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ORIGINAL RESEARCH

Predictive Value of Preoperative Diffusion Tensor Imaging for Evaluating Postoperative Outcomes of Supratentorial Glioma in the Motor Function Area

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Objective: This study aimed to assess the predictive value of preoperative diffusion tensor imaging (DTI) data for surgical outcomes of patients with supratentorial glioma in the motor function area.

Patients and Methods: This is a retrospective study of 43 patients receiving navigation-guided surgery for histopathologically demonstrated supratentorial glioma in the motor function area. All patients underwent preoperative 3 Tesla magnetic resonance imaging examinations with conventional and DTI sequences. Data on preoperative imaging and pre- and postoperative clinical characteristics of patients were retrospectively collected. Univariate and multivariate linear regressions were applied to analyze the relationships between preoperative parameters and pre- and postoperative muscle strength and the Karnofsky Performance Status (KPS) score.

Results: Fourteen patients had low-grade gliomas and 29 had high-grade gliomas. Although the corticospinal tract (CST) score did not differ significantly between tumor grades, edema and deviation were common in low-grade gliomas (64.3%), while destroyed and infiltrated lesions were common in high-grade gliomas (58.6%). Muscle strength improved after surgery in the deviated tract group (40%) more than in the infiltrated tract group (33.3%). Two independent indices, preoperative muscle strength ($p = 0.000$) and glioma-to-CST distance ($p = 0.001$), were linearly related to postoperative muscle strength. The preoperative KPS score was the only indicator that affected the postoperative KPS score ($p = 0.000$).

Conclusion: DTI should be considered in surgical management of supratentorial gliomas in the motor function area to determine the appropriate surgical strategy and predict the nature of the tumor and postoperative motor function.

Keywords: diffusion tensor imaging, supratentorial glioma, preoperative planning, surgical outcomes, motor cortex

Introduction

Glioma is the most common type of primary tumor of the central nervous system.[1] The treatment for glioma includes maximal resection of tumor volume combined with radiotherapy, chemotherapy, and monitoring for recurrence.[2] Surgery is performed to obtain histological samples, reduce clinical symptoms, increase survival, and limit the need for steroids.[3] Complete resection of gliomas, especially high-grade infiltrative tumors, is quite demanding. On average, about 6% of glioblastoma cells are found at a distance of 0–2 cm from the tumor margin; therefore, the resection area considered "radical" should not be less than 2 cm.[4] For tumors close to functional areas, maximal resection of the tumor can cause damage to imperative nerve fiber bundles, leading to postoperative neurological complications.[5,6] Therefore, it is crucial

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to localize white matter fiber tracts and preoperatively determine their anatomical relationship with the tumor to ensure maximal resection and reduce the risk of postoperative neurological deficits.[7]

Diffusion tensor imaging (DTI) is a noninvasive advanced magnetic resonance technique that determines the orientation and location of white matter fiber tracts on different planes based on anisotropic diffusion of water molecules in axons. Furthermore, analysis of the fractional anisotropy (FA) map and the color-coded orientation map helps to evaluate the characteristics and different patterns of glioma infiltration into the adjacent fiber tracts, including deviation, edema, infiltration, and destruction of tracts.[8] Studies have shown the value of preoperative DTI for surgical planning, changing surgical modality, and predicting surgical outcomes.[5,7–11] However, some studies have shown that DTI does not significantly alter the surgical strategy.[10,12] Therefore, we conducted this study to evaluate the utility of preoperative DTI in surgical planning, assessing tumor characteristics, and predicting the risk factors of operative treatment outcomes of supratentorial gliomas in the motor function area.

Patients and Methods

Study Population

This study was a retrospective investigation of 43 patients with solitary supratentorial masses in the motor function area. The patients underwent navigation-guided surgery and their masses were histologically confirmed as glioma at Viet Duc Hospital, Hanoi, Vietnam, from June 2021 to June 2022. All patients were observed preoperatively with 3 Tesla magnetic resonance imaging (MRI; GE SIGNA Pioneer, GE Healthcare, Chicago, IL, USA) with conventional and DTI sequences. Ethical clearance was received from the institutional ethics committee of Hanoi Medical University (Ref: 630/GCN-HĐĐĐNCYSN-ĐHYHN), and the need for informed consent of patients was waived. Our retrospective study was conducted adhering to the guidelines set forth in the Declaration of Helsinki.

Clinical data were obtained from patient records and included gender, age, clinical symptoms, complications after surgery, muscle strength, and the Karnofsky Performance Status (KPS) score before and three months after surgery. Pre- and postoperative muscle strength of the upper and lower limbs was assessed symmetrically according to the British Medical Research Council scale ranging from 0 to 5 and recorded the lowest level (5 = normal, full range of motion, full resistance; 4 = full range of motion, some resistance; 3 = full range of motion with gravity; 2 = full range of motion without gravity; 1 = slight contraction, no movement).[13]

Radiological Assessment and Diffusion Tensor Imaging/DTT Reconstruction

Imaging examinations were performed using a 3 Tesla MRI with a head coil with conventional sequences, including axial or sagittal T1-weighted image (T1W, repeat time [TR]/echo time [TE]: 2325/25 ms), axial fluid-attenuated inversion recovery (FLAIR, TR/TE: 8500/117 ms), coronal T2 gradient echo (T2 GE), and axial diffusion-weighted imaging (DWI, TR/TE: 5202/78 ms, 116×116 matrix, 5-mm slice thickness) with apparent diffusion coefficient map reconstruction. Contrast injection of gadolinium at 0.1 mmol/kg was administered intravenously with 18–20 G needle, followed by T1W after injection to reconstruct three directions, axial, coronal, and sagittal.

The DTI sequence was performed using a single-shot echo-planar imaging sequence on the axial plane, with the following parameters: TR/TE, 7000/84 ms; 4 mm slice thickness; 0.4 mm slice space; NEX 1 (number of excitations); 128×128 matrix; FOV 260×260 (field of view); 27 diffusion directions; and b-values of 0 and 1000 s/mm^2. The acquisition time was 3 minutes. All images were transferred to Workstation 4.7 (GE medical system) to generate an FA map and color-coded orientation map with a matrix of eigenvalues and eigenvectors. The fiber tracts were color-coded red, green, and blue to represent tracts running left to right, anterior to posterior, and superior to inferior, respectively.[14,15]

The imaging features of the lesion, including the site, the side of the lesion (left or right), the largest diameter of the tumor, and enhancement characteristics of the tumor, were collected. The closest distance from the margin of the solid tumor to the corticospinal tract (CST; glioma-to-CST distance [GCD]) was measured by combining the color-coded orientation map with the post-injection T1 image (Figures 1 and 2). The area of edema or infiltration around the tumor was not included in this distance measurement.[14]

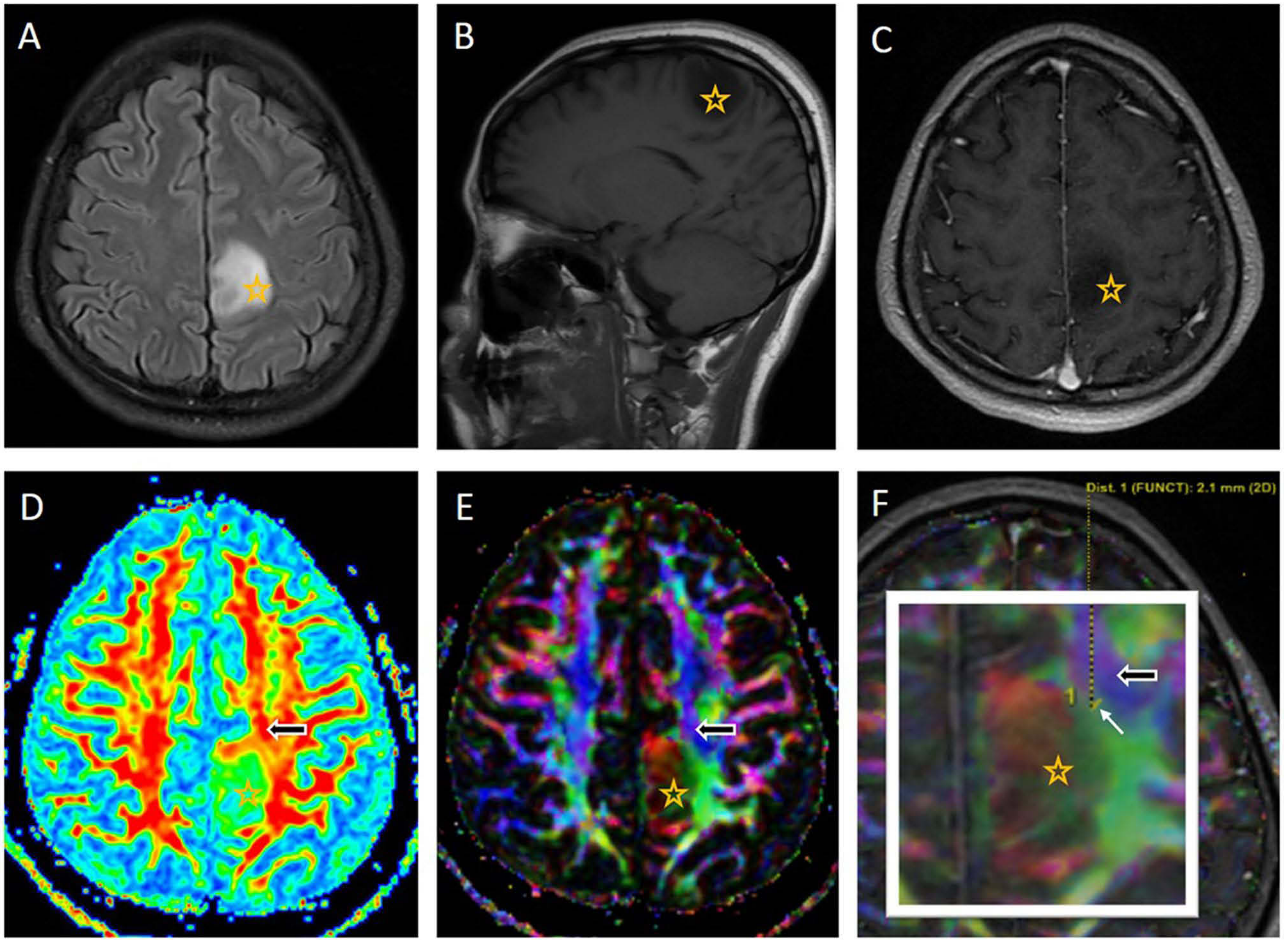

Figure 1 Diffusion tensor imaging of the brain of a 34-year-old woman with a left frontal–parietal diffuse astrocytoma (grade II). Axial fluid-attenuated inversion recovery (**A**), pre-contrast T1-weighted (T1W) (**B**), and post-contrast T1W (**C**) images show a homogenous tumor (indicated by a star in (**A**–**F**), with no enhancement and no peritumoral edema. The tumor appears to slightly and laterally compress the left corticospinal tract (CST) (indicated by black arrow in (**D**–**F**). The combination of the color-coded map and post-contrast T1W (**F**) shows a glioma-to-CST distance of 2.1 mm (indicated by white arrow).

Two radiologists with over ten years of neurological experience, who were blinded to the histopathology results, assessed the CST status and scored it using a scale ranging from 0 to 4 (0 = normal; 1 = deviated; 2 = edema; 3 = infiltrated; 4 = destroyed) based on the association between the FA map and the color-coded orientation map. The deviated pattern showed normal or only slightly decreased FA with abnormal location and/or direction. The edema pattern showed substantially decreased FA with normal location and direction (normal hues on color-coded maps). The infiltration pattern showed considerably decreased FA with abnormal hues on the color-coded map. The destroyed pattern consisted of isotropic (or near-isotropic) diffusion, which made the tract unidentifiable on both the FA map and the color-coded map.[15] The final CST score was based on the most severe axonal injury in each patient. Disagreements were handled by discussion.

Statistical Analysis

Data were analyzed using SPSS 20.0 software (IBM Corp., Armonk, NY, USA). Qualitative parameters are presented as number (n) and percentage (%), and quantitative parameters are presented as mean ± standard deviation (SD). The chi-square test was used to assess the relationship between CST score and tumor grading. The correlations between preoperative indices and postoperative muscle strength and KPS score were assessed using univariate linear regression. Indices significant at the $p < 0.05$ level were included in multivariate linear regression. A p-value of < 0.05 was considered statistically significant.

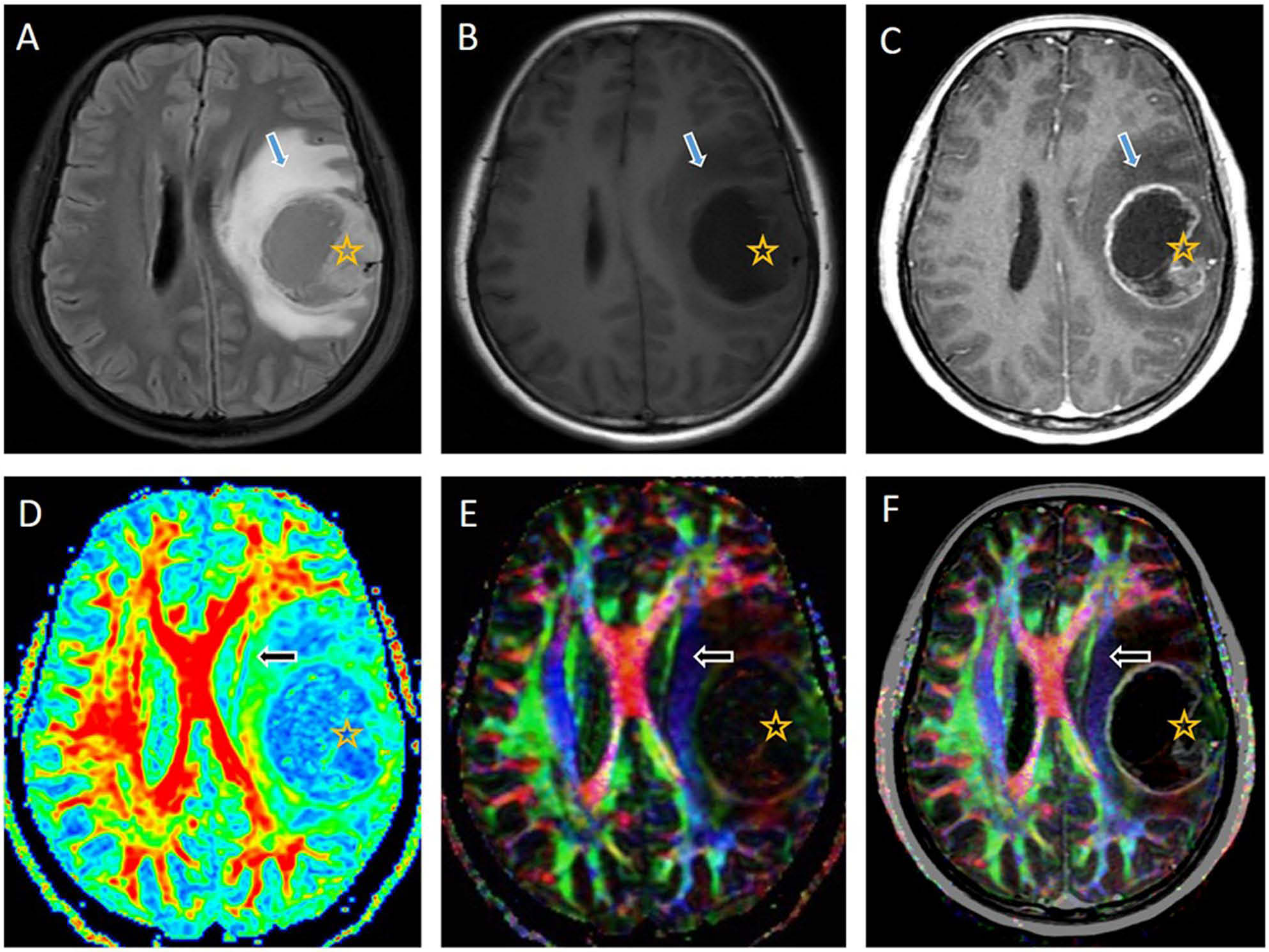

Figure 2 Diffusion tensor imaging of the brain of a 37-year-old woman with a left frontal anaplastic oligodendroglioma (grade III). Axial fluid-attenuated inversion recovery (**A**), pre-contrast T1-weighted (T1W) (**B**), and post-contrast T1W (**C**) images show a heterogeneous tumor (indicated by a star in (**A–F**) with central necrosis, ring enhancement, and peritumoral infiltration (indicated by blue arrow in (**A–C**). The tumor appears to infiltrate and medially compress the left corticospinal tract (CST) (indicated by black arrow in (**D–F**). The combination of the color-coded map and post-contrast T1W (**F**) shows tumor contact with the left CST, leading to a glioma-to-CST distance of 0 mm.

Results

Patient Characteristics and Radiological Findings

As shown as Table 1, of the 43 patients in this study, 48.8% were female and 51.2% were male. The mean age was 40.7 ± 16.5 years (the youngest patient was 9 years and the oldest patient was 70 years). The most common symptom was headache (100%). The KPS score after surgery (74.2 ± 14.5) was higher than that before surgery (72.8 ± 12.4). Twenty-three (53.3%) of the tumors were located only in the frontal lobe and 16 (37.2%) were in multiple lobes. Tumors were more common in the left hemisphere than in the right hemisphere. The mean maximum tumor diameter was 47.4 ± 19.39 mm. Most tumors (81.4%) were enhanced after injection, and only 18.6% did not show post-contrast enhancement. The pattern changes in the CST in descending order were infiltrated (n = 18), deviated (n = 10), edema (n = 8), destroyed (n = 4), and normal (n = 3). The average closest distance from the tumor to the CST was 0.351 ± 0.9 mm. Postoperative complications were encountered at a low rate (2.3% cases of surgical site infection, 4.7% cases of cerebral edema, and 2.3% cases of hemorrhage).

Relationships Between Pyramidal Tract Features in Diffusion Tensor Images and Tumor Grade and Muscle Strength Improvement After Surgery

As shown as Table 2 and Table 3, in the deviated tract group, four patients showed improved muscle strength after surgery and five patients maintained muscle strength. In the infiltrated group, 55.6% of the patients showed unchanged

Table 1 Summary of Clinical Data

Variable	Value	Range
Number of patients	43	
Sex, n (%)		
+ Males	21 (48.8%)	
+ Females	22 (51.2%)	
Median age, years	40.7 ± 16.5	9–70
Preoperative symptoms, n (%)		
+ Headache	43 (100)	
+ Blurred vision	3 (7.0)	
+ Seizure	11 (25.6)	
+ Weaker muscle strength	17 (39.5)	
+ Language disorder	6 (14.0)	
Median preoperative KPS score (%)	72.8 ± 12.4	40–90
Site of tumor, n (%)		
+ Frontal lobe	23 (53.3)	
+ Temporal lobe	2 (4.7)	
+ Parietal lobe	2 (4.7)	
+ Multiple lobes	16 (37.2)	
Side of tumor		
+ Left	23 (53.5)	
+ Right	20 (46.5)	
Mean maximum diameter of lesion ± SD, mm	47.4 ± 19.39	13–91
CST score, n (%)		
+ Normal	3 (7.0)	
+ Deviated	10 (23.3)	
+ Edema	8 (18.6)	
+ Infiltrated	18 (41.9)	
+ Destroyed	4 (9.3)	
Enhancement of lesion, n (%)		
+ With enhancement	8 (18.6)	
+ Without enhancement	35 (81.4)	
Median GCD, mm	0.351 ± 0.9	0–3.5
Median postoperative KPS score (%)	74.2 ± 14.5	40–90
Complications, n (%)		
+ Surgical site infection	1 (2.3)	
+ Cerebral edema	2 (4.7)	
+ Hemorrhage	1 (2.3)	
Pathology results, n (%)		
+ Low-grade gliomas	14 (32.6)	
+ High-grade gliomas	29 (67.4)	

muscle strength and 33.3% showed improved muscle strength. In the group with destroyed tracts, no patient showed postoperative improvement in muscle strength and 75% of patients maintained muscle strength. One patient each in normal, deviated, and destroyed groups and two patients in the infiltrated pattern group showed deterioration in muscle strength after surgery.

Table 2 Correlation Between Histopathologic Parameters and Preoperative Corticospinal Tract (CST) Score

CST Score / Grade	0–2 n %	3–4 n %	Total n %	*p*-value
Low-grade gliomas	9 64.3	5 35.7	14,100	0.203
High-grade gliomas	12 41.1	17 58.6	29,100	
Total	21 48.8	22 51.2	43,100	

Notes: CST score: 0 = normal; 1 = deviated; 2 = edema; 3 = infiltrated; 4 = destroyed. Normal lesions, edema, and deviated lesions were common in low-grade gliomas (LGG; 64.3%). In contrast, destroyed and infiltrated lesions were common in high-grade gliomas (HGGs; 58.6%). However, this difference was not statistically significant ($p > 0.05$).

Table 3 Relationship Between Preoperative Corticospinal Tract (CST) Score and Postoperative Muscle Strength Changes

Postoperative Muscle Strength		Preoperative CST Score				
		0	1	2	3	4
Improved	n %	0 0	4 40.0	0 0	6 33.3	0 0
Same	n %	2 66.7	5 50.0	8100	10 55.6	3 75.0
Deteriorated	n %	1 33.3	1 10.0	0 0	2 11.1	1 25.0
Total	n %	3100	10,100	8100	18,100	4100

Note: CST score: 0 = normal; 1 = deviated; 2 = edema; 3 = infiltrated; 4 = destroyed.

Risk Factors of Postoperative Muscle Strength

As shown as Table 4, univariate regression analysis showed an effect of preoperative muscle strength, preoperative KPS score, and GCD on postoperative muscle strength. Furthermore, preoperative muscle strength ($\beta = 0.591$, $p = 0.000$) had a greater effect than GCD ($\beta = -0.317$, $p = 0.001$) in multivariate regression.

Risk Factors of Postoperative Karnofsky Performance Scale Status Score

As shown as Table 5, in univariate regression analysis, preoperative muscle strength index, preoperative KPS score, and maximum lesion diameter had a significant effect on the postoperative KPS score. However, only the preoperative KPS score was linearly associated with the postoperative KPS score ($\beta = 0.806$, $p = 0.000$) in multivariate regression.

Table 4 Linear Regression Results for the Relationships Between Postoperative Muscle Strength and Preoperative Variables

Variable	Univariate Analysis		Multivariate Analysis	
	β	*p*-value	β	*p*-value
Age	−0.205	0.187		
Gender	0.045	0.773		
Preoperative muscle strength	0.749	**0.000**	0.591	**0.000**
Preoperative KPS score	0.699	**0.000**	0.237	0.054

(*Continued*)

Table 4 (Continued).

Variable	Univariate Analysis		Multivariate Analysis	
	β	*p*-value	β	*p*-value
Site of tumor	0.071	0.649		
Maximum lesion diameter	−0.259	0.094		
Enhancement of lesion	0.026	0.870		
CST score	−0.056	0.722		
GCD	−0.358	**0.018**	−0.317	**0.001**

Note: *P*-values in boldface type indicate statistical significance.

Table 5 Linear Regression Results for the Relationships Between Postoperative Karnofsky Performance Scale Status Score and Preoperative Variables

Variable	Univariate Analysis		Multivariate Analysis	
	β	*p*-value	β	*p*-value
Age	−0.063	0.649		
Gender	0.188	0.228		
Preoperative muscle strength	0.681	**0.000**	0.134	0.157
Preoperative KPS score	0.899	**0.000**	0.806	**0.000**
Site of tumor	−0.080	0.609		
Maximum lesion diameter	−0.363	**0.017**	−0.005	0.950
Enhancement of lesion	−0.152	0.330		
CST score	−0.090	0.567		
GCD	−0.177	0.255		

Note: *P*-values in boldface type indicate statistical significance.

Discussion

Multimodal techniques, including functional MR, neuronavigation, intraoperative MRI, and intraoperative electrophysiological monitoring, are increasingly being used in clinical practice to improve the safety of maximal brain tumor resection.[7,16–19] DTI is the only noninvasive tool for in vivo assessment of the anatomy, architecture, and microstructure of white matter tracts, as well as areas pathologically altered by the tumor, especially eloquent areas.[14]

In our study, the common preoperative neurological symptoms of supratentorial glioma included muscle weakness, epilepsy, speech disorder, and visual impairment. This result is similar to that of Bagadia and Khan et al who found that seizures and muscle weakness were the two most common symptoms.[5,20] The results of our study (67.4% HGG; 32.6% LGG) and those of Shalan's study[8] (70% HGG; 30% LGG) are similar, with displaced and infiltrated patterns being the two most common findings. DTI can potentially predict the malignancy of cranial tumors based on the change in white matter tracts.[5] Previous studies showed that HGGs are significantly associated with infiltration or disruption of tracts.[5,21] This study showed similar findings, although the difference was not significant ($p > 0.05$). This can be explained by the fact that HGGs are characterized by increased cellularity and vascularity with regions showing extended peritumoral infiltration.[22]

Preoperative assessment of the relationship between the tumor and the CST is highly important. This information is crucial when planning a surgical trajectory to avoid damage to eloquent tissue. In patients with HGG who have disrupted fibers and neurological deficits, complete resection of the tumor can be performed without attempting to preserve tracts. However, for patients with only compression fiber injury, the main goal of any surgical approach is to minimize injury to the vulnerable cortex and white matter tracts while maximizing brain function following surgical resection of tumors.[8] Our results agree with these views. A high percentage of patients (90%) in the group with axon compression injuries improved or maintained muscle strength index after surgery. This is due to the preoperative accuracy assessment of axonal injury by DTI.[5] On the other hand, the group with axon disruption showed no changes in the muscle strength score after surgery.

The relationship between preoperative motor fiber damage and improvement in neurological function after surgery has been investigated in several studies; however, the results are controversial.[5,20] Khan et al[5] showed no significant association between neurological outcome and fiber damage patterns. In contrast, Bagadia et al[20] showed that patients with only displacement on DTI had the best postoperative outcomes with a 77.27% likelihood, while patients with infiltration had an 84.61% chance of no clinical recovery. Our study obtained similar results; the group with axonal compression showed a higher rate of improvement in muscle strength after surgery (40%) compared to the group with the infiltrative form (33.3%), but no improvement was evident in the disruption group. Therefore, preoperative classification of CST infiltration by glioma can be valuable for predicting patients' motor function after surgery.

The linear relationship between the DTI features of fibers and postoperative neurological function is still controversial. Dali et al found no relationship between preoperative CST score and postoperative muscle strength.[23] Our study obtained similar results; there were no relationships between preoperative CST score and muscle strength and postoperative KPS score. However, Xiao et al's study of 54 brain stem glioma patients showed that the CST score had a linear and independent relationship with postoperative muscle strength (p <0.001) and modified raking scale score after surgery ($p = 0.016$).[16] Lin et al's study of 56 patients with supratentorial cavernous malformation showed that the CST score and the distance from the lesion to the CST had linear relationships with short-term surgery-related motor deficits, but only the CST score was associated with long-term deficits.[24] These differences may be explained by the differences between studies in the morphology of fiber injury and the anatomical location and nature of the lesion. Our study also showed that the distance from the tumor to the CST was an independent factor on the postoperative KPS score ($p < 0.05$). Lin et al showed that postoperative motor function deficit was significantly associated with tumor-to-fiber distance.[24] They suggested that 3 mm may be a safe distance for surgery in cavernous malformations.[24] In addition, maximum tumor diameter and postoperative KPS score were linearly related in univariate regression. The larger the tumor diameter was, the smaller the KPS score, corresponding to a lower quality of life of the patient. This result is similar to that of Khan et al who showed that the postoperative outcome depends on tumor volume, ie, an increase in tumor volume led to a higher risk of residual tumor or postoperative recurrence.[5]

This study has some limitations. Firstly, it focused only on motor function in assessing CST images and muscle strength characteristics, and did not consider other functional areas such as language and visual regions. Secondly, the displacement of the white matter tract can be changed during surgery due to gravity, the patient's head position, surgical equipment, edema, or loss of brain parenchyma.[7] Therefore, the position of the fiber tract in DTI may be altered, thereby reducing the reliability of preoperative DTI and intraoperative neurolocalization systems.[25] The lack of postoperative DTI data is another limitation of this study. Finally, the design of the retrospective study and small sample size may not accurately reflect the entire population of individuals with glioma. In future studies, larger samples, postoperative and intraoperative diffusion tension imaging should be performed to improve diagnostic accuracy.

Conclusions

Diffusion tensor imaging can provide useful information on the relationship between white matter tracts and tumor characteristics. This helps in surgical planning and predicting the safe maximum resection of the tumor and perioperative and postoperative follow-up clinical symptoms. Therefore, the DTI technique should be used as a routine neuroimaging procedure, especially for tumors in the eloquent areas of the cortex.

Data Sharing Statement

The datasets generated and/or analysed during the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request.

Ethical Approval

Ethical clearance was received from the institutional ethics committee of Hanoi Medical University (Ref: 630/GCN-HĐĐĐNCYSH-ĐHYHN).

Informed Consent

Informed consent was waived for the study's retrospective nature, and the analysis used anonymous clinical data.

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Disclosure

The authors declare no conflicts of interest in this work.

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