sGBM

The concept of patients who underwent regular follow-up being diagnosed with sGBM without newly occurring symptoms is similar to that of incidental glioma, in which glioma is diagnosed without any symptoms. Our results showed that a lack of newly occurring symptoms was a favorable independent prognostic factor for OS in patients with sGBM. These findings were consistent with those of a previous study that focused on OS in primary incidental low-grade glioma.[19] The good prognosis for incidental glioma in that study was due to the fact that these tumors were always small and easy to resect entirely. [20] Secondary GBM without newly occurring symptoms meant that the sGBM recurred in the original location and did not invade other functional cortices or subcortical structures. Hence, these tumors were also easy to resect completely. In addition, the postoperative KPS scores did not affect the OS of patients with sGBM in group R; therefore, GTR was recommended for these patients, even if the operation would

decrease their postoperative KPS. Likewise, this finding indicates that regular follow-up was necessary for patients with low-grade glioma; if a recurrent tumor is found, then reoperation should be performed in a timely manner.

The value of new epileptic seizures in patients with sGBM

A glioma-related history of epilepsy is a favorable prognostic factor for OS in patients with glioma.[21, 22] Our results showed that patients with sGBM and new epileptic seizures had prolonged OS. This finding corresponds with our previous finding that epileptic seizures were a favorable independent prognostic factor for OS in low-grade gliomas.[23] Additionally, this result was similar to that in studies on pGBM.[21, 24] We established two hypotheses that may explain these results. First, because sGBM originates from low-grade gliomas, some of the clinical and epidemiological characteristics of sGBM may be inherited from the low-grade glioma. Second, new seizures are likely correlated with the integrity of white matter fibers and, therefore, indicate the reduced ability of the tumor to infiltrate the white matter.[25] Neuron discharges can extend to the subcortical structures (e.g., the thalamus and basal ganglia) and induce epileptic seizures through the white matter. When the white matter fibers are not destroyed, the epileptic discharge pathway is preserved.[26] Thus, a glioma could have a higher chance to induce epilepsy than a more invasive glioma. Therefore, we can infer that the aggressiveness of a seizure-inducing sGBM is weaker than one that does not induce epilepsy, which might have infiltrated and destroyed its surrounding white matter fiber bundles.

Moreover, our results showed that a static or increased postoperative KPS score was a favorable independent factor for patients in group E, whereas GTR was not. This finding indicated that, for these patients, GTR might not be necessary if tumor resection would cause a further decrease in KPS.

The value of new neurological impairments in patients with sGBM

Patients with sGBM and new neurological impairments had worse OS than those without neurological deficits and primary low-grade glioma and GBM.[27] Our findings indicated that new neurological impairments were a detrimental factor for the OS of patients with sGBM. In addition, for patients in group F, GTR and a consistent or increased postoperative KPS score were favorable independent factors for OS. These findings indicated that GTR should be recommended if it will not decrease the quality of life of these patients. In contrast, if GTR would further damage the quality of life of these patients, it may not be necessary.

The value of other newly occurring symptoms in patients with sGBM

In the current study, patients with sGBM and other newly occurring symptoms (such as tumor-related headache and/or vomiting) had a shorter OS. If patients had these symptoms, it indicated that their intracranial pressure was high or they had a potential cerebral hernia induced by a large tumor.[28] For these patients, this observation indicated that the sGBM had significantly progressed. Hence, the OS of

these patients was poor, and no clinical characteristics were found to be benefit for their survival outcomes.

Although most of our results were expected, there are some limitations to the current study. The main limitation is the lack of molecular biomarker information, such as 1p/19q co-deletion and MGMT promoter methylation, because approximately half of the patients underwent primary surgery in other treatment centers. Another limitation is the lack of data on the tumor volumes and diameters; due to the follow-up time for these patients, we were unable to acquire DICOM imaging data or quantitative tumor data. In the future, a prospective observational study is needed to confirm our findings.

Conclusions

For patients with sGBM, GTR, increased postoperative KPS score, and diagnosis without newly occurring symptoms were favorable factors for OS. For patients diagnosed without newly occurring symptoms, we strongly recommend GTR even if GTR would impact their quality of life. For patients diagnosed with newly occurring symptoms, we recommend GTR, assuming that GTR would not impact their quality of life.

Abbreviations

IDH = isocitrate dehydrogenase, GTR = gross total resection, EOR = extent of tumor resection, sGBM = secondary glioblastoma, OS = overall survival, KPS = Karnofsky Performance Scale, ROC = receiver operating characteristic curve, HR = hazard ratio, CI = confident intervention, group E = patients with newly occurring epileptic seizures upon diagnosis with sGBM, group F = patients with newly occurring functional impairments, including paralysis, aphasia, and cognitive functional impairments, upon diagnosis with sGBM, group O = patients with other newly occurring symptoms, such as headache and/or vomiting, upon diagnosis with sGBM, and group R = patients without any newly occurring symptoms upon diagnosis with sGBM, based on T1 contrast-enhanced magnetic resonance imaging (MRI) during follow-up.

Declarations

1. Ethics approval and consent to participate

This study had been approved by IRB of Beijing Tiantan Hospital.

2. Consent for publication

All authors agreed that this manuscript was publicized with open access.

3. Availability of data and materials

Anonymized data will be made available on request.

4. Competing interests

There are no conflicts of interest to declare.

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6. Authors' contribution

- Study concept and design: Fang SY and Li YM.
- Data acquisition and analysis: Fang SY and Li YM.
- Statistics/verified analytic methods: Fang SY, Li YM, and Wang YY.
- Drafting the paper: Fang SY and Li YM.
- Supervision of the study: Li YM, Wang YY, and Jiang T.
- Read and approved the final version: All authors.

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8. Authors' information

Not applicable

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Figures

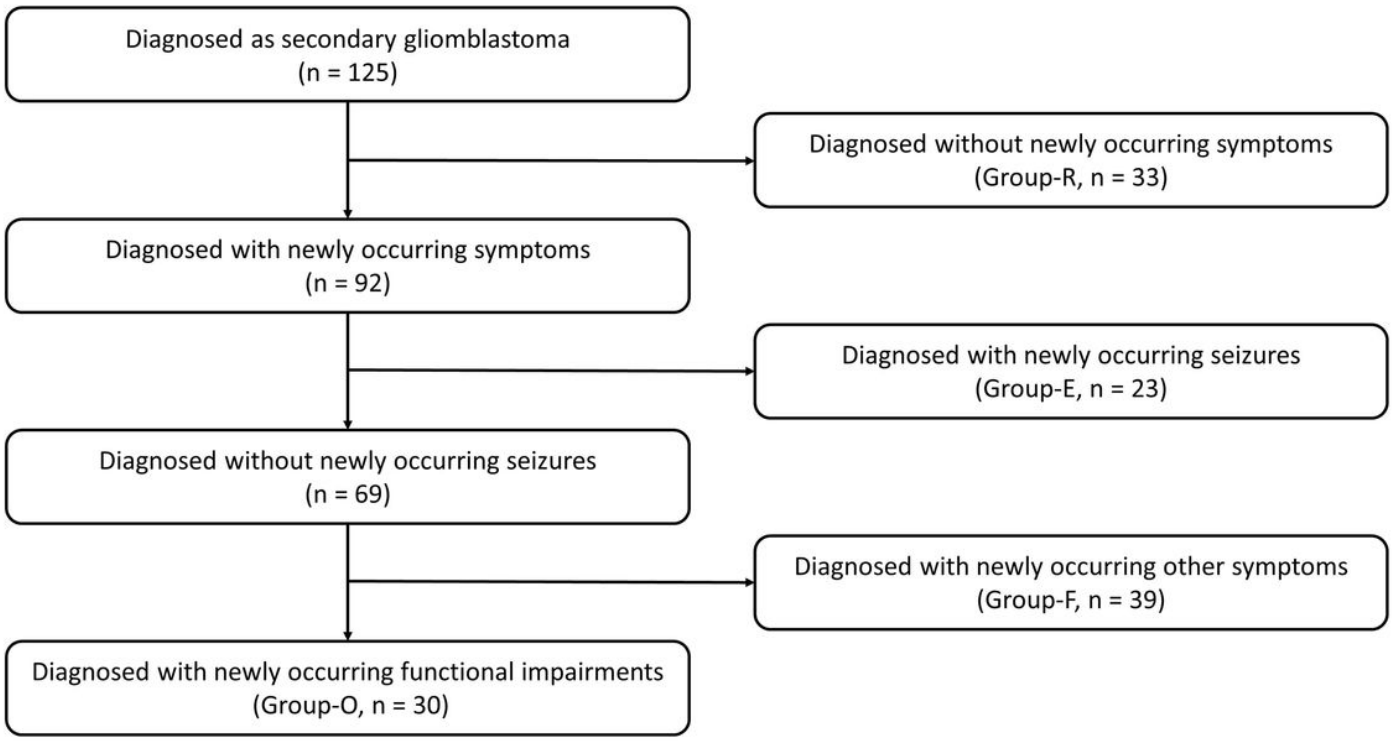

Figure 1

Distribution of patients with secondary glioblastoma (sGBM) in different sub-groups. Group R included patients without any newly occurring symptoms upon diagnosis with sGBM based on T1 contrast-enhanced magnetic resonance imaging (MRI) during follow-up; Group E included patients with new epileptic seizures upon diagnosis with sGBM; Group F included patients with new functional impairments, such as paralysis, aphasia, or cognitive functional impairments, upon diagnosis with sGBM; Group O included patients with other newly occurring symptoms, such as headache and/or vomiting, upon diagnosis with sGBM.

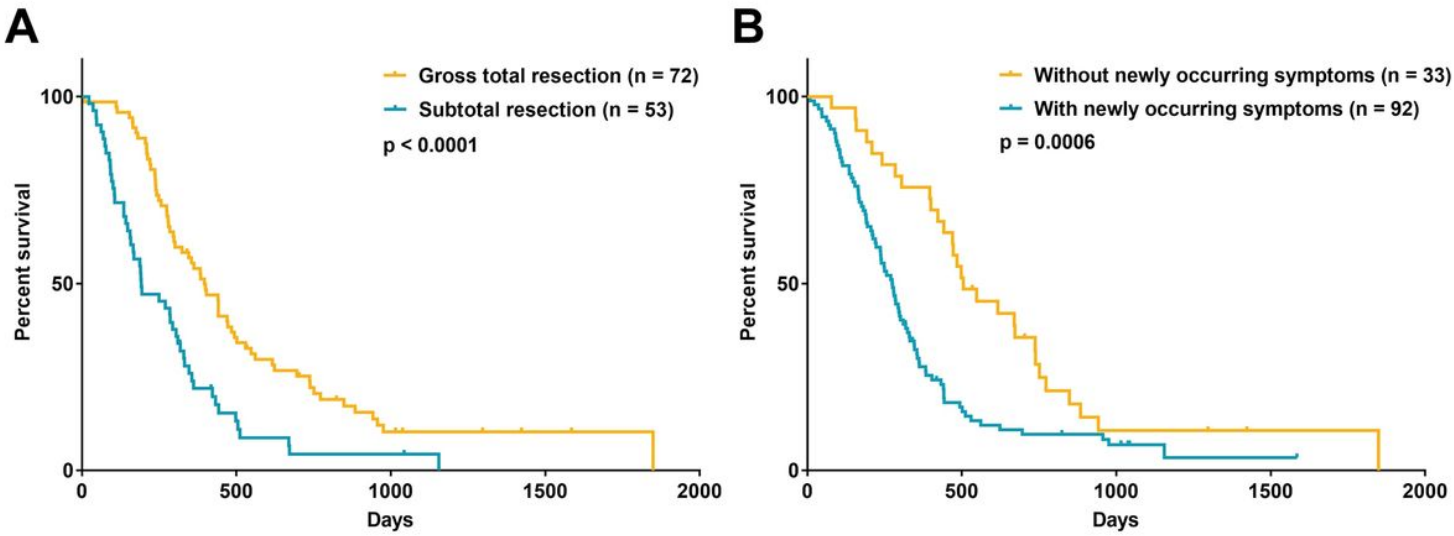

Figure 2

Kaplan–Meier survival curve analysis for different independent prognostic factors for overall survival (OS) in patients with secondary glioblastoma (sGBM). (A) Different OS outcomes in patients with sGBM with different extents of resection. (B) Different OS outcomes in patients with sGBM based on whether the sGBM was diagnosed without newly occurring symptoms.

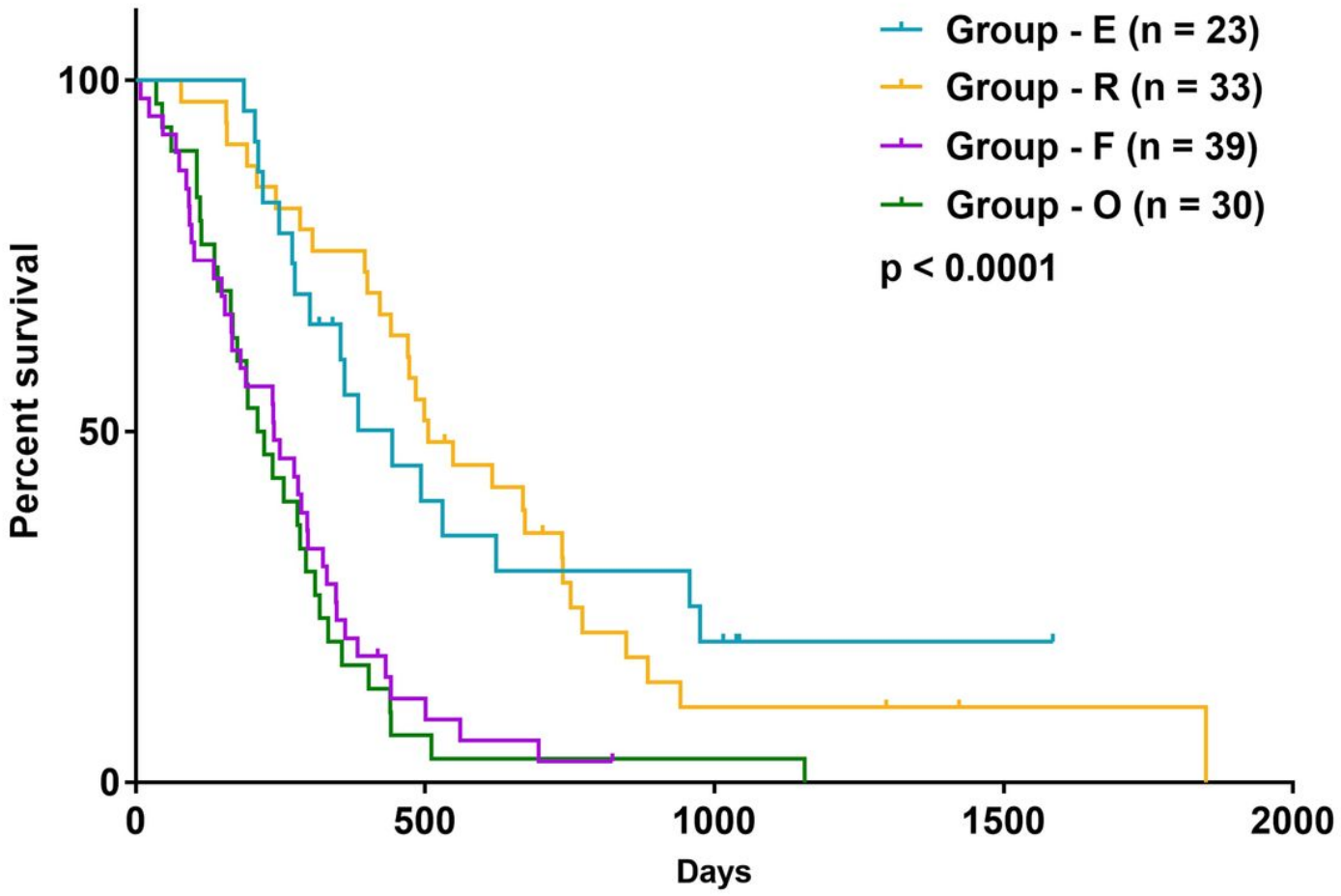

Figure 3

Kaplan–Meier survival curve analysis for different sub-groups. Group E included patients with new epileptic seizures upon diagnosis with secondary glioblastoma (sGBM); Group R included patients without any newly occurring symptoms upon diagnosis with sGBM based on T1 contrast-enhanced magnetic resonance imaging during follow-up; Group F included patients with new functional impairments, such as paralysis, aphasia, or cognitive functional impairments, upon diagnosis with sGBM; Group O included patients with other newly occurring symptoms, such as headache and/or vomiting, upon diagnosis with sGBM.

Supplementary Files

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