# **Prevalence and Radiographic Characteristics of Cerebral Infarction after Surgery in Patients with Glioma: A Retrospective Study**

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AIM: The aim of our study was to analyze risk factors for postoperative cerebral infarction in patients with glioma in our hospital, and to compare medical imaging techniques for early diagnosis of postoperative cerebral infarction.

METHODS: A retrospective analysis was conducted on 178 patients (male: 78, female: 100) who underwent glioma surgery at our hospital between May 2015 and October 2023. They were divided into two groups based on the presence of postoperative cerebral infarction within 7 days: the cerebral infarction group ( $n = 85$ ) and the non-cerebral infarction group ( $n = 93$ ). Magnetic resonance imaging (MRI) was used to assess the location, distribution, and volume of the tumor before surgery. During the perioperative period, patient postoperative time, intraoperative blood loss, and other relevant data were documented. Computed tomography perfusion (CTP) and diffusion-weighted imaging (DWI) imaging techniques were employed to evaluate the occurrence, area, location, and shape of cerebral infarction. The imaging characteristics of postoperative cerebral infarction were noted. Apparent diffusion coefficient values, apparent diffusion coefficient (ADC) of whole-brain CTP parameters, cerebral blood flow (CBF), cerebral blood volume (CBV), time to peak (TTP), mean transit time (MTT), and DWI parameters were measured. The sensitivity and specificity of CTP, DWI, and their combined diagnosis for postoperative cerebral infarction were compared, with consistency assessed using the Kappa value.

RESULTS: This study found that 85 patients (47.8%) experienced postoperative cerebral infarction. Significant risk factors included tumor location in the temporal lobe, tumor volume *<sup>≥</sup>*23.57 cm<sup>3</sup> , number of surgeries *>*1, World Health Organization (WHO) grade *>*3, and intraoperative blood loss *>*79.83 mL (*p <* 0.05). Imaging examinations revealed that CTP combined with DWI diagnosis detected cerebral infarctions in 84 patients, showing lower CBF and CBV, and higher TTP, and MTT in the infarct group (*p <* 0.05). The Kappa values for CTP, DWI, and the combined diagnosis were 0.762, 0.833, and 0.937, respectively ( $p < 0.001$ ).

CONCLUSIONS: The prevalence of cerebral infarction in patients with glioma is high and is affected by many factors. Timely imaging examination can detect and predict the occurrence of cerebral infarction in patients after surgery, which is of great significance for improving the prognosis of patients.

**Keywords:** glioma; whole-brain computed tomography (CT) perfusion; magnetic resonance diffusion-weighted imaging; cerebral infarction; perfusion parameters

# **Introduction**

Brain glioma is the most common central nervous system (CNS) tumor, accounting for approximately 85%–90% of all primary CNS tumors [1,2]. The most common regions include the central sulcus, basal ganglia, thalamus, and brainstem, in addition to other important sites. The degree of surgical difficulty is extremely high, with poor prognosis and a high recurrence rate for patients. Approximately 55% of these gliomas will progress to glioblastoma, resulting in survival of less than 1 year after diagnosis for most patients [3,4]. There have been few major advances in the prevention, early detection, and treatment of glioblastoma over the past decades, so that patient 5-year survival has only increased from 4% to 7% [5]. At present, the treatment methods for brain glioma include surgery, electric field therapy, targeted therapy, and immunotherapy [6,7], among which the maximum safe resection of tumor has become the gold standard for brain glioma surgery [8,9]. Moreover, the prognosis of patients improves with an increase in the extent of surgical resection [10]. However, craniotomy cannot avoid damage to surrounding brain tissues and blood vessels, resulting in ischemic changes in peripheral nervous tissue, and potentially leading to cerebral infarction [11]. Therefore, early detection of the blood supply to the patient's brain is of great significance for preventing the patient from suffering ischemic cerebral infarction and for improving the prognosis. Both computed tomography perfusion (CTP) and diffusion weighted imag-

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ing (DWI) of the whole brain can detect cerebral ischemia in patients [12,13]. At present, there are few clinical studies on the relationship between postoperative cerebral infarction and tumor size, location, and surgical process in patients with brain glioma, and relevant predictive indicators are lacking. Only symptomatic treatment is provided for postoperative complications. In this study, we retrospectively analyzed the imaging data of patients with brain glioma before and after surgery in our hospital, compared the imaging characteristics of postoperative cerebral infarction and preoperative tumors, and identified risk factors for postoperative cerebral infarction.

# **Materials and Methods**

#### *General Data*

The clinical data of patients who underwent surgical treatment for brain glioma in our hospital from May 2015 to October 2023 were retrospectively analyzed. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study has been approved by the Ethics Committee of Central Hospital Affiliated to Shandong First Medical University (Approval No. 2023-124- 01). Informed consent was obtained from all individual participants included in the study.

#### *Inclusion Criteria*

The inclusion criteria were (1) Diagnosed brain glioma according to the World Health Organization (WHO)'s diagnosis of Grade 2–4 newly diagnosed or recurrent diffuse brain glioma [14], and diagnosed cerebral infarction according to the diagnostic criteria for cerebral infarction in the Guidelines for Diagnosis and Treatment of Acute Ischemic Stroke in China; (2) Age *≥*18 years; (3) Surgical treatment of brain glioma in our hospital; (4) Complete clinical data.

#### *Exclusion Criteria*

The exclusion criteria were (1) Patients with severe heart, liver, or kidney abnormalities; (2) Patients with other malignant tumors; (3) Patients with other nervous system diseases or mental disorders; (4) Patients with a history of severe brain trauma in the past 6 months.

#### *Preoperative Imaging Examination of Brain Glioma*

Patients' brain magnetic resonance imaging (MRI) scans and other imaging data were independently assessed preoperatively by the same radiologist and neurosurgeon, who were blinded to individual patient clinical data. MRI examination was conducted using Philips 3.0T magnetic resonance scanner (Philips Corporation, Amsterdam, Netherlands). Conventional sequence: 1 T1 weighted image (T1WI), Turbo Spin Echo (TSE), echo time (TE) 2.3 ms, repetition time (TR) 250 ms; 2 T2 weighted image (T2WI)

TSE, TE 80 ms, TR 2505 ms; Fluorous-Attenuated Inversion Recovery (FLAIR), inversion recovery (IR) 2200 ms, TE 107 ms, TR 7000 ms. Layer spacing 1 mm, layer thickness 6 mm, number of excitation 1, reversal angle 75°, field of view 230 mm *×* 182 mm *×* 125 mm, matrix 128 *×* 128. Recondition the intravoxel incoherent motiondiffusion weighted imaging (IVIM-DWI) sequence, axial scan: TE 59 ms, TR 2500 ms, excite twice, and apply dispersion sensitive gradient fields in X, Y, and Z axis directions. Post-processing software: The original data were transmitted to the post-processing software to obtain D and F, which were read by two experienced radiologists. The tumor region with the maximum perfusion fraction of IVIM was selected to avoid inhomogeneous areas such as large blood vessels, liquefaction, calcification, hemorrhage, necrosis, and cystic degeneration.

#### *Surgical Techniques*

Routine craniotomy was performed for patients diagnosed with brain glioma, and the surgical treatment was completed by physicians at the deputy chief level or above with more than 10 years of neurosurgical experience. The location of the patient's tumor lesion was identified according to the imaging data of the patient before surgery, and positioning marks were made. After preoperative preparation, the patient was given general anesthesia. After successful anesthesia, a surgical incision was made according to the marked position, the bone flap was removed, the meninges were cut open to fully expose the center and surrounding infiltrated parts of glioma, and the tumor tissue was removed under the microscope. During surgery, the tumor tissue was removed to the maximum extent possible while preserving function. At the same time, it was necessary to decide whether to remove the bone flap in combination with the brain tissue bulge of the patient, and the resected tumor tissue was sent for pathological examination. Adequate hemostasis was performed, the dura mater was tightly sutured, all layers of the scalp were sutured layer by layer, and a drainage tube was placed subcutaneously.

# *Postoperative Imaging Procedures*

#### CTP Examination

A Philips Brilliance iCT 256-slice spiral CT machine was used for head scanning. The parameters were set as tube voltage 100 kV, current 250 mA, slice thickness 5 mm and spacing 5 mm. The non-ionic contrast agent iopromide 370 mgI/mL was injected, followed by 40 mL of normal saline, and then CTP was performed. The tube voltage, tube current, slice thickness, and spacing were set at 80 kV, 250 mA, 5 mm, and 5 mm respectively. Images were collected for 40 seconds to collect data such as cerebral blood volume (CBV), cerebral blood flow (CBF), mean transit time (MTT), and time to peak (TTP).

#### MRI and DWI Examination

MRI examination was conducted using a Philips 3.0T magnetic resonance scanner for brain examination. Sagittal and axial scans were routinely performed, and the regular sequence was set. 1 T1 weighted image (T1WI) sequence: echo time (TE) 1.6 ms, repetition time (TR) 110 ms; 2 T2 weighted image (T2WI) sequence: TE 110 ms, TR 3961 ms, field of view (FOV) 23 cm, number of excitation (NEX): 2, matrix  $232 \times 144$ , spacing 1.2 mm, slice thickness 6 mm.

DWI scanning was conducted using the spin echo-planar image (SE-EPI) technology for DWI examination, with a matrix of  $152 \times 105$ , FOV of 23 cm, scan spacing of 5 mm, interlayer spacing of 1 mm, slice thickness of 8 mm, TE of 73 ms, and TR of 2112 ms. The diffusion sensitivity coefficient was based on  $b = 1000 \text{ s/mm}^2$ , and the dispersion gradient in 3 directions was selected for DWI scanning. After obtaining the image with post-processing software, the region of interest was delineated to obtain the mirror area of the symmetrical unaffected side, and the apparent diffusion coefficient (ADC) value and average diffusion coefficient (DCavg) were calculated. The clinical symptomrelated blood supply area showing focal hyperintensity was positive, otherwise, it was negative.

## *Observation Indicators*

The location, distribution, and volume of the patient's tumor were observed by MRI before surgery; the postoperative time, intraoperative blood loss, and other information of patients were recorded during the perioperative period; CTP and DWI were used after surgery to observe the incidence, size, location, and shape of postoperative cerebral infarction; the imaging characteristics of postoperative cerebral infarction were observed; whole-brain CTP parameters, DCavg value, and ADC value were measured; the sensitivity and specificity of CTP, DWI, and the two methods combined for diagnosing postoperative concurrent cerebral infarction were compared, and their consistency was analyzed using the Kappa value.

#### *Statistical Analysis*

Statistical analyses were performed using SPSS Statistics software (version 26.0, IBM Corp., Armonk, NY, USA). In this study, normality was tested by Kolmogorov-Smirnov (KS) tests. After testing variables for normality, the *t*-test or a non-parametric test was selected to compare groups. Normally distributed variables were expressed as  $(\bar{x} \pm s)$ , and those not normally distributed were expressed as median (interquartile range [IQR]). Univariate and multivariate logistic regression analyses were performed on risk factors that may cause postoperative cerebral infarction in patients. *p* values *<* 0.05 were considered statistically significant.

## **Results**

#### *Comparison of General Data between the Two Groups*

A total of 178 patients were included in this study. According to whether the patients had postoperative cerebral infarction within 7 days after surgery, they were divided into a cerebral infarction group ( $n = 85$ ; 41 males, 44 females) and a non-cerebral infarction group ( $n = 93$ ; 37 males, 56 females). The general information of patients is shown in Table 1. Of the 178 patients included in the study who underwent brain glioma surgery, 85 (47.8%) had a postoperative cerebral infarction, of which 26 (30.6%) were marginal, 38 (44.7%) were fan-shaped, 14 (16.5%) were mixed marginal and fan-shaped, and 7 (8.2%) were distal infarcts. The results of univariate logistic regression analysis showed that the risk of cerebral infarction increased with the patient's age, tumor location in the temporal lobe, tumor size, World Health Organization (WHO) classification, reoperation, and intraoperative hemorrhage ( $p < 0.05$ ). However, the patient's sex, tumor location, number of surgeries, surgery time, past medical history of radiotherapy and chemotherapy, history of cerebrovascular disease, and history of diabetes mellitus were not associated with postoperative cerebral infarction ( $p > 0.05$ ) (Table 1).

## *Multivariate Logistic Regression Analysis*

The results of multivariate logistic regression analysis showed that tumor location in the temporal lobe, tumor volume *<sup>≥</sup>*23.57 cm<sup>3</sup> , number of surgeries *>*1, WHO classification *>*3, and intraoperative hemorrhage *>*79.83 mL were all risk factors for postoperative cerebral infarction (Table 2).

#### *Imaging Characteristics of Postoperative Cerebral Infarction*

The postoperative imaging characteristics of the two groups are shown in Table 3. For the CTP examination method, a higher number of cases with abnormal perfusion were associated with cerebral infarction (67 cases) compared to those without cerebral infarction (4 cases). Similarly, a larger number of cases with positive findings on DWI displayed cerebral infarction (72 cases) compared to those without cerebral infarction (3 cases). When considering the combined diagnosis, the majority of cases diagnosed with cerebral infarction exhibited abnormal findings in both CTP and DWI (84 cases).

#### *Comparison of Whole-Brain CTP Parameters between the Two Groups*

The CBF and CBV of patients with cerebral infarction were significantly lower than those without cerebral infarction (*p <* 0.05), whereas the TTP and MTT of patients with cerebral infarction were higher than those without cerebral infarction  $(p < 0.05)$  (Table 4).

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\*Values are reported as n (%) unless otherwise indicated.

WHO, World Health Organization; SD, Standard Deviation.

*Comparison of DWI Parameters between the Two Groups*

The values of DCavg and ADC in the cerebral infarction group were significantly lower than those in the noninfarction group  $(p < 0.001)$  (Table 5).

*Diagnostic Value of CTP, DWI, and Their Combination in Postoperative Cerebral Infarction after Glioma Surgery*

Based on Table 6, which presents the consistency of CTP, DWI, and their combined diagnosis in the detection of cerebral infarction following glioma surgery, it is evident that

Risk factors	B	S.E.	Wald $\chi^2$	$\boldsymbol{p}$	OR (95% CI)
Age $>65$ years	1.10	0.672	2.700	0.100	3.016(0.808~11.258)
Tumor is in the temporal lobe	0.83	0.421	3.900	0.048	$2.297(1.006 - 5.242)$
Tumor volume $>23.57$ cm <sup>3</sup>	1.25	0.416	9.040	0.003	$3.493(1.546 \sim 7.894)$
Number of surgeries $>1$	1.36	0.683	3.950	0.047	3.888 (1.018~14.829)
WHO classification $>$ Grade 3	1.38	0.403	11.649	0.001	$3.957(1.796 - 8.718)$
Intraoperative blood loss $>79.83$ mL	1.01	0.411	6.001	0.014	$2.737(1.223 - 6.125)$

**Table 2. Multifactorial regression of risk factors for posterior cerebral infarction.**

WHO, World Health Organization; OR, odds ratio; CI, Confidence Interval.

The B-value is the regression coefficient and intercept (constant term), and Wald is a chi-square value equal to B divided by the square of its standard error (S.E.).





CTP, computed tomography perfusion; DWI, diffusion weighted imaging.





Note: Compared with the group without cerebral infarction,  $\dot{p}$  < 0.05.

CTP, computed tomography perfusion; CBF, cerebral blood flow; CBV, cerebral blood volume; TTP, time to peak; MTT, mean transit time.





Note: Compared with the group without cerebral infarction,  $\dot{p}$  < 0.05.

DWI, diffusion weighted imaging; DCavg, average diffusion coefficient; ADC, apparent diffusion coefficient.

#### **Table 6. Consistency of CTP, DWI, and their combination in the diagnosis of cerebral infarction after glioma surgery.**



CTP, computed tomography perfusion; DWI, diffusion weighted imaging.

all three methods demonstrate substantial agreement in their diagnostic capabilities. The Kappa values for CTP, DWI, and the combined diagnosis are 0.762, 0.833, and 0.937, respectively. Each of these values, coupled with their associated *p* values of less than 0.001, indicates strong agreement beyond what would be expected by chance. Additionally, the narrow range of standard error values further supports the reliability of these results (Table 6).

## **Discussion**

At present, the treatment methods for brain glioma mainly include surgical treatment and chemoradiotherapy [15]. A large dose of radiation, far exceeding what normal brain tissue can bear, would be required to effectively inhibit brain glioma in clinical practice. Thus, the potential efficacy of radiotherapy is greatly reduced [16]. Therefore, chemotherapy has become one of the most important treatments for patients with brain glioma after surgery [17], and its efficacy is directly related to the quality of life of patients. Nitrogen mustard was used for chemotherapy of tumors in the 1950s, and since then, clinicians have made progress in using chemotherapeutic drugs to treat tumor-related diseases [18]. However, due to the existence of the blood-brain barrier, macromolecules and most small-molecule drugs are prevented from entering brain tissue [19,20]. In addition, the cerebral blood flow only accounts for one-fifth of the systemic blood flow. To achieve effective chemotherapy, a high dosage is inevitably required, which causes substantial systemic toxicity and side effects [21], thus greatly reducing the efficacy of chemotherapy for patients with brain glioma. Although maximal tumor resection is a good option for patients with brain gliomas, postoperative ischemic lesions commonly develop around the area of resection, and vascular occlusion cannot be avoided by meticulous sub-basal dissection. Considering the differences in patients' age, tumor location, tumor size, and other factors, the probability of permanent neurological deficit after surgery is approximately 8.0%–12.2% [22,23]. Gempt *et al*. [24] found that approximately 31% of patients developed new postoperative ischemic lesions after initial glioma resection, whereas approximately 80% of patients developed new postoperative ischemic lesions after recurrent glioma resection. However, Strand *et al*. [25] found that there was no significant difference in the probability of ischemic cerebral infarction between initial versus recurrent resection procedures. The results of the present study showed that the probability of cerebral infarction complications after reoperation for brain glioma was significantly higher than that of patients undergoing initial surgery. The reason may be that reoperation increases the risk of surgical trauma and hemorrhage, which may lead to complications such as vascular injury and thrombosis [26], thus increasing the risk of cerebral infarction. Tumor recurrence may also lead to local blood vessel compression, stenosis, or obstruction, thus increasing the risk of cerebral infarction.

With the continuous development of imaging technology, CTP and DWI play an increasingly important role in improving the diagnostic efficacy for cerebral infarction [27,28]. CTP is a neuroimaging technique that can be used

to assess the patient's cerebrovascular condition and determine whether the brain tissue is ischemic or hypoxic [29]. DWI is a neuroimaging examination technology based on the diffusion of water molecules in brain tissue [30]. Under normal circumstances, water molecules in brain tissue are randomly diffused. When local brain tissue ischemia occurs, the degree of diffusion of water molecules changes, and DWI can reveal this subtle change. The results of this study showed that the combination of CTP and DWI diagnosis had higher sensitivity and specificity than singleexamination diagnosis of postoperative cerebral infarction in patients with brain glioma. The combination of the two methods can exclude false-positive or false-negative results. CTP is more accurate for the measurement of blood flow in cerebral gray matter and white matter, while DWI is more sensitive for the detection of small-scale cerebral infarction [31]. CT perfusion imaging cannot directly show cerebral infarction, while DWI is susceptible to image artifacts [32]. Therefore, in the clinical assessment of the prognosis of patients with brain glioma, the combination of the two will greatly improve the accuracy of diagnosis, which is of great significance for timely detection and prevention of possible risks.

The results of this study showed that the patient's age, tumor distribution, tumor volume, WHO classification, number of surgeries, and intraoperative hemorrhage were all risk factors for postoperative cerebral infarction. Specifically, the risk of cerebral infarction increased with age, tumor location in temporal lobe, tumor volume, WHO classification, reoperation, and intraoperative hemorrhage. Although surgeons have tried to minimize the damage caused by surgery, there is still a lack of surgical methods to reduce postoperative complications in patients after brain glioma surgery. Smith *et al*. [33] evaluated 44 patients after glioma resection and found that 64% of patients developed new ischemic lesions after surgery. It has been shown that the relationship between perioperative hemodynamics, postoperative infarction and overall survival, diastolic blood pressure, positive fluid balance, and duration of surgery was correlated with postoperative infarct volume [34]. Although different grades of glioma are associated with differences in blood supply, this study did not reveal a significant correlation between tumor grade and postoperative cerebral infarction. The larger the patient's tumor volume, the more severe the compression on surrounding tissues, leading to a relatively difficult surgical resection. Therefore, the amount of intraoperative hemorrhage may also be greater, resulting in a relatively poor postoperative brain blood supply and a higher risk of postoperative cerebral infarction for patients. The results of this study showed that patients with tumors located in the temporal lobe have the highest probability of cerebral infarction after surgery. The temporal lobe is in the lower lateral part of the brain, surrounded by many important structures, such as the middle cerebral artery and cranial nerves. Moreover, the blood supply of temporal lobe

tumors is usually abundant, and bleeding is common during surgery. Overall, the surgery is difficult, and patients are at high risk of postoperative ischemic changes.

In this study, we conducted a comprehensive analysis of risk factors associated with postoperative cerebral infarction in glioma surgery patients, highlighting key clinical and imaging features. Our findings offer valuable insights for further research in assessing postoperative complication risks. Additionally, we observed strong agreement between CTP and DWI imaging methods, providing a reliable means for early postoperative cerebral infarction diagnosis. Future studies should explore additional clinical parameters and imaging indicators to enhance the risk assessment model. Furthermore, verification through multicenter large-sample studies will bolster the generalizability and stability of our findings, offering a robust scientific foundation for clinical practice.

This study is subject to certain limitations due to methodological constraints. Firstly, generalizing the findings to the broader patient population may be challenging because the research was conducted at a single hospital without multicenter data support. Secondly, being a retrospective study, it lacked intervention control and random allocation, thus hindering the establishment of causality. The results could have been impacted by confounding variables or unaccounted factors, highlighting the need for further prospective studies to confirm the conclusions. Unfortunately, we were unable to provide details regarding the anesthesia method, anesthetic concentration, and dosage due to restrictions on data access.

Despite these limitations, the study exhibits several strengths. Firstly, it offers an initial exploration of the risk factors associated with postoperative cerebral infarction, providing valuable references and insights for future research within related fields. Additionally, despite the modest sample size, the study leverages the analysis of real-world clinical data to obtain results with reliability and applicability. Lastly, by investigating the risk factors for post-surgical cerebral infarction, the study aids clinicians in identifying high-risk patients and implementing appropriate preventive measures, thereby contributing to reduction of surgical risk.

# **Conclusions**

Patients with brain glioma have a high incidence of postoperative cerebral infarction, among which marginal infarction and fan-shaped infarction are the most common. The occurrence of postoperative cerebral infarction in patients is related to various factors such as patient age and tumor size. Timely imaging examination after surgery can detect and predict the occurrence of cerebral infarction in patients, which is of great significance for improving the prognosis of patients.

# **Availability of Data and Materials**

Data to support the findings of this study are available on reasonable request from the corresponding author.

# **Author Contributions**

JZ and MZ designed the research study. JZ drafted the article. YL and ZS performed the research. JZ and YL analyzed the data. All authors revised the manuscript critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

# **Ethics Approval and Consent to Participate**

This study has been approved by the Ethics Committee of Central Hospital Affiliated to Shandong First Medical University (Approval No. 2023-124-01). Informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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# **Conflict of Interest**

The authors declare no conflict of interest.

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