Original Article

Significance of radiation therapy in frontal glioblastoma patients and exploration of optimal treatment modality: a real-world multiple-center study based on propensity score matching

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Background: Glioblastoma (GBM) exhibits diffuse and invasive growth patterns, with a 5-year overall survival (OS) rate of 5–10%. In addition, approximately 40 percent of GBMs are localized in the frontal lobe, a region closely linked to essential life functions including cognition, so that it cannot be completely eradicated through surgical intervention, leading to very poor prognosis. Postoperative therapy is an essential treatment modality. The aim of this study is to explain the possible role of radiation therapy (RT) in the treatment of frontal GBM, providing more evidence for clinical application.

Methods: In the study, patient information pertaining to frontal GBM patients was collected from the Surveillance, Epidemiology, and End Results (SEER) database for the period 2000 to 2018 with 9,904 patients deemed appropriate for inclusion in this study. A 1:2 propensity score matching analysis was conducted to balance the non-radiotherapy and radiotherapy group. This study is a retrospective study.

Results: Before matching, the median OS, tumor specific survival (TSS) and hazard ratio (HR) were 3 months, 3 months and 4.408 [95% confidence interval (CI): 3.762–4.535, P<0.001] in the non-RT group compared to those of 13 months, 14 months and 2.463 (95% CI: 2.247–2.936, P<0.001) in the RT group. After matching, the median OS, TSS and HR were 3 months, 4 months and 1.433 (95% CI: 1.387–1.692, P<0.001) in the non-RT group compared to those of 8 months, 8 months and 1.427 (95% CI: 1.374–1.682, P<0.001) in the RT group.

Conclusions: Radiotherapy is an important local therapy, which can significantly improve the tumor-specific survival and OS of frontal GBM patients. With the arrival of the era of precision radiotherapy, the continuous progress of radiotherapy technology may bring more benefits to frontal GBM patients.

Keywords: Radiotherapy; glioblastoma (GBM); frontal lobe tumor; propensity score matching (PSM)

Submitted Dec 30, 2023. Accepted for publication Aug 15, 2024. Published online Sep 26, 2024.
doi: 10.21037/qims-23-1871
View this article at: https://dx.doi.org/10.21037/qims-23-1871

Introduction

Glioma is a common central nervous system tumor. According to the global tumor data released in 2022, there are 308,102 new patients with central nervous system tumor worldwide every year, and about 251,329 related death (1). Glioblastoma (GBM) has poor prognosis due to its aggressive growth (2). An increasing number of studies have been conducted on GBM, including tumor vaccines, inhibitors targeting epidermal growth factor receptor (EGFR) amplification and other emerging therapeutic approaches, with minimal improvement in prognosis (1,3).

The frontal lobe is the most common site of disease (40%) followed by the temporal lobe (4). The frontal lobe is an important functional area of the brain. Zhang *et al.* (5) reported that frontal lobe glioma has a specific form of atrophy, which further affects the cognitive function of patients. Liu and colleague (6) reported a case of frontal lobe tumor with epilepsy, including loss of consciousness, nonresponse to call, myotonia, and convulsions. Patients with primary tumors in the right hemisphere have worse prognosis than those in the left hemisphere. Tumors localized in the non-dominant hemisphere may grow larger before symptoms appear, leading to delayed diagnosis (7). However, Coluccia *et al.* (8) suggests that tumors located in the left hemisphere are associated with short disease-free survival. Tumor location and laterality may also be factors affecting patient outcomes.

GBM is rarely associated with extracranial metastasis. The most common finding is intracranial metastasis. Conventional chemotherapy does not penetrate the blood-brain barrier, which is an additional factor leading to poor prognosis of GBM (9). As the standard of care, radiotherapy is an affective treatment modality for local control in the treatment of primary and secondary malignant tumors. Radiation therapy (RT) can alter the permeability of the blood-brain barrier, thereby improving chemotherapy penetration (10). In this study, the important role of radiotherapy in frontal lobe GBM is demonstrated through retrospective study of multi-center Surveillance, Epidemiology, and End Results (SEER) data. We aim to provide a strong basis for the improvement of radiotherapy techniques and clinical application moving forward.

This study mainly focused on frontal lobe GBM, a special category of GBM, which should receive extensive attention due to the special location of the primary tumor. Unfortunately, there are few studies on this category, and this study focuses on the survival prognosis of this type of patients, which has important clinical value. The prognosis of tumors at different sites will be analyzed in the future, and their similarities and differences will be compared to improve accuracy and in-depth analysis. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1871/rc).

Methods

Research object and data acquisition

The study collected patients with GBM who visited health care facilities in each state of the United States of America between 2000 and 2018. Appropriate cases were qualified using SEER*Stat 8.4.0 software: included data from Incidence-SEER Research Plus Data, 18 Registries, Nov 2020 Sub [2000–2018]. ICD-O-3/WHO 2008=brain was selected. Data were access from https://seer.cancer.gov/. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data screening process

After computer screening, data of 99,928 patients were collected, and only patients with frontal lobe GBM confirmed by pathology were included in the study. The medical records of the included patients were complete, and each patient had a unique ID code. 9,904 eligible cases were deemed appropriate to be included in this study (*Figure 1*).

Inclusion criteria

- Patients with GBM between 2000 and 2018;
- Age >18 years old;
- Pathology confirmed GBM.

Exclusion criteria

- Not the only primary malignant tumor or the primary site is not frontal lobe;
- The patient's basic condition or identity code record is unknown;
- Survival time and status records are unknown;
- Treatment protocol records are unknown.

Statistical analysis methods and chart making

X-tile software was used to transform numerical variables into categorical variables. Univariate and multivariate Cox

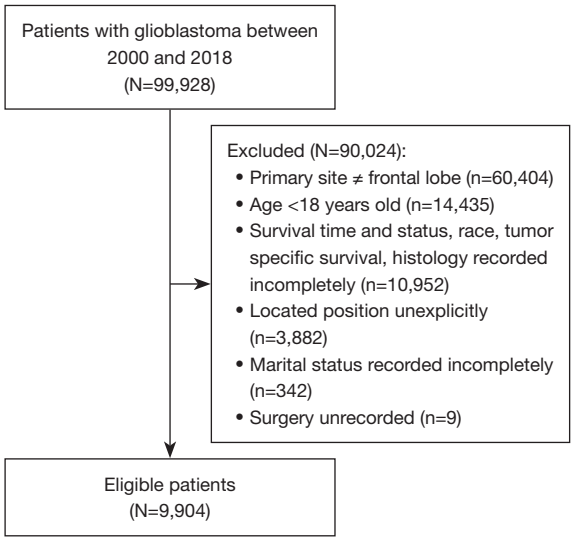

Figure 1 The screening process of the study.

regression analyses were performed using rms and survival package in R studio, hazard ratio (HR) values and 95% confidence intervals (CIs) were calculated respectively. All cases were grouped according to whether they received radiotherapy or not. The caliper value was set as 0.03 by the propensity scoring method, and the selected cases were matched according to the radiotherapy group and the non-radiotherapy group, with the matching tolerance of 1:2. The propensity scoring matching model was based upon age, sex, marital status, race, laterality, chemotherapy, and surgery. The propensity scoring was completed using https://www.mstata.com software.

In this study, survival analysis was performed on Graphpad 7.0, and Log-rank (Mantel-Cox) testing.

Results

Clinical baseline data of patients

A total of 9,904 patients were included in the study, including 5,409 males (54.61%) and 4,495 females (45.39%). 7,247 (73.17%) received radiotherapy and 2,657 (26.83%) did not (*Table 1*).

Multivariate Cox regression results

The variables of age, sex, marriage, race, laterality, surgery, radiotherapy, chemotherapy, which were significantly associated with survival in the univariate COX analysis were included in the multivariate COX analysis. Multivariate Cox regression results showed that age at diagnosis, tumor hemiformity, surgery, radiotherapy and chemotherapy were all independent risk factors affecting tumor specific survival (TSS) in frontal GBM patients, and the results before and after propensity score were consistent (*Tables 2*,*3*).

Overall survival (OS) results before and after matching

Before matching, the median OS was 3 months in the no-RT group and 13 months in the RT group, with a HR of 4.408 (95% CI: 3.762–4.535, P<0.001). After propensity score matching, the median OS of the no-RT was 3 months, and the median OS of the group with radiotherapy was 8 months, and the HR was 1.433 (95% CI: 1.387–1.692, P<0.001), respectively (*Figure 2A*,*2B*).

Tumor-specific survival results before and after matching

Before matching, the median TSS was 3 months in the no-RT group and 14 months in the RT group with radiotherapy, with a HR of 2.463 (95% CI: 2.247–2.936, P<0.001), respectively. After propensity score matching, the median TSS of the matched no-RT group was 4 months, and the median TSS of the RT group was 8 months, with a HR of 1.427 (95% CI: 1.374–1.682, P<0.001) (*Figure 3A*,*3B*).

Discussion

Gliomas are tumors originating from glial cells and nerve cells in neuroectoderm, accounting for about 32% of all primary central nervous system tumors. According to World Health Organization (WHO) classification, gliomas can be divided into four grades with progressively increasing malignancy (1,3,11-13). In China, the annual incidence rate of glioma is 5–8/100,000, and the 5-year mortality rate ranks third among systemic malignant tumors, among which high-grade glioma accounts for more than half of adult primary brain tumors, GBM is a subtype of WHO grade Ⅳ, and the median OS time is about 1 year (11,12,14,15). GBM has a short disease-free survival, high intracranial recurrence rate and poor prognosis (12). It can also lead to the occurrence of symptoms related to raised intracranial pressure, which can compress functional areas, resulting in corresponding neurological deficits (1).

The frontal lobe is located at the forefront of the cerebral hemisphere and is the center of voluntary movement and higher mental activities, such as executive ability, spatial

Table 1 Baseline covariates before and after matching

Variables	Level	Before matching				After matching			
		RT (n=7,247)	No-RT (n=2,657)	SMD	P	RT (n=1,363)	No-RT (n=1,131)	SMD	P
Age (years)	18–60	3,728 (51.4)	740 (27.9)	–0.526	<0.001	501 (36.8)	385 (34.0)	–0.044	0.01
	61–78	3,094 (42.7)	1,245 (46.9)	0.083		675 (49.5)	541 (47.8)	–0.031	
	>78	425 (5.9)	672 (25.3)	0.447		187 (13.7)	205 (18.1)	0.081	
Sex	Female	3,194 (44.1)	1,301 (49.0)	0.098	<0.001	603 (44.2)	491 (43.4)	–0.036	0.708
	Male	4,053 (55.9)	1,356 (51.0)	–0.098		760 (55.8)	640 (56.6)	0.036	
Marital	Single	2,298 (31.7)	1,227 (46.2)	0.29	<0.001	531 (39.0)	296 (26.2)	–0.253	<0.001
	Married	4,949 (68.3)	1,430 (53.8)	–0.29		832 (61.0)	835 (73.8)	0.253	
Race	Black	392 (5.4)	141 (5.3)	–0.005	0.903	83 (6.1)	68 (6.0)	–0.016	0.007
	White	6,431 (88.7)	2,369 (89.2)	0.014		1,199 (88.0)	960 (84.9)	–0.1	
	Asian or Pacific Islander	394 (5.4)	138 (5.2)	–0.011		74 (5.4)	100 (8.8)	0.159	
	American Indian/ Alaska Native	30 (0.4)	9 (0.3)	–0.013		7 (0.5)	3 (0.3)	–0.015	
Laterality	Left	3,309 (45.7)	1,214 (45.7)	0.001	<0.001	586 (43.0)	307 (27.1)	–0.331	<0.001
	Right	3,763 (51.9)	1,321 (49.7)	–0.044		742 (54.4)	756 (66.8)	0.266	
	Bilateral	175 (2.4)	122 (4.6)	0.104		35 (2.6)	68 (6.0)	0.152	
Chemotherapy	No/unknown	905 (12.5)	2,426 (91.3)	2.797	<0.001	905 (66.4)	902 (79.8)	0	<0.001
	Yes	6,342 (87.5)	231 (8.7)	–2.797		458 (33.6)	229 (20.2)	0	
Surgery	No	957 (13.2)	1,079 (40.6)	0.558	<0.001	302 (22.2)	312 (27.6)	0.095	0.002
	Yes	6,290 (86.8)	1,578 (59.4)	–0.558		1,061 (77.8)	819 (72.4)	–0.095	

Data are presented as number (%). SMD, standardized mean difference; RT, radiation therapy.

vision, memory, insight, verbal fluency, fluid intelligence, etc. Studies have shown that the incidence and severity of cognitive impairment in patients with frontal lobe tumors are greater than those without frontal lobe tumors, and the phenomenon is more obvious in elderly patients (16,17). Frontal lobe tumors, especially those in the dorsolateral prefrontal lobe, tend to cause executive dysfunction. Executive response time is always prolonged in both high-grade and low-grade glioma patients, suggesting that frontal glioma impairs attention. Frontal lobe tumors account for a large proportion of intracranial tumors and should be paid attention to.

GBM is mainly invasive and diffuse, and tumor cells can release more dissolved substances and tissue toxins (1,14,18,19), which is highly malignant, so it is difficult to achieve biological complete resection by simple surgery (1,20,21). Therefore, postoperative adjuvant therapy is particularly important. The standard of care is adjuvant chemoradiotherapy per the Stupp protocol for local control (1,6,22). It is important to note that extracranial metastases of gliomas are rare (9,23). The existence of glioblastoma stem cells (GSCs) indicate that they are capable of self-renewal and differentiation and involve multiple lineages. GBM relapse/recurrence is common, so the observed curative effect is poor (10). Yan's team found that GSCs are less expressed in primary glial tumors, while GSCs are more expressed in glioma tissues that relapse after chemoradiotherapy. The results indicated that postoperative adjuvant therapy was mainly targeted at common tumor cells, and Glioma Stem Cells had strong radiotherapy and chemotherapy resistance, which could supplement the killed tumor cells. Glioma stem cells have self-replication, multidirectional differentiation, and proliferative potential, thus determining their malignant biological behavior. GBM

Table 2 COX multivariate prognostic analysis before propensity score matching

Variable	TSS			OS		
	HR	95% CI	P	HR	95% CI	P
Age (years)						
18–60	1	–	Ref.	1	–	Ref.
61–78	1.842	1.756–1.932	<0.001	1.857	1.772–1.946	<0.001
>78	2.993	2.766–3.238	<0.001	3.043	2.819–3.285	<0.001
Sex						
Female	1	–	Ref.	1	–	Ref.
Male	1.038	0.993–1.086	0.099	1.054	1.009–1.101	0.019
Marriage						
Single	1	–	Ref.	1	–	Ref.
Married	1.023	0.976–1.073	0.342	1.002	0.957–1.049	0.934
Race						
Black	1	–	Ref.	1	–	Ref.
White	1.118	1.013–1.235	0.027	1.092	0.992–1.203	0.071
Asian or Pacific Islander	0.908	0.792–1.041	0.168	0.9	0.789–1.028	0.121
American Indian/Alaska Native	1.034	0.709–1.508	0.863	1.109	0.778–1.582	0.566
Laterality						
Left	1	–	Ref.	1	–	Ref.
Right	1.031	0.942–1.129	0.506	1.035	0.991–1.081	0.123
Bilateral	1.284	1.030–1.600	0.026	1.486	1.312–1.682	<0.001
Surgery						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.544	0.492–0.602	<0.001	0.596	0.563–0.630	<0.001
Radiotherapy						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.622	0.570–0.679	<0.001	0.607	0.567–0.650	<0.001
Chemotherapy						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.577	0.523–0.636	<0.001	0.557	0.522–0.594	<0.001

TSS, tumor specific survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; Ref. reference.

is highly radiation-resistant in part due to the presence of glioma stem cells promoting G2/M checkpoints and efficient DNA repair. This is also considered to be a primary reason for glioma recurrence (3,11,24,25). Isocitrate dehydrogenase (IDH) is a key rate-limiting enzyme in the tricarboxylic acid cycle, which can catalyse the oxidative decarboxylation of isocitrate to carbon dioxide and alpha ketoglutaric acid. The IDH mutation rate in primary GBM is about 5%. Studies have shown that IDH is a common molecular index and genetic change index of glioma, and the prognosis of high-grade glioma patients with IDH gene mutation is better than IDH wild type (12,26).

Table 3 Cox multivariate prognostic analysis after propensity score matching

Variable	TSS			OS		
	HR	95% CI	P	HR	95% CI	P
Age (years)						
18–60	1	–	Ref.	1		Ref.
61–78	1.848	1.676–2.037	<0.001	1.867	1.698–2.054	<0.001
>78	2.62	2.291–2.997	<0.001	2.693	2.363–3.068	<0.001
Sex						
Female	1	–	Ref.	1	–	Ref.
Male	1.005	0.921–1.096	0.911	1.022	0.939–1.113	0.613
Marriage						
Single	1	–	Ref.	1	–	Ref.
Married	1.027	0.935–1.129	0.578	1.026	0.936–1.124	0.587
Race						
Black	1	–	Ref.	1	–	Ref.
White	1.164	0.966–1.403	0.111	1.092	0.992–1.203	0.071
Asian or Pacific Islander	1.068	0.837–1.362	0.597	0.9	0.789–1.028	0.121
American Indian/Alaska Native	0.918	0.425–1.983	0.827	1.109	0.778–1.582	0.566
Laterality						
Left	1	–	Ref.	1	–	Ref.
Right	1.031	0.942–1.130	0.506	1.035	0.991–1.081	0.123
Bilateral	1.284	1.030–1.600	0.026	1.486	1.312–1.682	<0.001
Surgery						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.544	0.492–0.602	<0.001	0.596	0.563–0.630	<0.001
Radiotherapy						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.622	0.570–0.679	<0.001	0.607	0.567–0.650	<0.001
Chemotherapy						
No/unknown	1	–	Ref.	1	–	Ref.
Yes	0.577	0.523–0.636	<0.001	0.557	0.522–0.594	<0.001

TSS, tumor specific survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; Ref. reference.

Studies have confirmed that patients over 60 years of age, tumor diameter >6 cm, Karnofsky Performance Status (KPS) score <80 points prior to radiotherapy, subtotal resection of tumor, high-grade pathological grade, EGFR amplification, IDH status are risk factors for prognosis of patients (1,27-30). Mizuhata's study on GBM recurrence pattern showed that the recurrence originated from the excision margin (31).

Despite trimodality therapy with surgery and chemoradiotherapy with concurrent temozolomide, median survival is 10–14 months for adult patients (4). The blood-brain barrier is a selective permanent, tightly regulated physiological and chemical barrier between blood and

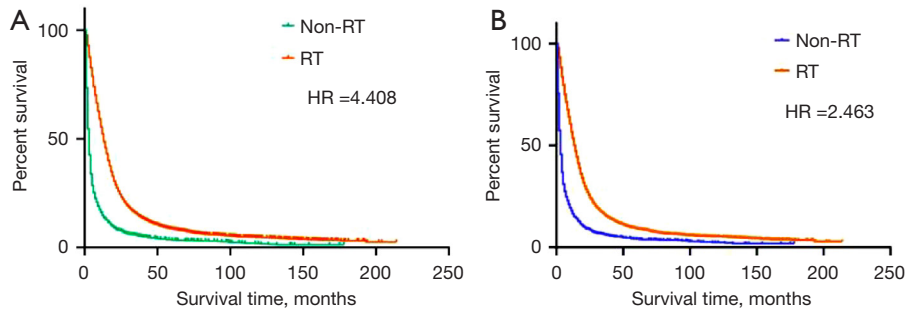

Figure 2 Effect of radiotherapy on overall survival. (A) Before PSM. (B) After PSM. RT, radiation therapy; HR, hazard ratio; PSM, propensity score matching.

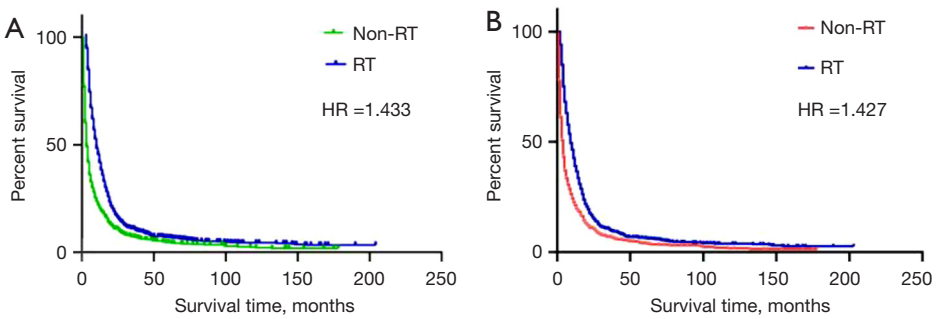

Figure 3 Effect of radiotherapy on tumor specific survival. (A) Before PSM. (B) After PSM. RT, radiation therapy; HR, hazard ratio; PSM, propensity score matching.

brain parenchyma. Between 24 hours and 4 weeks after radiotherapy, the blood-brain barrier appears to deteriorate and become more permeable, therefore facilitating drug penetration (9,32).

This study shows that radiotherapy can significantly improve the median survival of frontal glioma patients. In several studies, radiotherapy did not improve OS. However, in GBM, we found that radiotherapy can significantly improve the survival of patients. The primary reason for this may be related to the biological behavior of GBM. The main reason for its treatment failure is local recurrence. And radiotherapy is a good local treatment modality that provides better local control than surgery alone. Current research on GBM focuses on the interval between radiotherapy and surgery and the segmentation mode of radiotherapy.

Results of a meta-analysis showed that delayed postoperative radiotherapy, an interval of more than 6 weeks, can significantly reduce the local control rate of tumors, thus affecting the OS of patients (29). Postoperative radiotherapy can leave enough time for the wound to heal and reduce the risk of postoperative infection. Brain edema caused by surgery will gradually disappear and brain tissue displacement caused by edema will improve (28). Irwin's retrospective analysis of 172 patients with grade 3 and 4 glioma who underwent postoperative radiotherapy showed an 8.9% increase in mortality for each week of delay in hazardous radiotherapy. If start of radiotherapy is delayed by 2 to 8 weeks, median survival time is reduced by 11 weeks. Delayed radiotherapy significantly reduces OS (33).

The standard dose and fraction is 60 Gy in 30 fractions over 6 weeks. That significantly improves OS than 40–45 Gy in 15 fractions over 3 weeks in the younger group. Therefore, the standard course of OS was longer, but the recurrence pattern of the short course (40 Gy/15 Fx) was similar to that of the standard treatment. Short courses of radiotherapy plays a vital role in the elderly population, not only in disease-free survival, but also in relapse patterns. It should be noted that the standard prescription dose of 60 Gy/30 Fx was excluded for over 70-year-old individuals (31,34). Yao's study showed that, for elderly patients, the

effect of radiotherapy is mainly related to pathological subtypes, and there is no obvious correlation with radiotherapy dose (35,36). The reason for the phenomenon may be that GBM is more aggressive to elderly patients and has stronger tolerance to radiotherapy (35,36). In the past, for patients treated with GBM surgery, after the routine 55 Gy irradiation, the normal brain tissues and organs around the tumor could not tolerate it and could not continue to increase the dose of radiotherapy, thus affecting the therapeutic effect (15). Elderly patients have higher expression level of tumor angiogenic endothelial factor and better induction of angiogenic ability, so the tumor is more aggressive, and therefore the postoperative recurrence rate is higher than that of patients with cerebral glioma (1,27). The molecular characteristics of elderly patients with GBM are worse than those of young patients, which is consistent with the above conclusions (37). Bozdag analyzed data from the Cancer Genome Atlas and found that elderly patients (≥70 years old) showed a pro-angiogenic phenotype compared to GBM. Young patients (≤40 years old) were analyzed using computational high-throughput genomic data (38).

The study by Norton showed that tumor growth was often at the peak of Gompertz curve and relatively slow (29,39). When the tumor is surgically removed, the residual small tumor cells grow more rapidly and begin to proliferate rapidly with increased radiosensitivity. However, with the passage of time, the tumor growth rate gradually slows down and the radiosensitivity also decreases. Although the model can explain the biological characteristics of tumors and early interventional radiotherapy, some scholars believe that early interventional radiotherapy, such as within three weeks after surgery, may cause serious neurological damage (29,40).

However, the standard of care of surgery and chemotherapy also has some disadvantages. Intrinsic factors such as tumor hypoxia, radiation-resistant glioblastoma stem cells, and up-regulated DNA damage response mechanisms have been shown to contribute to the treatment of drug resistance and tumor recurrence. Traditional therapy induces lymphocytopenia, and decreased lymphocyte count is an independent predictor of poor clinical prognosis and is associated with higher recurrence and infection rates (11). Proton therapy is an emerging therapy that can improve patient survival while preserving normal tissue and reducing neurocognitive complications.

In terms of clinical observation, patients with GBM have been treated with carbon ion radiotherapy (CIRT) in combination with primary radiotherapy and re-irradiation for recurrent tumors. CIRT has been reported to be well tolerated with minimal toxicity (11). The possibility of proton beam therapy and CIRT in combination with DNA damage repair inhibitors to overcome therapeutic resistance to GBM suggests that different radiological modalities should be paired with specific agents to maximize clinical benefit. With the continuous emergence of new radiotherapy technologies, immune checkpoint inhibitors and tumor vaccines, the survival of GBM patients will gradually improve (28).

It is worth noting that the marital status of patients was mentioned in the inclusion and exclusion of patients in this study, and patients with unknown marital status were excluded. It's an interesting decision, but one based on a number of studies. A classic study was conducted by Professor Yu's team at Tianjin Medical University. In the study of 4,282 glioma patients, multivariate COX regression analysis found that marital status was an independent prognostic factor for patient survival ($P<0.05$), and widower was still an independent risk factor for patients with the same gender, age range and surgical treatment ($P<0.01$). This study shows that marital status is closely related to the survival of glioma patients, and the death of a spouse increases the risk of death (41).

There are also some shortcomings in the study. Firstly, this study is a multi-center retrospective study without adjusting radiotherapy dose and radiotherapy target area, and differences in radiotherapy techniques and means with different units may lead to bias. Secondly, the status of IDH is an important basis for evaluating the prognosis of GBM, which was not included in the study. Thirdly, the study included patients with frontal GBM from 2000 to 2018. Although the number of patients included was large and the statistical confidence was relatively high, it should be noted that RT techniques have changed significantly during the 18 years. From the era of conventional radiotherapy to intensive-modulated radiotherapy, including the emergence of current volume-modulated and stereotactic radiotherapy technology, radiotherapy has become more and more accurate and standardized, and has shown an improvement in local control rate in various malignant tumors. Therefore, there are obvious differences in radiotherapy equipment and technology that were available to the included patients from different periods. This can lead to underestimation of tumor-specific and OS. Last but not least, the prognosis of concurrent chemoradiotherapy is significantly better than that of radiotherapy or chemotherapy alone. However, clinicians would fully evaluate the patient's survival, general

condition, and coordination when selecting treatment options. If a patient has a low KPS score, single treatment is being more inclined to rather than combination therapy. There are also some patients who have indications for chemotherapy but refuse chemotherapy, directly affecting the survival of patients. In future prospective clinical studies, we will fully evaluate the general condition of the patient and the risk factors that may affect the prognosis.

Conclusions

Radiotherapy is an essential adjuvant therapy after frontal GBM surgery, which can significantly improve OS and tumor-specific survival, and has positive prognostic significance. Proton therapy and other new radiotherapy methods may overcome the shortcomings of traditional radiotherapy and be used in the treatment of GBM.

Acknowledgments

Funding: This research was supported by the Government Subsidizes the Training Program for Clinical Medical Talents (No. ZF2024068) and Traditional Chinese Medicine Scientific Research Project (No. 2024279).

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-23-1871/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-23-1871/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Cite this article as: Li N, Hao S, Cao X, Lin Y, Li Y, Dai T, Liu M. Significance of radiation therapy in frontal glioblastoma patients and exploration of optimal treatment modality: a real-world multiple-center study based on propensity score matching. Quant Imaging Med Surg 2024;14(10):7576-7586. doi: 10.21037/qims-23-1871