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The concept of the "Hexahedron" in the supratotal resection of the frontal gliomas: A technical note

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Research Article

Keywords: Frontal gliomas, Supratotal resection, Microsurgical techniques, Hexahedron

Posted Date: October 14th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-926821/v1

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Abstract OBJECTIVE

To evaluate the value of the concept of the "Hexahedron" in the supratotal resection (SPTR) of frontal gliomas in both dominant and nondominant hemispheres .

METHODS

All consecutive patients who underwent SPTR for frontal gliomas under the guidance from the concept of the "Hexahedron" were retrospectively analysed for lesion location, pathology, extent of resection (EOR), and complications from May 2020 to June 2021. Volumetric EOR was measured and classified as SPTR, (in which the volume of the postoperative cavity was larger than the preoperative tumour volume), gross total resection (GTR, > 95% by volume) or subtotal resection (STR, \leq 95% by volume) after independent radiological review.

RESULTS

Six men and two women (mean age: 47.13 years; range: 26–69 years) were included. All eight patients underwent frontal craniotomy combined frontotemporal craniotomy for resection of frontal gliomas. Neuropathological examination confirmed a diagnosis of glioblastoma WHO Grade IV in 4 patients, anaplastic oligodendroglioma WHO Grade III in 1, anaplastic astrocytoma WHO Grade III in 2 and diffuse astrocytoma WHO Grade II in 1. SPTR was achieved in six patients and STR was achieved in two. The main postoperative complications were contralateral paresis in 2 patients and memory disturbances in 1 patient. There were no cases of rebleeding or secondary operation during hospitalization.

CONCLUSIONS

In the presented eight cases the concept of the "Hexahedron" allowed for safe surgical supratotal resection of frontal gliomas.

Introduction

The management of gliomas has been extensively studied, and consistently, surgery is said to play a central role in their treatment. The consistency of available data supports the long-held principle that safe, maximal tumour resection including high-grade (HGG) and low-grade glioma (LGG) improves symptom management, quality of life, progression-free survival (PFS), and overall survival (OS) in glioma patients[1].

For maximally resecting frontal gliomas, we proposed the concept of the "Hexahedron" based on their growth range and the functional characteristics of the frontal lobe. The six sides and different boundaries of the frontal resection area were defined following guidance from the "Hexahedron" concept.

Material And Methods

This retrospective study included all consecutive patients who underwent the resection of the frontal gliomas under guidance from the concept of the "Hexahedron" at Chongqing Sanbo Jiangling Hospital and Yunnan Cancer Hospital, China between May 2020 and June 2021. There were no age exclusion criteria. A total of eight patients were enrolled in this study, including six males and two females, with an average age of 47.13 (26\%69) years. Patient medical records, clinical visits, and imaging studies were reviewed until the last available follow-up. Tumour pathology, postoperative complications, and clinical outcomes were collected (Table 1).

Table 1

Clinical and Tumor Characteristics of Adult Patients With Low-Grade and High-Grade Glioma Evaluated for Extent of Surgical Resection (N = 8)

Characteristic	No. of Patients	%
Sex		
Male	б	75
Female	2	25
Age at diagnosis, years		
< 40	2	25
40-60	4	50
> 60	2	25
Meidan	47.13	
Range	26-69	
KPS at diagnosis		
80	2	25
90	4	50
100	2	25
Meidan	90	
Range	80-100	
Presentation		
Seizure	2	25
Incidental	2	25
Headache	4	50
Side of tumor		
Left	4	50
Right	4	50
Tumor location		
Frontal lobe	7	87.5
Frontal lobe, basal ganglia and thalamus	1	12.5
Tumor subtypes		

Characteristic	No. of Patients	%
Glioblastoma	4	50
Anaplastic astrocytoma	2	25
Anaplastic oligodendroglioma	1	12.5
Diffuse astrocytoma	1	12.5
Postoperative chemotherapy		
No	1	12.5
Yes	7	87.5
Extend of tumor resection(%)		
70-89 (STR)	2	25
>100 (SPTR)	6	75
Abbreviations: KPS, Karnofsky performance score; STR, subtotal resection; SPTR, supratotal resection.		

Resection rates were considered as follows: supra-total removal (SPTR), in which the margin for tumour resection is extended beyond the abnormal area detected by magnetic resonance imaging (MRI); gross total removal (GTR), where no residual tumour is visible on immediate postoperative MRI; and subtotal removal (STR), where < 90% of the lesion is resected. This retrospective study was approved by the Academic Committee of Chongqing Sanbo Jiangling Hospital.

Surgical Technique

With the patient in the supine position, a coronary incision was performed, and the flap was reversed forward. The frontal and temporal bone windows were exposed, 2 holes were drilled in the frontal bone, and a bone flap measuring approximately 10x7cm² was removed with a bone knife. The lower boundary of the bone flap was near the superior part of the frontal sinus, which was not left open. The superior boundary of the bone flap was close to the coronal suture, the medial boundary was attached to the midline, and the lateral boundary was attached to the squamous suture.

The dura was opened and turned to the midline and anterior skull base to expose the frontal lobe and lateral fissure. The differences between normal brain tissue and tumour tissue were identified carefully under a microscope. Some tumours could be identified by their appearance: LGGs were greyish white, while HGGs were greyish red. Some tumours were not easy to distinguish visually from normal brain tissue and thus had to be identified by differences in texture and blood supply and preoperative anatomical localization.

Tumors with clear boundaries were removed along the tumour boundary. First, the medial side of the tumour was removed as most of the blood supply of frontal gliomas are derived from the pericallosal artery and the callosomarginal artery; removing the medial side of the tumour was thus equivalent to disconnecting its main blood supply. Then, the boundary between the tumour and brain tissue was gradually pushed apart with cotton strips or gelatine sponge, allowing removal of the entire tumour. If the tumour partially crossed the midline, however, it was difficult to remove the tumour in one piece on the opposite side of the midline, and it thus had to be resected in blocks. In these cases, the branches of the pericallosal artery and the callosomarginal artery needed to be carefully identified to protect large branches (Fig. 1) (Fig. 2). Some tumours invaded the basal ganglia and the thalamus, and were thus also difficult to remove.

After the tumour was resected, extended resection of the surrounding frontal lobe tissue was performed. The whole resection range could be defined as an irregular hexahedron (Fig. 3) surrounded by 6 surfaces and 8 points. The anterior surface (frontal sinus surface) is surrounded by the nasal frontal suture, the lateral orbital point, the medial point above the frontal sinus and the root of the sphenoid ridge. The inferior surface (sphenoid plateau surface) is surrounded by the nasal frontal suture, the lateral end of the orbit, the root of the lateral fissure and the cranial entry point of the optic nerve. The posterior surface (hypothalamus and ventricular surface) is surrounded by the cranial entry point of the optic nerve, the root of the lateral fissure, the intersection point of the coronal suture and the midline, and the intersection point of the coronal suture and the inferior frontal sulcus. The superior surface (frontal surface) is surrounded by the medial point above the frontal sinus, the root of the sphenoid ridge, the intersection point of the coronal suture and the midline, and the intersection point of the coronal suture and the posterior part of the inferior frontal gyrus. The medial surface (midline surface) is surrounded by the nasal frontal suture, the entry cranial point of the optic nerve, the medial point above the frontal sinus, and the intersection point of the coronal suture and the midline. The lateral surface (lateral fissure surface) is surrounded by the lateral end of the orbit, the root of the sphenoid ridge, the intersection point of the coronal suture and the inferior frontal sulcus, and the root of the lateral fissure.

For gliomas with unclear boundaries and infiltration to the lateral ventricle, basal ganglia, thalamus and the opposite side of the midline, complete removal while maintain the integrity of important functions was impossible; this also applied to tumours that had partially infiltrated the basal ganglia and the thalamus. In these cases, our overall surgical strategy was to remove most of the tumour tissue and the resectable portion of the frontal lobe within a safe range according to the concept of the "Hexahedron". During the operation, the actual surgical strategy was to remove part of the tumour tissue in blocks that were not along its boundary. Then, under guidance from the concept of the Hexahedron, the tissue of the frontal lobes were removed to the greatest extent possible in a safe range along the six surfaces.

Results

The pathological anatomical diagnosis was glioblastoma WHO Grade IV in 4 patients, anaplastic oligodendroglioma WHO Grade III in 1, anaplastic astrocytoma WHO Grade III in 2 and diffuse

astrocytoma WHO Grade II in 1.

For postoperative imaging, high-grade gliomas were mainly analysed with enhanced MRI, and low-grade gliomas were analysed with T2 fluid-attenuated inversion recovery (FLAIR) sequences. Achievement of SPTR was defined as tumour resection extending beyond the abnormal MRI- verified area, which indicated that the volume of the postoperative cavity was larger than the preoperative tumour volume. Six patients received SPTR and two patients received STR (due to invasion of the basal ganglia and thalamus). In the two patients who underwent STR, except for the part invading the basal ganglia and the thalamus, the other interfaces of the tumour were resected according to the concept of the Hexahedron. The postoperative imaging of the six patients who received SPTR was basically consistent with the range of the Hexahedron that we determined during the operation.

The main postoperative complications were contralateral paresis in two patients and memory disturbances in one patient. There were no cases of rebleeding and secondary operation during hospitalization.

Adjuvant Therapies

In our study, postoperative pathology revealed diffuse astrocytoma WHO Grade II in one patient, which received STR. The other seven patients had WHO Grade III and Grade IV tumors. These seven patients underwent adjuvant radiotherapy and chemotherapy after the operation, while the eighth patient underwent adjuvant radiotherapy alone. The patient who achieved STR received radiotherapy, chemotherapy and tumour treating fields (TTF) therapy.

Long-term Follow-up

One patient (WHO Grade IV) died 4 months after the operation. Two tumours (1 glioblastoma and 1 anaplastic astrocytoma) recurred 8 months after the operation. The mean clinical follow-up of the surviving patients was 7.86 months (range: 2–15 months), and no patient was lost to follow-up. The median overall survival of the eight patients was 7.38 months (range: 4–15 months).

Discussion

Gliomas are a major cause of morbidity and mortality in China. Low and high-grade gliomas [World Health Organization (WHO) grades II-IV] have proven difficult to treat due to their propensity to infiltrate deep into surrounding parenchyma; however, an increasing body of evidence suggests that extent of resection affects overall survival, progression-free survival, time to malignant transformation and seizure control.

Surgical resection is now considered for asymptomatic, incidentally found low-grade gliomas. A few studies favour increasing the extent of resection to improve overall and progression-free survival in cases

of low-grade glioma[2–10]. These studies showed a mean survival benefit from 61.1 to 90 months with maximal resection. A large population-based natural history study of Norwegian patients offered additional insight in their analysis of 153 glioma patients treated in two hospitals serving adjacent geographical regions[4, 11], where the approach to the care of gliomas in individualized patients was dependent on residential address. The median survival in this study was 5.9 years for patients receiving tumour biopsy, while the group receiving early resection did not reach median survival by the end of the study period, suggesting a survival benefit for those treated with early surgery. Furthermore, the 5-year survival was 60% for biopsy patients and 74% for those receiving early surgery. GTR impacts the natural history of low grade glioma. The time to malignant transformation for low-grade gliomas ranges from 4 to 29 months, and approximately 45% of patients with diffuse low-grade WHO grade II glioma will experience transformation to anaplastic (WHO grade III) glioma within 5 years[5, 12, 13]. Smith et al. analysed 216 patients with hemispheric low-grade gliomas, and identified a median time to progression of 5.5 years and median time to malignant transformation of 10.1 years for patients undergoing a greater than 90% extent of resection. Moreover, individuals with an extent of resection at least 90% have 5-year survival rates of 97%, while patients with less than 90% extent of resection have 5-year survival rates of 76%[5].

We reviewed the significance of the extent of resection in improving overall and progression-free survival for patients with primary and recurrent high-grade gliomas found in a few reports[1, 14–19]. The preponderance of evidence supports using the extent of resection as a significant predictor of overall and progression-free survival in high-grade glioma. After GTR, overall survival improves to 64.9–75.2 months for WHO grade III gliomas and to 11.3–18.5 months for WHO grade IV gliomas[20, 21]. Although limited by selection bias, a retrospective analysis of 107 patients with recurrent glioblastoma revealed that patients who initially received subtotal resection experienced a survival benefit when GTR was achieved at recurrence (19 months overall survival for GTR vs. 15.9 months overall survival for STR)[22]. It has been further suggested that an extent of resection threshold of at least 80% is the minimum needed to offer a survival benefit in recurrent glioblastoma[23].

GTR or SPTR can be difficult to achieve in many cases due to glioma infiltration into cortical and subcortical regions important for language, motor, and neurocognitive function. However, neurosurgeons should strive to improve the surgical technology and achieve GTR or SPTR of glioma. A firm understanding of neuroanatomy is critical to performing a safe operation for glioma resection.

Our research focused on the frontal lobe which are the most common site of gliomas. GTR can be performed for frontal gliomas with clear boundaries, while for gliomas growing in the direction of the paraventricular nucleus, basal ganglia or thalamus, complete removal of the parts infiltrating into the deep structures can be difficult. Existing relevant studies have reflected the idea of extended glioma resection [1, 3, 5, 16, 18, 24], which can reduce the recurrence rate of gliomas and prolong the survival time of the patients. Due to the relatively wide space in the frontal lobe, it is possible to expand the resection of frontal gliomas. Based on the above ideas, removing the frontal tumour and frontal lobe

tissue as much as possible within the safe range without damaging the important functions of movement and language can be challenging.

According to our previous surgical experience, we defined the maximum range of safe resection for frontal gliomas from an anatomical perspective: the anterior skull base as the anterior boundary, the midline as the medial boundary, the inferior frontal sulcus as the lateral boundary, and the coronal suture as the posterior boundary; resection according to these safe boundaries cannot cause damage to important functions. Based on this idea, we propose the concept of the Hexahedron for maximum safe resection of frontal gliomas. The Hexahedron is an irregular hexahedron surrounded by 6 surfaces and 8 points. The anterior surface (frontal sinus surface) is surrounded by the nasal frontal suture, the lateral orbital point, the medial point above the frontal sinus and the root of the sphenoid ridge. The front range is the smallest surface, and includes the front end of the straight gyrus and the orbital gyrus. The location of the frontal surface is deep and does not need to be completely exposed during craniotomy. This part can be removed by adjusting the angle of the microscope during operation. The inferior surface (sphenoid plateau surface) is surrounded by the nasal frontal suture, the lateral end of orbit, the root of the lateral fissure and the cranial entry point of the optic nerve. The inferior surface mainly includes the olfactory nerve, olfactory tract, optic nerve and optic tract which are adjacent to the hypothalamus and basal ganglia. This part can be observed under direct vision during the operation. The posterior surface (hypothalamus and ventricular surface) is surrounded by the cranial entry point of the optic nerve, the root of the lateral fissure, the intersection point of the coronal suture and the midline, and the intersection point of the coronal suture and the posterior part of the inferior frontal sulcus. The posterior surface is the main interface of the tumour and includes the hypothalamus and lateral ventricle interface. The superior surface (frontal surface) is surrounded by the medial point above the frontal sinus, the root of the sphenoid ridge, the intersection point of the coronal suture and the midline, and the intersection point of the coronal suture and the posterior part of the inferior frontal sulcus. The superior surface is the largest surface and includes the main part of the superficial part of the tumour. The medial surface (midline surface) is surrounded by the nasal frontal suture, the cranial entry point of the optic nerve, the medial point above the frontal sinus, and the intersection point of the coronal suture and the midline. When dealing with the midline interface, we mainly focus on protecting the pericallosal artery and the callosomarginal artery. The lateral surface (lateral fissure surface) is surrounded by the lateral end of the orbit, the root of the sphenoid ridge, the intersection of the lateral side of the coronal suture and the posterior part of the inferior frontal gyrus, and the root of the lateral fissure.

On preoperative imaging, some tumours have clear approximate boundaries, which can be completely moved under the microscope. The resection strategy for this kind of tumour is to remove it along the tumour boundary first, which is helpful for comlete tumour removal and avoiding residual tumour. Then, the resection is expanded to the six surfaces according to the range of the Hexahedron.

For tumours diffusely infiltrating the ventricles, basal ganglia, thalamus and contralateral hemisphere, a part of the tumours is removed first, and then most of the remaining tumours and the expandable frontal lobe are removed together according to the guidance of the Hexahedron.

Many skills are involved in the process of tumour resection, and the experience in different neurosurgical centres is different. According to our experience, the operators should first focus on removing the straight gyrus and orbital gyrus piece by piece at the bottom of the frontal lobe under the arachnoid when close to the inferior surface of the Hexahedron (sphenoid plateau). It is best to leave a thin layer of arachnoid to observe and avoid damaging the deep optic nerve. When close to the posterior surface of the Hexahedron (hypothalamus and ventricular surface), the position of the bottom of the hypothalamus and the front of the hypothalamus can be determined by the direction of the optic nerve. By removing the thin layer of tissue in front of the frontal horn of the lateral ventricle, the pulsation of the anterior horn of the lateral ventricle can be observed carefully to judge the range of anterior ventricular resection.

This study mainly defined the range of SPTR of the frontal gliomas from an anatomical perspective. Since the posterior boundary of the Hexahedron was defined as the coronal suture and the lateral boundary as the inferior frontal sulcus, no motor or language disorders were produced in this study. Because the frontal gliomas of this group were mainly limited to the frontal lobe, intraoperative techniques such as awake craniotomy, neuronavigation and image-guided surgery were not applied.

Conclusions

In this small series, the concept of the "Hexahedron" was shown to provide a safe, effective, and maximum extent of excision in the SPTR of the frontal gliomas.

Abbreviations

LGG Low-grade glioma HGG High-grade glioma GTR Gross total resection SPTR Supratotal resection STR Subtotal removal WHO World Health Organization 0S Overall survival PFS Progression-free survival.

Declarations

Acknowledgements

Not applicable.

Authors' contributions

HY performed the surgeries and proposed the idea. PC and GB carried out the clinical data collection, statistical analysis, and manuscript drafting and modification. JP and YL helped in the clinical data collection and statistical analysis. SC participated in the design of the study and the modification of the manuscript. FL conceived of the study and participated. All authors read and approved the final manuscript.

Funding

This work was not supported by any research program and projects.

Availability of data and materials

The data used during the current study are available from the corresponding author on reasonable request. The additional supporting files of the images of the cases has been submitted.

Ethics approval and consent to participate

This study was approved by the Chongqing Sanbo Jiangling Hospital Ethics Committee. In the process of research, we strictly followed the relevant management regulations of medical ethics and carried out relevant work under the supervision of the Chongqing Sanbo Jiangling Hospital Ethics Committee. The research conforms to the relevant provisions of the Chongqing Sanbo Jiangling Hospital Ethics Committee. Committee.

Consent for publication

Written informed consent for publication was obtained from all participants.

Competing interests

The authors declare that they have no competing interests.

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Figures



Figure 1

Cranial CT and MRI reveal a right frontal glioma. Preoperative CT and MRI (a-f); postoperative CT and MRI (g-l).



Figure 2

a skin incision; b the exposed area of the frontal lobe measures approximately 7x8cm2; c the olfactory nerve and the anterior skull base are exposed (white arrows); d the midline surface is exposed (white arrows); e the choroid plexus of the lateral ventricle is exposed (white arrows); f the resected area of the tumour and the frontal lobe measures approximately 7x8cm2.



Figure 3

Schematic diagram of the "Hexahedron ". FSS represents the frontal sinus surface; SPS represents the sphenoid plateau surface; HVS represents the hypothalamus and ventricular surface; FS represents the frontal surface; MS represents the midline surface; LFS represents the lateral fissure surface. The "Hexahedron" is composed by the eight points (the lateral end of the orbit; the nasal frontal suture; the medial point above the frontal sinus; the root of the sphenoid ridge; the root of the lateral fissure; the entry cranial point of the optic nerve; the intersection point of the coronal suture and the midline; the intersection point of the coronal suture and the midline; the

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